THE PHYSIOLOGIST

A Publication of the American Physiological Society Volume 33, Number 4 August 1990

What's Happening in APS?

Shu Chien

There has been much happening in the American Physiological Society recently. Because it is likely that not all members are aware of all these new developments, I would like to share the following with our members.

While APS will continue to hold its annual meeting in the spring, beginning next year the traditional once-a-year APS fall meeting will be replaced by specialty meetings on specific topics at the forefront of research. This change was made to allow for the in depth presentation of selected topics at the cutting edge of the physiological sciences and to provide a forum for free exchange among scientists with common interests (somewhat analogous to the Gordon Conferences, but slightly more structured and larger in size). The first APS Specialty Meeting will be held from October 6-10, 1990 in Orlando, FL. This meeting, organized by the Comparative Physiology Section, has the theme of "In Search of Physiological Principles: The Use of Animal Diversity and Novel Technology." All indications are that this will be an excellent meeting with a superb scientific program. This meeting will be larger than envisioned for specialty meetings because it represents a transition from the fall meeting to the specialty meeting format.

In 1991, there will be a specialty meeting on "Interactions of the Endocrine and Cardiovascular Systems in Health and Disease" (September 29 - October 3, San Antonio, TX). In 1992, there will be two specialty meetings: "The Cellular and Molecular Biology of Membrane Transport" and "Exercise Physiology." The organization of these meetings is well under way. However, the Program Committee welcomes suggestions for specialty meetings for 1993 and onward. The current plan is to have two specialty meetings per year until 1995. Based on an evaluation of the specialty meetings, the Society might make changes in their format and increase the frequency of the meetings. The Society's primary interest is to sponsor small meetings that present the best science in a given area. In special circumstances, the Society will also consider the sponsorship of intersociety meetings.

Many of you have already heard about the changes taking place in the Federation of American Societies for Experimental Biology (FASEB). It was felt that FASEB, currently composed of six corporate societies, was not representative of the biomedical research community. Furthermore, the large assessment placed by FASEB on its

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Deadline for submission of material for publication: Dec. 5, February issue; Feb. 5, April issue; April 5, June issue; June 5, August issue; Aug. 5, October issue; Oct. 5, December issue. **If you change your address or telephone number, please notify the central office as soon as possible.**

Headquarters phone: (301) 530-7164. TELEFAX: (301) 571-1814.

Letter to Editor

I am responding to your editorial in the April 1990 issue of *The Physiologists.* Your analogy comparing animal facility break-ins to rape is well taken, but only for those who have suffered break-ins. For the wider population of those of us who do research with animals, the more appropriate analogy may be to the situation of a person who is raped, conceives, then tries to avail herself of a legal abortion. Both animal research and therapeutic abortion have solid standing under the law. Both have financial support of the federal government (or have had). Both have vocal minorities (all polls taken of the general public indicate solid support of both) who are unafraid of breaking other laws to oppose animal research and abortion. Thus, both activities have congressional (and some times executive) opposition in Washington. It is unlikely that a wave of strong opposition could be mounted against laws and penalties against rape (even when the "rape is caused by the raped" mentality of a minority of individuals), but such is not the case with legal abortion or with animal research. Thus, our support base of the majority is eroded by the visibility and rancor of the minority. Obviously, the majority must be heard.

Thanks for a well-written editorial and for a newsletter that continues to inform.

Lee A. Meserve
Bolling Green State University

PUBLISHING OPPORTUNITY

Photos, slides and movies needed for an educational videodisc biology program. Please contact Stephanie Petron at Optical Data Corporation, 1-800-248-8478.

WHAT'S HAPPENING IN APS?

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member societies (over $60 per member last year) not only was a severe impediment for the recruitment of new societies, but it also greatly reduced the flexibility of member societies in scheduling their spring meeting. The latter results from the fact that the member societies currently offset their assessments by using income generated from the spring FASEB meeting. Some of these issues were clearly outlined in an Editorial by Past President Vernon Bishop (*The Physiologist,* 32:53, 1989).

In response to the concerns of APS, the FASEB Board held a retreat in Williamsburg, VA, in September 1989 to re-examine the relationship between FASEB and its constitutent societies. After three days of deliberations, it was agreed that FASEB should be restructured with an aim to broaden its representation of biomedical sciences societies. As a result of several Board meetings and the arduous work of several committees, major changes were recommended in the structure and operation of FASEB. These changes were adopted by the Board at its meeting on June 18, 1990 and became effective on July 1, 1990. The salient points are summarized below.

Member societies will no longer pay annual assessments to FASEB, but instead will pay annual dues that will be reduced progressively from $45 per member this year to $15 per member by 1994. This reduction will be made possible by rendering all FASEB functions (except for administrative office and public affairs) self-sufficient, by raising rents paid by tenant societies on the FASEB campus, by properly charging associated services to tenants (e.g., mail service), and by other cost-reducing and income-generating approaches. Most service departments will become self-sufficient immediately, whereas others will be expected to achieve that goal within a given time. The FASEB Journal has until the end of 1992 to be either (a) available to members with no charge on dues, or (b) put on a subscription basis. As mentioned above, the income generated from the FASEB meeting was traditionally used to meet the assessment. From now on, if FASEB meetings continue to generate significant income, we may come out ahead financially. The most important effect of this reduction in dues is that it will make it possible to recruit new societies. The approved plan will allow new member societies to join FASEB with an annual dues of $10 per member (without the directory). This two-tier system will disappear by 1995, at which time every society will pay the same amount.

Under the new FASEB Constitution and Bylaws, the initiation of new programs will require a 2/3 majority vote of the FASEB Board members. However, any society voting against a program will not be obligated to provide financial support for the new program. The restructured FASEB Board will be composed of two members from each society serving staggered four-year terms. The President-elect of FASEB will be elected by the Board from those Board members in their second year of service. During the past year, FASEB has conducted an extensive search for a new Executive Director, selecting Michael J. Jackson, Dean for Research and Professor of Physiology at the George Washington University Medical Center.

Under the restructured FASEB, scientific meetings will be initiated by member societies, although FASEB may be asked to manage the meetings. From 1991 to 1997, APS is committed to meeting with other FASEB member societies in the spring. However, APS is actively exploring the possibility of meeting with other societies outside the FASEB framework in the years after 1997. Because of the need to book meeting sites many years in advance, most societies have already scheduled their meetings through 1999. For this reason, APS must plan for future meetings well in advance.

Together, we can ensure a bright future for physiology and APS.

The APS has experienced a steady growth in membership, which now exceeds 7,000. What we need most at this point is the recruitment of more young members, including students. I hope every regular member will help to recruit one new young member to APS. The application form is available from the APS Membership Office.

Currently, applications for regular and corresponding members are voted on by APS regular members at the spring and fall business meeting, the procedure needs to be changed in order to continue to have two rounds of voting per year. The newly proposed procedure involves the publication of a slate approved by Council in *The Physiologist* twice a year to be voted on by regular members by mail. In order to implement this change, an amendment to the Bylaws will be submitted to the membership at the spring business meeting.

The 1989 budget for the Society (including society operating and publications funds) had an income over expenses of $290,627. During 1989, the journal subscription prices were increased by 21% over 1988 prices. In 1990, there was no increase in journal subscription prices, and the projected budget has a deficit of $3,397 (out of a total budget of $8.45 million). In order to balance the budget in 1991, it will be necessary to increase journal income. This will be accomplished by increasing the institutional subscription price by 12% and by increasing page charges from $30 to $40. The question of a manuscript handling fee was considered but postponed for one year for further review. A plan has been initiated to move toward a three-tier subscription rate schedule in which APS members (presently paying 1/2 institutional rate) will ultimately pay 1/3 of the institutional rate and nonmembers (presently paying the institutional rate) will pay 2/3 of the institutional rate. To attain these goals, the in-

dividual subscription rates for 1991 will remain unchanged from those in 1990.

In order to develop a long-range strategic plan based on the Society's financial resources, the Council will be focusing on this area during its next several meetings. The Finance Committee has been asked to make a projection of the financial picture for the next five years that will provide the Council with a realistic framework for the deliberation of fundamental policy issues. The program will be reported in *The Physiologist* and input from members will be sought at various stages.

The APS journals are continuing to do well. *Physiological Reviews* ranks number one among physiological journals in frequency of citation, and the *American Journal of Physiology* and the *Journal of Neurophysiology* also rank very high. There has been a 20% increase in journal pages and published articles in 1989. Two new journals (*AJP: Lung Cellular and Molecular Physiology* and *Advances in Physiology Education*) have been published since last year. In addition, an effort has been made to reduce the time to publication by accepting an increasing number of manuscripts on author provided disks.

The in-house book publication program has been successfully phased out and Oxford University Press has taken over this program. Handbooks on Muscle and Motility and on the Cardiovascular System have been approved. Others on the Nervous System, Adaptation to the Environment, Comparative Physiology, Exercise, and Aging are being considered.

In recent years, the Society's structure and function has evolved in response to the changing times. The governance of APS has been strengthened by the establishment of Sections. Most Sections have been increasingly effective in communicating with Section members, but a few Sections are still in the process of getting their members to participate with enthusiasm. In order to improve communications, the APS Council and the Section Advisory Committee have started holding annual joint meetings. For the last three years, the slate for Society officers has been developed by a Nominating Committee composed of representatives from Sections. This new procedure has worked well.

We are all seriously concerned about the progressive decline in Federal support for research and training. APS has been actively working to improve these conditions. Cooperating with other societies in FASEB, APS has communicated the importance of improved biomedical research funding to congressional representatives. APS is a member of the American Association of Medical Colleges Ad Hoc Group for Medical Research Funding, which has been effective in unifying requests to Congress for medical research funding. Members of the Executive Cabinet (Vernon Bishop, Aubrey Taylor and I) have made personal visits to the Hill to express our views on research funding and on the use of animals in research. Our elected representatives have urged us to encourage more scientists to do the same. I know many APS members have written to and/or visited their congressional representatives, but we need more. These individual efforts are extremely important; they complement the endeavors of the Society and have a personal touch that is invaluable.

The APS is a chief advocate for animal research, an area where experimental physiologists are facing difficult problems at this time. Again, we need to redouble our efforts to express our views to our elected representatives. In dealing with the issue of animal research, we need to be more active rather than always on the defensive. In this regard, APS has drafted a model animal facilities bill to be used to counter state or local legislation proposed by animal activists. The Society is also preparing a statement on the feasibility of the consolidation of animal care and use regulations, guidelines and standards, with the aim of having one set of policies from the Federal government. A sourcebook on animal care and use issues and a brochure on some "do's and don'ts" for use in interpreting the animal regulations and for obtaining the official approval of NIH are being prepared.

APS is sponsoring a High School Teachers Summer Research Program this summer. From 30 applications submitted by high school teachers, 12 were selected and matched with mentors in various universities and colleges. A scientific session with presentations by the teachers to be followed by a luncheon is planned at the 1991 spring meeting. This program is supported by $50,000 allocated by APS plus institutional cost-sharing and funds from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). This program will be continued next year.

APS has several Fellowship programs that recognize outstanding graduate students and postdoctoral fellows who submit papers for presentation at its annual meeting. APS, with the support of NIDDK, has run a successful and meaningful program to sponsor the attendance of underrepresented minority students at APS meetings. We will continue this program and amplify it by seeking funding support from other sources. Other awards for graduate students and postdoctoral fellows include the Procter and Gamble Awards and the Caroline tum Suden Professional Opportunities Awards.

At the invitation of the Chinese Physiological Society in Taiwan, a joint meeting will be held from November 2-5, 1990 in Taipei with 6 symposia, 1 workshop and sessions of free communications. Letters have been sent to members regarding this meeting. The APS conducts a US/USSR Bilateral Exchange Program, under which there have been exchanges of four physiologists from each side. APS has been asked by AAAS to send 2-3 members to Nigeria in 1991 to conduct a 1-2 week workshop to update Nigerian physiology teachers on recent advances. A Poster/Discussion session on "Research in Developing Countries" will be held at the 1991 spring meeting.

APS is continuing to interact actively with other related disciplines such as bioengineering, biophysics and clinical physiology. There has been an increasing incorpora-

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Minority Recruitment Physiology Instruction on the Crow Indian Reservation

Robert G. Carroll, PhD
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Greenville, North Carolina

As physiologists, we are acutely aware of the shortage in scientists projected for the end of the century. One response to this problem is the recruitment of previously underrepresented minority students into biomedical careers. The Porter Physiology Development Program was established with this goal in mind, and recently supported my participation in a pilot science program. In this program, a two-week laboratory demonstration course was designed for the Crow Indian tribal college, the Little Big Horn College (LBHC) in Crow Agency, Montana.

A certain amount of apprehension preceded my arrival in Crow Agency. In spite of good intentions (or more often because of bad intentions), native Americans have often suffered in the hands of the predominantly European settlers of this country. A certain amount of resentment would be normal, and my blue eyes and fair skin would identify my non-native background to even a casual observer. My discovery that the Crow were employed as scouts by Custer and had advised against the attack on Crazy Horse and his confederates, reduced some of this apprehension. The open and friendly personalities of the Crow people at the college eliminated any remaining doubts.

Crow Agency is the administrative center of the Crow Indian reservation and home to a hospital, a few administration buildings, and the LBHC. A few shops supply necessary items, but there is little to offer employment. On the reservation, unemployment remains a major problem. The lack of employable skills and the seasonal nature of farm work keep the majority of Crow families on the reservation at or below the poverty line. The tribal leaders are seeking to remedy this problem, primarily through improved access to education.

The Little Big Horn College is one of the tribally controlled colleges that has been founded in the past 15 years. In addition to standard associate level coursework, the college serves as a basis for continuing adult education (culminating in the GED). An additional charge, and possibly the most important, is to serve as a repository for the written and oral history of the Crow nation.

Since its founding in 1980, the college has modified its primary structure (an old basketball gymnasium) into classroom, library, administration, and office space. Particular emphasis was placed on the science and computing facilities, and successful grant applications have funded both construction of appropriate facilities and the acquisition of modern computing equipment. There are currently 15 fulltime faculty members and over 350 students enrolled.

Robert G. Carroll, East Carolina University, with the Crow Indian Reservation students.

The pilot science program was initiated to improve the instruction in the two quarter anatomy and physiology course. Students enrolled in this course generally plan to continue their education at one of the state universities after graduating from LBHC, and earned credits are transferrable.

The initial laboratory session introduced the experimental approach to physiology as a part of the scientific method. Future experiments were based on testing a hypothesis. The data gathered were analyzed statistically, and the results were used to support, modify, or reject the original hypothesis. The majority of the experiments were modified from a laboratory manual being prepared by the International Union of Physiological Sciences for use in developing countries. Donation of a polygraph, preamplifiers, and transducers by Gould Inc. and an oscilloscope card and software by R. C. Electronics outfitted the laboratory for the experiments. Additional experiments utilized the computing facilities for simulations (HUMAN, by Jim Randall and Tom Coleman).

Robert G. Carroll, East Carolina University, with the Crow Indian Reservation students.

Generally, the students enrolled in the anatomy and physiology course are not "traditional" students. Most have long since completed their high school education, and many are trying to juggle the demands of family, an outside job, and the coursework. The seven students in the anatomy and physiology course, however, managed to balance these tasks and remain enthusiastic and inquisitive throughout the laboratory experiments.

Teaching at the college level, however, was markedly different from medical school physiology. The students were in their first semester of physiology, and attempts at integration of the information were not always successful. Particularly important was stressing the difference between cause and effect. The students were usually willing to accept simultaneous occurrences as causative. Apart from this caution, the students appeared to grasp the physiological principles underlying the experiment.

The majority of these students will continue their education, usually at one of the state schools. Often, a career in nursing or other health related profession is their stated career goal. A future in academic medicine is not considered, primarily because the students do not realize that such a career exists. Their interest in biomedical sciences, however, indicates that these students may be a source of future physiologists.

One of the more promising events in the reservation primary schools is the introduction of "discovery" science, where the students are encouraged to explore the world around them. Because these students are encouraged to question and interpret events, these students may be more attuned to careers in the investigative sciences. Additionally, LBHC runs a science camp for primary school students, staffed by the faculty and students on the campus. With native American role models, future generations should be more inclined to pursue science careers. It will take time to see any benefits from such a program, but the future should be promising.

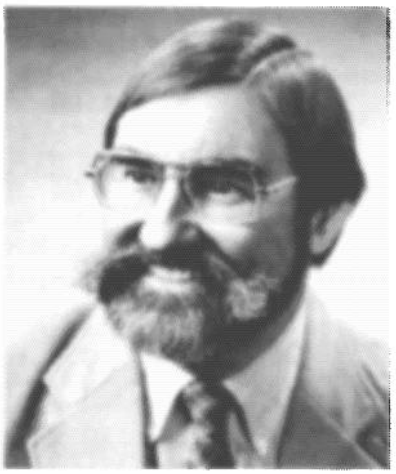
The lack of extensive physiological training at the community college level is not necessarily unique to the tribal colleges. Because the continued health of our society depends on the recruitment of qualified individuals, I feel the APS must become involved in improving the perception of physiology as an active, investigational science. The students readily appreciate the relevance of this knowledge and can apply physiological principles to understand many of their subjective experiences. Involvement at the collegiate and precollege levels of instruction, however, are required to further attract students to our profession.

The past two weeks have allowed me to observe an essentially foreign culture, where English is a second language. Particularly noteworthy are the efforts of LBHC to become the center for preservation of the Crow culture, while simultaneously preparing its graduates for life in the state college system. The opportunities to witness a pow-wow on a neighboring indian reservation and listen to discussions of dance and "drum" competitions within the pow-wow provided an insight not available to the casual tourist. Additionally, the white culture of the area is different from that of North Carolina. Ranching, farming, and mountain-based recreation color most aspects of Montana life. I do confess to trying my luck at trout fishing on the Big Horn River with moderate success.

The transgressions of the "white" world against native Americans are as legendary as the ill-fated attack by Custer against Chief Crazy Horse about three miles from the site of the college. The Crow Indians, however, follow the advice of their last chief, Plenty Coups, and seek to regain control of their own destiny through education. Currently, native Americans represent an untapped human resource, particularly in the field of higher education. A small effort by the APS may entice some of these individuals to consider careers in biomedical sciences, and the discipline of physiology would benefit from an early and effective exposure at the tribal college level.

Introducing . . .

William H. Dantzler



William H. Dantzler, a professor of physiology at the University of Arizona, has been appointed editor of the *American Journal of Physiology: Regulatory, Integrative, and Comparative.* He had been an associate editor of the journal for nine years.

Dantzler earned his medical degree at Columbia University and his PhD degree at Duke University under the direction of former APS president, Bodil Schmidt-Nielsen.

The new editor has had an active role in the Society's publications. In addition to his tenure as an associate editor, he served four years as a member of the editorial board of the *American Journal of Physiology: Renal, Fluid, and Electrolyte Physiology,* and three years on the editorial boards of the *American Journal of Physiology* and *Journal of Applied Physiology.*

He also has been a member of the APS Membership Committee and the Committee on Committees and has served as secretary and chairman of the Renal Section, councillor and chairman of the Section on Water and Electrolyte Homeostasis, and councillor and treasurer of the Comparative Physiology Section.

His research involves comparative renal physiology with particular emphasis on the renal tubular transport of organic molecules. He also maintains a broad interest in fluid and electrolyte balance.

In an introductory editorial, Dantzler noted the growth of the journal under the direction of his predecessor, David Ramsay, wherein the number of manuscripts increased 3-fold to approximately 600 manuscripts annually.

"I hope to continue the trend," Dantzler said, adding that there is no intention of limiting subjects considered or techniques used. "We wish to continue to attract papers from physiologists who are united by a broad interest in regulation, integration, and homeostasis."

He also plans to increase the number of editorial reviews, which in recent years have attracted wide attention and frequently are cited in the literature. His goal is to eventually publish one editorial review each month. The Journal also, on occasion, will publish symposia presented at national and international meetings.

Dantzler also noted the rate of manuscript review was improved during Ramsay's editorship, and he hopes to further reduce the review time by utilizing modern electronic communications.

Computerized Editing

Can you supply a disk for your **accepted** manuscript? The APS Publications Office is encouraging the submission of disks for accepted manuscripts for the *American Journal of Physiology* and the *Journal of Applied Physiology.* Disk manuscripts can be created with any popular word-processing software and may be submitted on 3.5- or 5.25-inch low- or high-density diskettes. For information: Krysia Moore (301/530-7169).

WHAT'S HAPPENING IN APS?
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tion of new biology (molecular and cellular) into APS meetings and journals. At the same time, we have continued to emphasize excellence in research at the levels of tissues, organs, systems and the whole body. These efforts are aimed at elucidating the molecular and cellular bases of physiological functions and toward establishing the physiological significance of molecular and cellular biological research. Such evolutions can be evidenced by the topics of the symposia organized by APS for the 1991 spring meeting. It is also encouraging to note that APS has been approached by several genetic engineering companies regarding the training and employment of physiologists with expertise in classic physiology.

The above represents only a fraction of the activities of the American Physiological Society, but I think it provides a picture of a dynamic, effective and vigorous society as it enters the fourth year of its second century. While we are doing well, for APS and physiology to continue moving ahead with vigor, we need the active participation of our members in society activities. We need your participation in publications, meetings, committees and other activities of the Society. Together, we can ensure a bright future for physiology and APS.

American Physiological Society 143rd Business Meeting

Time: 5:45 PM, Wednesday, April 4, 1990
Place: Grand Hyatt Hotel, Washington, DC

I. Call to Order

The meeting was called to order by President **Vernon S. Bishop,** who welcomed the members to the 143rd Business Meeting of the Society. The agenda, Election Ballot for new members, a list of 1990 APS Award Recipients, and a list of future Society meetings.

The President appointed Loring B. Rowell, University of Washington, as parliamentarian.

II. Report on Membership

President-Elect Shu Chien presented a report on the status of the Society membership and deceased members since the last meeting.

A. Summary of Membership Status

The Society membership continues to grow. As of March 6, 1990, the membership increased to 6,896 (4,809 regular, 719 emeritus, 25 honorary, 256 corresponding, 826 associate, 13 associate corresponding, and 248 student), a net increase of 189 members since October.

B. Deaths Reported Since the Fall Meeting

With a deep sense of sorrow, the names of the 21 deceased members were read. The membership observed a moment of silence in tribute to their dedication to physiology (p. 121).

III. Election of Officers and Society Affairs

A. Election of Officers

The Nominating Committee, composed of representatives from the six sections, identified the slate of candidates nominated by the membership.

Martin Frank, announced that **Norman C. Staub** was elected President-Elect and will take office on April 5, 1990. The newly elected Councillors, **Allen W. Cowley, Jr.** and **David J. Ramsay,** will take office at the close of the spring Council meeting. A total of 1,762 ballots were cast.

B. Society Affairs

The Society offices are located on the FASEB campus in Bethesda, Maryland. A dedicated staff of forty-two works for the Society in membership, programming, and publications to ensure that the services desired by the membership are provided. One major change of importance to note is the computerization of the Publications Department, which has increased the number of manuscripts on disks that are handled by the editorial staff. This has enhanced the ability to edit manuscripts and decreased the turn-around time from receipt to publication of manuscripts.

IV. Election of Members

A. Appointment of Tellers

The membership was instructed to strike those names from the ballot for whom they did not wish to vote. Tellers **Edward G. Schneider** and **William S. Spielman** were asked to collect and count the ballots.

B. Election of New Members

President-Elect Chien announced that 105 votes were cast unanimously electing 189 candidates to membership in the Society, a total increase of 327 new members since the October 1989 fall meeting (p. 110).

V. State of the Society

"It is an exciting age for physiologists. With the advances in molecular biology and imaging, we can investigate regulatory processes at all levels," stated President Bishop.

"One of the responsibilities of the American Physiological Society, your Society, is to assist its members to take advantage of the new opportunities associated with the expanding technologies. In this respect, the Council is striving to implement programs to respond to the needs of our membership. Whether the need is for a journal or a special scientific meeting, the Society endeavors to meet your needs.

"Reviewing the state of the Society, I would like to highlight some of the opportunities and initiatives to which we are responding.

"No matter what the Society does, it is imperative that we mount a public information campaign to ensure that biomedical research will be adequately funded in the 1990s and that animals will be available for the research needs of the investigator community. This campaign has already begun, but it needs your help.

"Recently, you received a letter and information from me urging you to write your elected representatives to ask for their support on HR 3270—the Animal Research Facilities Protection Bill introduced by Charles Stenholm. You were also asked to write to ask their support for additional monies by providing support for 6,000 new and competing renewal grants in the NIH appropriations for fiscal year 1991. I know many of you have already written to your representatives, but for those of you who have not, I must urge you

to write, to become active, and, if possible, to visit your elected representatives.

"Through its committees—Public Affairs, Animal Care and Experimentation, and Government Relations Initiatives Programs—the Society is beginning its pro-active campaign. At this meeting alone, there were three events designed to increase your awareness on the animal issue. For two of these, 'A Review of the New Animal Welfare Act Regulations: Are They Good or Are They Bad?' as well as 'How to Develop Grassroots Organizations in Support of Animal Research,' reports will appear in *The Physiologist.* The third was a workshop 'Media Training for the Scientist: How to Meet the Media,' which was so successful, it will be repeated next year.

"For the Society to succeed, we must have the financial resources to take advantage of new opportunities and to develop new programs. **Norman R. Alpert,** as chairperson of the Finance Committee, is responsible for ensuring the financial well being of the Society. Since Norman was not able to stay for the Business Meeting, he has submitted a report for me to read to the membership.

"The charge to the Finance Committee from the Council is to develop a budget so that the Society does not lose money in any fiscal year. It is also charged with having a plan that will enable the Society to accumulate a reserve fund that will cover one to two years of operation. The Finance Committee has taken that charge seriously and is in the process of accumulating such reserves.

"However, as we approach that goal, the Finance Committee is also working on a five-year financial plan for the Society. This will enable us to have a better view of the year-to-year progress toward achieving financial stability. It will also serve as the basis of a five-year strategic plan being developed in conjunction with the Council. It should be clear that the financial strength of this organization permits the Society to develop new programs to strengthen our meetings and to provide the membership with an expanding list of benefits. Such financial strength has allowed the Society to take initiatives, such as the new high school science teachers research program, and to start new journals and new program formats.

"The Finance Committee is responsible for: *1*) a financial overview of the Society for the past year and the development of future budgets; *2*) the audit of the Society by Coopers and Lybrand; and *3*) overseeing the management of our reserve accounts. During the 1989 fiscal year, the Society had an income of $8,182,039 with expenditures of $7,891,411, representing $290,627 income over expenses.

"The major source of funding for the Society is the publications activities. The journal program generated income of $6,810,338 while the expenses were $6,405,341 with an income over expenses of $404,887. This resulted from understaffing in the editorial office, savings in printing and engraving costs and other savings generated by the editorial staff. However, the decision not to increase subscription rates for this year will result in a $550,000 negative shift in this relationship. The Handbook Series budget registered a loss for this year of $50,000 while the Society General Fund had a loss of $60,000.

"The Society's finances and accounting procedures were audited by Coopers and Lybrand. They reported to the Finance Committee that the financial statements were accurate and that the Society was in excellent financial health."

"As Norman indicated in his report," stated President Bishop, "the Society is financially healthy, but that health is fragile when one considers that our decision not to raise subscription prices will result in a half million dollar shift in our balance sheet in 1990. Because of that, the Council has decided to raise subscription prices for 1991. However, the message is not all bad. After consultation with the Finance and Publications Committees, we have decided to exempt members' rates from this increase. Indeed, members' rates

APS Council. *Top Row (L-R):* W. S. Spielman, R. B. Reeves, B. R. Duling, M. Frank, P. D. Wagner, A. W. Cowley, Jr., J. S. Cook, C. V. Gisolfi. *Front Row (L-R):* G. Giebisch, A. E. Taylor, S. Chien, V. S. Bishop, B. Bishop, A. R. Alpert.

should remain stable for the next several years as we move to a three-tiered subscription level with members paying one-third the institutional rate, and non-member individuals paying two-thirds the institutional rate. The ability of the Society to provide this benefit to the members is a result of our financial health.

"The publications program of the Society continues to grow in size and prestige. In 1989, the journals received more than 5,000 manuscripts and published more than 25,000 pages, an increase of 20%. This represents the combined effort of over 815 scientists who serve as editors and members of the editorial boards. In 1989, the Society also published two new journals—*APS: Lung Cellular and Molecular Physiology* and *Advances in Physiology Education.*

"For 1990, the Publications office is working to reduce the time between manuscript receipt and publication by accepting manuscripts on disks. Our members are encouraged to take advantage of this new benefit.

The Publications Committee has just appointed **Dale Benos,** University of Alabama at Birmingham, as editor of *AJP: Cell Physiology.* **Luis Reuss** has been appointed editor of *Physiological Reviews* to replace **Gerhard Giebisch.** The committee is also seeking candidates for *AJP: Endocrinology and Metabolism* and *AJP: Gastrointestinal and Liver Physiology.* Anyone interested in these positions should contact the committee chairperson, **John Cook.**

In conjunction with Oxford University Press, our partner in publishing, the Society is making plans to publish several new handbooks and other physiology books. Our relationship with Oxford improves our marketing ability, while reducing our financial burden.

One of the evolving strengths of the APS is its ability to put on 'cutting edge' scientific programs for our members. At the 1990 FASEB meeting, APS members contributed over 40% of the volunteered abstracts. In addition, the program included numerous symposia, workshops and tutorials contributed by APS. However, FASEB only represents one aspect of our meeting program,

APS Business Meeting, Washington, DC, April 1, 1990.

and I would like to call on **Carl Gisolfi,** chairperson of the Program Committee, to tell you more about our new initiatives in programming."

"The Program Advisory Committee, which consists of 18 different sections and groups of the Society, has been working very hard to improve the quality of your meetings," stated Gisolfi. "The fall meeting has been evolving over the last five years going from multiple themes to a single theme meeting. Committed to expanding programs, the Society will sponsor two fall speciality meetings in 1992. The format of a specialty meeting is different from what has been experienced in the last few years. It will be a three-day meeting attracting up to 500 people with no more than one overlapping session.

"Two proposals have been accepted for specialty meetings in 1992. The Cellular and Molecular Biology of Membrane Transport, organized by **Lazaro Mandel, Douglas Eaton** and **William Agnew,** will be a three-day meeting held in Sarasota, Florida in October. The Exercise Physiology Specialty Meeting, organized by Peter Wagner, is to be a three-day meeting scheduled in early September in Colorado Springs.

"The 1991 FASEB spring meeting to be held in Atlanta, Georgia, April 21-25, will be the last six-society meeting. After that, the biochemists will no longer meet with FASEB. The theme of that meeting will be Molecular Aspects of Experimental Biology. Twenty-six APS symposia have been selected for presentation, and the Education Committee will sponsor a workshop, 'Single Ion Channels.' The 1991 specialty meeting, 'Interaction of the Endocrine and Cardiovascular Systems: In Health and Disease,' will be held September 29-October 3, San Antonio, Texas. The organizers are **David Wasserman, George Hedge, Hershel Raff, Ronald Freeman,** and **Joseph Haywood.**

"**Larry Crawshaw** has organized a superb specialty meeting entitled 'In Search of Physiological Principles: The Use of Animal Diversity and Novel Technology,' to be held at the Orlando Hyatt Hotel, Florida, October 6-10, 1990. Participating societies are the Divisions of Comparative Endocrinology and Comparative Physiology and Biochemistry, American Society of Zoologists; Comparative Physiology and Biochemistry Section, Canadian Physiological Society; Society of Experimental Biology (UK), Comparative Respiratory Society, and the APS sections.

"The APS' primary interest is generating good science," said Gisolfi, "I leave you with the request to provide us with ideas for a specialty meeting in 1993. I encourage you to contact me or your Section's Program Advisory Committee representative. If we provide the science, the APS will provide the financial support. The deadline for receipt of proposals for the 1993 specialty meeting is February 1, 1991. Please send your ideas in."

Continuing his State of the Society report, President Bishop said, "I would

also like to share with you information about a new program for high school science teachers initiated this year to help increase the understanding of science and animal use in the schools. Under the auspices of the Education Committee, this program is designed to give high school science teachers an experimental education in modern physiology. In response to announcements of the program in teachers' professional journals and to the APS membership, 30 applications were received. After careful review, the committee selected 12 teachers to serve as APS summer research fellows. Hopefully, each of you will consider being of assistance to a high school teacher during the coming year even if you are not a recipient of an award.

"These are just some of the activities that reflect on the State of the Society. I will not enumerate on others at this time. However, I do want to say that the Society's committees and Council are seeking new ideas on how to strengthen the Society and benefit our members. For those ideas we rely on you, The Members.

"The State of the Society would not be complete without providing you with an update on the happenings in FASEB. As you may recall, last year the Council issued a resolution calling for FASEB to 'essentially eliminate' the assessment so new societies could be attracted to FASEB membership and APS could meet independently of the FASEB meeting, if desired. I am pleased to inform you that all the elements are coming together. Current plans call for FASEB to go from an assessment-based to a dues-based budget. Plans call for the dues to be reduced from the current $47.00 per member to $10-$15 per member in 1995. New societies joining FASEB would pay $10 per member, and I am pleased to say there are a number of interested societies. In addition, the Bylaws are being changed to make FASEB more representative and more responsive. All that is lacking is an executive director, and we are in the process of interviewing candidates.

"Overall the American Physiological Society is in good health. However, the health of the Society depends on you The Members. I urge you to get involved.

"This represents my last report to you as President of the Society. I would like to take a moment to thank you for giving me the opportunity to serve you and the Society in this capacity. It has been my pleasure."

VI. Awards and Presentations

A. Ray G. Daggs Award

The Ray G. Daggs Award was presented to **Robert M. Berne,** 45th President of APS (see p. 86).

B. Orr E. Reynolds Award

The Orr E. Reynolds Award, named for the Society's second Executive Secretary-Treasurer, is given annually to the APS member judged to have written the best historial article.

The Award was established in 1986 in recognition of Orr Reynolds' contributions to the Society and his interest in the history of physiology. Articles submitted for the award may deal with any aspect of the history of physiology.

President Bishop was pleased to present the 1990 Orr E. Reynolds Award to **Clark T. Sawin,** Chief, Endocrine-Diabetes Section at the Boston Veterans Medical Center, and professor of medicine and physiology at Tufts University School of Medicine for his paper entitled "Defining Thyroid Hormone: Its Nature and Control," which was published in *People and Ideas, Endocrinology.*

In accepting the award, Clark Sawin expressed surprise and gratitude to be the recipient of the award. He said, "My view of history is more than chronology—the who, what, when, and where—or interesting anecdotes, important though these are. History viewed as the study of human behavior over time aims at finding out why things happen and so attempts to illuminate the present. We need to know better why we, as scientists, do what we do and how we have come to be what we are. With this knowledge, imperfect though it may be, one is a professional; without it, I fear, one remains a technician. A thorough knowledge of the development of physiology may even help the Society figure out what physiology is today and what it might become. Thank you."

Arthur M. Brown, Baylor College of Medicine, presenting the Walter B. Cannon Lecture—Physiology in Perspective, Washington, DC, April 4, 1990. The lecture, sponsored by the Grass Foundation, was entitled, "The Heartbeat and Its Regulation by G Proteins."

1990 Ray G. Daggs Award

"One of the pleasures of my tenure as President of the American Physiological Society is the honor of presenting the Ray G. Daggs Award. What makes this presentation special is that this year we close a loop so to speak," announced President Vernon Bishop.

The Daggs Award, named for the Society's first full-time executive secretary, is given each year in recognition of a physiologist who is judged to have provided distinguished service to the science of physiology and the American Physiological Society.

The award was established by the APS Council in 1973 when **Robert Berne** was President. The loop is closed by honoring him as the 1990 recipient of the Ray G. Daggs Award.

Bob's journey into physiology was to have been a two-year stint because his sights were set on a career as a cardiologist. To prepare for such a career, he believed it was necessary to gain some basic science training in cardiovascular physiology, and he obtained a postdoctoral fellowship with Carl Wiggers at the Western Reserve University Medical School.

As things developed, Berne became so engrossed in and excited by his research with Wiggers that he continually postponed his pursuit of cardiology. Moreover, his research career has continued along the same avenues he began with Wiggers: cardiovascular physiology, in general, and local chemical regulation of tissue blood flow, in particular.

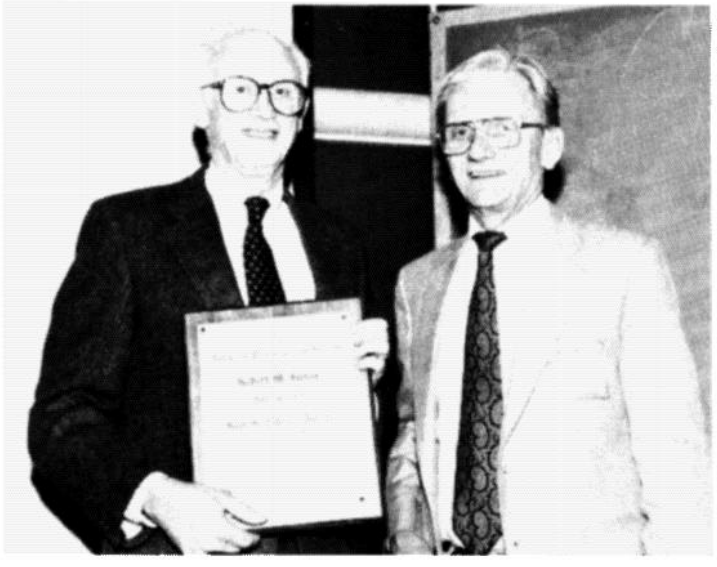
Bob has not been one to confine his interests in the cardiovascular system to the laboratory and the classroom because he has served a variety of editorial boards and committees of scientific societies and associations in addition to giving countless hours to the American Physiological Society.

Although he was elected to membership in the Society in 1951, Bob did not begin an active role in the affairs of APS until the early 1960s, serving first on the Program Committee. He later served two separate terms on the Finance Committee, was chairperson of the Long-Range Planning Task Force, and was a member of the Publications, the Perkins Award, and the Long-Range Planning Committees. He also was editor of the circulation section of the *American Journal of Physiology,* served four years on the editorial board of the *American Journal of Physiology,* and a member of the steering committee for the revision of the cardiovascular section of the *Handbook of Physiology* and editor of volume 1 on the heart.

Bob was elected to Council in 1970 and elected President-Elect the following year. Procedures by which APS conducts its affairs probably changed more during his presidential years than any other time in recent Society history. The most dramatic change, perhaps, was the change in the voting procedures for the election of President and Councillors.

Traditionally, any item that required a decision by the membership was considered only at the spring meeting, including the election of Councillors and Officers. Bob was successful in gaining an amendment to the Bylaws to permit election of office by mail. The first mail election was held in 1975, and 1,677 votes, approximately 45 percent of the membership, were cast compared to the 150 to 300 votes usually cast in the spring meeting elections.

Responding, Robert Berne said, "Thank you all for this great award. I am deeply honored. It really has a very special meaning for me because I had the good fortune to work with Ray Daggs and got to know him quite well. As indicated, it was during my tenure as President that this award was initiated, and I wish he were here. It is accepted with great appreciation. Thank you."



Robert M. Berne receiving the 1990 Ray G. Daggs Award from President Vernon S. Bishop, APS Business Meeting, Washington, DC, April 4.

Ray G. Daggs Award Recipients

1974	H. H. Brookhart
1975	M. B. Visscher
1976	J. D. Hardy
1977	J. H. Comroe
1978	H. Rahn
1979	J. R. Papenheimer
1980	J. R. Brobeck
1981	A. C. Guyton
1982	R. W. Berliner
1983	C. L. Prosser
1984	E. F. Adolph
1985	A. C. Barger
1986	D. B. Dill
1987	O. E. Reynolds
1988	H. W. Davenport
1989	B. Schmidt-Nielsen
1990	R. M. Berne

APS/FASEB Spring Meeting
Atlanta, Georgia April 21–25, 1991

APS Sponsored Symposia

The regulation of glucose transport in skeletal muscle.
Chair: R. J. Barnard

Flow-sensitive regulation of vascular tone.
Chair: J. A. Bevan and G. Kaley

Cellular and molecular aspects of muscle disease.
Chair: K. P. Campbell

Molecular biology of myocardial growth and development.
Chairs: K. R. Chien and S. Chien

Avian foregut function.
Chair: G. Duke

Pathophysiology of hypertension in blacks.
Chair: J. C. S. Fray

Mechanisms of renal ammonium transport.
Chairs: L. L. Hamm and D. W. Good

Molecular aspects of renal phosphate transport.
Chair: S. A. Kempson

Interactions of anion and cation transport in cell volume and pH regulation.
Chairs: P. A. Knauf and S. Grinstein

Mechanisms involved in the coupling of excitation to sarcoplasmic reticulum Ca^{2+} release in the heart.
Chair: E. G. Lakatta

Calcium and the heart.
Chair: G. A. Langer

Interactions between energy metabolism and cardiovascular regulation in exercise.
Chair: S. F. Lewis

Segmental epithelial electrolyte transport in pulmonary system with relevance to cystic fibrosis.
Chair: C. M. Liedtke

Advances in integrative human neurocirculatory physiology.
Chair: A. L. Mark

Modern history of the nervous system.
Chair: L. H. Marshall

Regulation of extracellular matrix formation during lung development and repair.
Chair: S. E. McGowan

The heart and control of renal excretion: neural and endocrine mechanisms.
Chairs: T. V. Peterson and B. A. Benjamin

Endocrine adaptation to hypoxia.
Chairs: H. Raff and M. F. Dallman

Is growth hormone a growth factor?
Chairs: J. Schwartz and C. Carter-Su

Tissue remodeling by inflammatory cells.
Chair: R. M. Senior

Renal ion channels: molecular biology and signal transduction pathways.
Chairs: B. Stanton and D. Eaton

Comparative biology of adhesion.
Chair: H. Waite

Molecular endocrinology of gastrointestinal hormones.
Chairs: J. A. Williams and T. Yamada

Membrane transport of cations in vertebrates red blood cells: the lessons of diversity.
Chair: J. S. Willis

Lactate kinetics: physiological and methodological issues.
Chair: R. R. Wolfe

AAP/APS Symposium

Application of molecular biology to the study of vascular endothelium.
Chairs: M. G. Grimbone, Jr. and S. Chien

AIN/APS Symposium

Human milk proteins: structure and function.
Chair: M. C. Neville

Workshops

Single ion channels.
Chair: J. T. Herlihy

National Institute on Deafness and Other Communication Disorders mission workshop.
Chair: J. Pearl

Biomedical research in developing countries.
Chair: D. Richardson

APS Public Affairs Workshop

Media training for the scientist: how to meet the media.

Special Lectures

Annual Space Life Sciences Lecture

Bowditch Lecture: W. S. Ammons, Thomas Jefferson Univ.

Walter B. Cannon Memorial Lecture: P. Needleman, Washington Univ.

BMES Symposia

Molecular aspects of cell adhesion.
Chair: L. V. McIntire

Shear stress effects on vascular endothelial cells.
Chair: R. M. Nerem

SEBM Symposium

The role of endogenous factors in tumor promotion.
Chair: H. C. Pitot

12 High School Science Teachers Selected for APS Summer Research Program

Twelve high school science teachers have been selected for a 10-week summer research program sponsored by the American Physiological Society.

The Society started the program this year as a means to provide high school science teachers with experiences in modern physiology research. The teachers' experiences will be shared with students with the hope that students will take an interest in pursuing a career in the biological sciences.

Recent studies show there is a decline in student interest in the biological sciences during the high school years and fewer students are making or seeking advanced degrees in science. This growing lack of scientific background hinders the public from making informed decisions about important scientific issues such as the human genome project and the use of animals in research.

The 12 teachers, selected in a national competition, were awarded grants that included a $5,000 stipend plus $750 to support the teacher's attendance at the April 1991 FASEB meeting in Atlanta, where they will be honored at a luncheon.

Listed are the teachers and their high schools, followed by the host institutions and the mentors:

- Lesli Adler, Wootton High School, Rockville, MD; Armed Forces Radiobiology Research Institute, Gregory King.
- Belinda B. Banks, Fairborn (OH) High School; Wayne State University School of Medicine, Robert W. Putnam.
- Travis Barnes, Granbury (TX) High School; Texas College of Osteopathic Medicine, H. Fred Downey.
- Barbara Doyle, Northeast High School, Oklahoma City; University of Oklahoma Health Sciences Center, Robert Foreman.
- George H. Gould, Firestone High School, Akron, OH; University of Akron, Daniel Ely.
- Lana Hays, Simon Kenton High School, Independence, KY; University of Cincinnati School of Medicine, Nicholas Sperelakis.
- Kenneth J. Mann, Lourdes High School, Rochester, MN; Mayo Medical School, Franklyn G. Knox.
- Kent W. Osborn, Batavia (NY) High School; University of Rochester Medical Center, Richard J. Connett.
- Clemontene Rountree, Alice Deal School, Washington, DC; Howard University College of Medicine, Laval Cothran.
- Linda Sandoval, North High School, Denver, CO; Colorado State University, Alan Tucker.
- Michael Stormo, Vermillion (SD) High School; University of South Dakota School of Medicine, Barbara E. Goodman.
- Michael J. Zanatian, Chamberlain High School, Tampa, FL; University of South Florida College of Medicine, Carleton H. Baker.

Call for Symposia Topics—Spring 1992

Members are urged to submit proposals for APS symposia to their Section Program Advisory Committee representative. Organizers should consider multidisciplinary approaches with other sections and the contribution by experimentation at multiple levels of investigation.

What specific questions will the symposium address? Are there two or three conflicting issues that warrant presentation and discussion? What does the symposium offer to the intended audience? Are future directions considered in the material to be presented?

Symposia proposals are welcome for the 1992 APS/FASEB spring meeting. Submit proposals to the appropriate Section Program Advisory Committee representative by January 15, 1991. All proposals should include the following: *1)* Title; *2)* Organizer and address; *3)* Abstract (150 words); *4)* Number of half-day sessions; *5)* Names of session chairperson(s); *6)* Presentors/Discussants—approximately six per half day (list the participant's name and title of presentation as it would appear in the program); *7)* Brief biographical sketch (2-3 sentences) of each speaker in the symposium; *8)* Budget information. To coordinate fund-raising efforts by the national office, the anticipated costs to support the travel and lodging of symposia speakers are needed. Symposia are evaluated on the basis of their scientific merit. Organizers will be notified immediately on acceptance of the symposia.

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MYOBIO Group
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APS Code of Ethics

A Code of Ethics for members of the American Physiological Society was adopted by the Council at the fall meeting in Rochester, MN.

CODE OF ETHICS

Membership in the American Physiological Society includes the acceptance of and the responsibility to uphold the following Code of Ethics.

The role of the physiologist is to advance the field through teaching, research, and service. In the process physiologists shall be honest in their reporting of research findings and ethical in their dealings with others. Moreover, physiologists shall be humane in the treatment of human and nonhuman subjects. Physiologists shall also have the professional responsibility to bring to the attention of appropriate authorities apparent violations of these principles.

Physiologists recognize the Society's responsibility to consider breaches of ethical behavior and to take any response deemed necessary in accordance with the Society's Bylaws, Article IX, Section 5 and as defined in the Operational Guide.

APS Specialty Meetings

For several years the American Physiological Society has been transforming its fall meeting from one encompassing all aspects of physiology to one embracing selected themes. From 1985 through 1987, the meetings had multiple themes, and in 1988 the Program Advisory Committee endorsed a program with a single theme. The 1989 meeting offered the most focused program to date, featuring the theme "Mechanisms of Smooth Muscle Function."

The format of the fall meeting continues to evolve. In fact, what was once a single meeting designed for all Society members with annual Society events (Bowditch Lecture, Past President's Address) will become multiple meetings for "specialized groups." The Bowditch Lecture and Past President's Address will be held during the spring FASEB meeting.

The specialty meetings of the Society will be held anywhere from August through February and will be organized by the different Sections of the Society or by small groups of Society members. Moreover, beginning in 1992, specialty meetings will be managed by the APS central office staff rather than by FASEB. This means that the organizing committee of a specialty meeting will have the opportunity to participate in the selection of the meeting site. These meetings offer the Society membership the ultimate in programming opportunities. In general, the organizing committee will select the theme, format, abstract categories, method of presentation (slide/poster), and duration of the meeting. The APS office will be responsible for negotiating the site and space allocation for the meeting, advertising the meeting, and managing all financial and logistic aspects of the program. In essence, the Society is simply asking you to help organize a program that presents the best science and it will provide the space and resources to support you. What more could you possibly ask?

Listed below are more specific guidelines to follow in organizing a specialty meeting of the APS. Any questions regarding the organization of such a meeting should be directed to Carl V. Gisolfi, Department of Physiology & Biophysics, University of Iowa, Iowa City, IA 55242, or Martin Frank at the APS office.

Specialty Meeting Guidelines

Scope

These meetings should focus on a circumscribed area of physiology that attracts a limited (100–500) audience. A concerted effort should be made to integrate overlapping fields of study and levels of investigation, i.e., from molecular biology through systemic physiology.

Organizing Committee

The Program Committee should provide direction by identifying select persons, groups, or perhaps Sections and requesting them to organize a specialty meeting. The "organizing committee" and the chairperson of that committee will work with the chairperson of the APS Program Committee to develop the framework of the meeting. The organizing committee will be responsible for providing APS with: *1*) a list of potential meeting sites; *2*) contacts from other societies who may wish to attend or participate in the meeting; *3*) potential outside funding; and *4*) a budget detailing the cost of the meeting.

Management

The APS staff will be responsible for booking site selection, advertisement, setting the registration fee, attracting exhibitors if desired, and solicitation of supporting funds.

Abstracts

Inclusion of volunteered papers on the program will be left to the discretion of the meeting organizers. There should be a format that provides graduate and postdoctoral students the opportunity to present their data if the material falls within the scope of the theme. Abstracts will be accepted without evaluation and published by the Society. The organizing committee will be responsible for generating a list of topic categories that fall within the scope of the theme.

Location

Will be flexible. The Society requires at least two years advance notice of proposed meeting sites to book meeting space.

Duration

The meeting should be scheduled for two to three days, preferably over a weekend to take advantage of travel costs.

Program Advisory Committee

Will evaluate and contribute to the framework of the meeting. Once the PAC has had the opportunity to evaluate and contribute to the meeting, and the Program Committee has given its approval, the final content will be presented to Council for their final endorsement and approval.

Joint Sponsorship

With other societies will be considered.

Number of Meetings

Will depend upon the needs of the membership. From 1992 through 1995, not more than two meetings per year will be sponsored by the Society.

Reimbursement Policy

Partial reimbursement for member and nonmember invited speaker expenses may be provided by the Society based on availability of funding.

Time of Year

June through December (to avoid overlap with preparations for the FASEB meeting).

Recipients – 1990 APS Awards

Ray G. Daggs Award

Robert M. Berne, University of Virginia

Orr E. Reynolds Award

Clark T. Sawin, Veterans Administration Medical Center, Boston, MA: "Defining Thyroid Hormone: Its Nature and Control"

Caroline tum Suden Professional Opportunities Awards

Kay K. Azuma, University of Southern California
Najia Jin, Indiana University, Indianapolis
Li Lu, University of Michigan
Lawrence C. Starke, University of Texas, Galveston
Xiao-Ping Sun, Harbor, University of California, Los Angeles
Jun Yu, University of Manitoba, Winnipeg

1990 Caroline tum Suden Professional Opportunities Awardees with Catherine Chew *(L)*, Chair, Women in Physiology Committee, Washington, DC, April 4, 1990.

NIDDK Minority Fellowship Awards

George T. Blevins, Jr., University of Arkansas
Dayne Jo-Ann Clarke, University of Florida
Claude A. Davis, Tuskegee University
Alarico Fernandez, University of Florida
Xavier Flores, Medical College of Ohio
Theodore Ford, Northwestern University
John Galan, St. Mary's University
Cynthia Ann Jackson, University of California, Davis
Patricia A. Warren Marks, Little Rock, Arkansas
Todd V. Robinson, University of Tennessee, Memphis
Arnold L. Silva, University of Arizona
Alice Renee Villalobos, University of Arizona
Joyce Marie Wright, Southfield, Michigan

John F. Perkins, Jr. Fellowship Awards

Visiting Scientists and Hosts

Peter Bergsten, University of Uppsala, Switzerland
Mark Levine, National Institutes of Health, Bethesda, MD

Rod Dimaline, University of Liverpool, England
John H. Walsh, University of California, Los Angeles

Wu-Xin Huang, General Hospital, Chengdu, PRC
Sukhamay Lahiri, University of Pennsylvania, Philadelphia

Rodrigo Iturriaga, Catholic University of Chile, Santiago
Sukhamay Lahiri, University of Pennsylvania, Philadelphia

Chang-Lin Lu, Second Military Medical College, Shanghai, PRC
Allan Siegel, University of Medicine and Dentistry, Newark

Howard Mitchell, University of Western Australia, Nedlands
Ronald Coburn, University of Pennsylvania, Philadelphia

Christopher McCormack, University College, Dublin, Ireland
Beth Burnside, University of California, Berkeley

Procter & Gamble Professional Opportunities Awards

Cardiovascular Section

Karen M. Anderson, University of North Carolina (James E. Faber)
Lewis D. Fannon, University of Florida (M. Ian Phillips)
Evangeline Motley, Smith Kline & Beecham (Frankl C. Barone)
Jeffrey Paul, University of Medicine & Dentistry of New Jersey (Walter Duran)

1990 NIDDK Fellows, spring meeting, Washington, DC

1990 Procter and Gamble Professional Opportunities Awardees with Ted Logan *(seated 4th from the L),* Procter and Gamble Company, sponsor.

Cell and General Physiology Section
Matthew P. Anderson, University of Iowa (Michael J. Welsh)
John V. Frangioni, Harvard Medical School, Physiology Labs (Claude Lechene)

Endocrinology and Metabolism Section
Michael S. Jasper, Brown University (William C. Engeland)

Environmental and Exercise Physiology Section
John D. Griffin, Ohio State University (Jack A. Boulant)

Gastrointestinal Physiology Section
Johnson W. McRorie, Michigan State University (Jacob Krier)
Marc Post, University of Michigan (David C. Dawson)

Nervous System Section
Caroline L. Szymeczek, University of North Carolina (David Millhorn)

Neural Control & Autonomic Regulation Section
Hong Gu, Texas College of Osteopathic Medicine (James L. Caffrey)
Meredith Hay, University of Texas, San Antonio (Vernon S. Bishop)

Renal Physiology Section
Maria Trolliet, University of Florida (M. Ian Phillips)

Respiratory Physiology Section
Michael Emery, University of Washington (Michael P. Hlastala)
Denise Hocking, Albany Medical College, VA Med Ctr (Arnold Johnson)

Water and Electrolyte Homeostasis Section
Lawrence D. Nelson, Medical College of Wisconsin (Jeffrey L. Osborn)

Biomedical Research in Developing Countries

Special Poster Discussion 1991 APS/FASEB Meeting

In recent years several members of the American Physiological Society have been involved in research and/or teaching projects in developing countries throughout the world. The purposes of this special session are to increase the awareness of the biomedical science community of these activities, to provide a showcase of the type of research conducted in developing countries, and to provide an opportunity for interested FASEB members to learn how they can become involved.

If you have been involved in research and/or teaching in a developing country, you are invited to present a poster of your activities at this special session, which will be held on Tuesday, April 23, 1991 4:45-6:45 p.m. in Atlanta, Georgia.

Interested individuals should obtain the FASEB Call for papers and submit an abstract by the abstract deadline of December 3, 1990. Contact FASEB Office of Scientific Meetings, 9650 Rockville Pike, Bethesda, MD 20814. Telephone 301-530-7010, Telefax 301-571-1855.

APS and Section Awards

Society Awards

Caroline tum Suden Professional Opportunity Awards

The annual Caroline tum Suden Professional Opportunity Awards ($500, complimentary registration, and placement service fees) are granted to as many as six graduate students or postdoctoral fellows who present a contributed paper at the APS/FASEB spring meeting. Candidates must be the first author of an abstract submitted to APS. An accompanying letter, signed by the sponsor of the abstract, must contain *1*) certification that the author is a student or postdoctoral fellow and *2*) the approximate date the nominee will be available for employment. Awardees are notified by the Selection Committee prior to January 31 and presented with their awards during the APS Business Meeting.

NIDDK Travel Fellowships for Minority Physiologists

NIDDK Travel Fellowships for Minority Physiologists are open to advanced undergraduate, predoctoral, and postdoctoral scientists who have obtained their undergraduate education in Minority Biomedical Research Programs (MBRP) and MARC eligible institutions, as well as students in the APS Porter Development Program. Applications may also be submitted by minority faculty members at the above institutions. Funds will provide transportation, meals, and lodging to attend the annual APS/FASEB spring meeting. The specific intent of this award is to increase participation of the pre- and postdoctoral minority students in physiological sciences. Applicants need not be members of the APS but should be a US citizen or hold a permanent resident visa. Applications should include *1*) information on academic background and experience; *2*) a written statement of interest in research in physiology; *3*) a letter of recommendation from the applicant's mentor; *4*) a list of publications, if available; *5*) a statement indicating the underrepresented minority (Black, Hispanic, or American Indian) with which the applicant identifies himself/herself; *6*) an estimate of required travel and per diem expenses. The deadline for receipt of completed applications is December 15.

John F. Perkins, Jr. Memorial Fellowship

The American Physiological Society invites applications for the John F. Perkins, Jr. Memorial Fellowships. The Perkins Fellowships are designed primarily to provide supplementary support to foreign physiologists who have already arranged for fellowships or sabbatical leave to carry out scientific work in the United States.

The supplementary support is intended to help foreign scientists bring their families to the United States and thus enable them to take fullest advantage of other cultural benefits inherent in international exchange.

Preference will be given to physiologists working in the fields of respiratory physiology, neurophysiology, and temperature regulation. Applications from scientists in developing countries will also be given special attention.

Application should be made by both the visiting scientist and his/her host. To qualify, the host must be a member of the American Physiological Society. The application should contain an account of these arrangements with a brief description of the proposed scientific work and an account of how visitors and their families intend to make use of cultural opportunities during their stay. Deadlines for receipt of applications are May 1 and November 1. Applications may be obtained from the Executive Director, American Physiological Society, 9650 Rockville Pike, Bethesda, MD 20814, USA.

Orr E. Reynolds History Award

The Orr E. Reynolds Award is given annually by the American Physiological Society for the best historical article submitted by a member of the Society.

Articles may deal with any aspect of the history of physiology including the development of physiological ideas and their application, instrumentation, individual and collective biography, departmental and institutional history, history of societies including APS, and physiology in its public context. Manuscripts submitted for the award should represent original research and be adequately documented. Articles published in APS journals or books during the prior calendar year are also eligible for the award upon request by the author(s). The award is open to all classes of APS membership except for those members who have advanced degrees in the history of science and medicine. A member may receive the award only once.

The awardee will receive $500 plus expenses to attend the APS/FASEB spring meeting. If the awardee wishes, and there is a suitable place on the program, an oral presentation will be made at the spring or subsequent fall meeting at the beginning of an appropriate scientific session. It is hoped that, after appropriate peer review, the article will be published in one of the APS journals.

Manuscripts will be evaluated by a committee consisting of three members of APS appointed annually by Council in consultation with the chair of the History of Physiology Group. At least one of the members will be a professional historian.

Manuscripts should be typed and double-spaced with wide margins on 8½ × 11 paper and should conform to the style used in APS journals. (Instructions will be sent on request.) Three copies should be submitted for use of the review committee. Manuscripts should be sent to The Orr E. Reynolds Award, American Physiological Society, 9650 Rockville Pike, Bethesda, MD 20814, by December 1. The recipient of the award will be announced at the APS/FASEB spring meeting.

Section Awards

Procter & Gamble Professional Opportunity Awards

The Procter & Gamble Professional Opportunity Awards (provides $500 and complimentary registration for the APS/FASEB spring meeting) are granted to at least 17 predoctoral students who present a contributed paper at the meeting. Candidates must be the first author of an abstract submitted to APS and within 12–18 months of completing his/her PhD degree. All recipients must be US citizens or hold a permanent resident visa. An accompanying letter, signed by the sponsor of the abstract, must contain *1*) certification that the author is a predoctoral student and *2*) the approximate date of degree completion. Awardees will be notified before February 15. Awardees are selected by the following Sections of the APS: Cardiovascular, Cell & General Physiology, Comparative Physiology, Endocrinology and Metabolism, Environmental and Exercise Physiology, Gastrointestinal Physiology, Nervous System, Neural Control & Autonomic Regulation, Renal Physiology, Respiratory Physiology, Teaching of Physiology, and Water & Electrolyte Homeostasis.

Cardiovascular

The Cardiovascular Section presents three annual awards—Fellowship, the Lamport Award, and the Carl J. Wiggers Award. Nominations for **Fellowship Awards** must be made by at least two existing fellows with supporting letters sent to the steering committee for vote. The total number of fellows cannot exceed 5% of the APS regular members who have published meritorious research in cardiovascular physiology. The **Lamport Award** is presented to a young investigator under the age of 36 showing outstanding promise in his/her field of cardiovascular research. The recipient, who receives a certificate and a $200 check, is selected by the Wiggers awardee of the previous year. The **Carl J. Wiggers Award** honors a founder of the section and is presented to a scientist who has made outstanding and lasting contributions to cardiovascular research.

Comparative Physiology

The Comparative Physiology Section **Scholander Award** is presented annually to recognize an outstanding young investigator presenting a paper as first author in a comparative physiology slide session at the APS/FASEB spring meeting. Candidates must be graduate students or postdoctoral fellows, not more than five years beyond their highest degrees. The recipient receives a cash award of $100 and a certificate from the APS.

Environmental and Exercise Physiology

The Environmental and Exercise Physiology Section presents two annual awards. The **Young Investigator Award** ($150) is for the recognition of excellence in research by a graduate student. The **Honor Award** ($200) is given to a member of the section who has had a lifetime of outstanding research. Candidates must be first author on a paper presented at a previous APS meeting. Honoring Harwood S. Beling, the awards are presented at the section dinner.

Gastrointestinal Physiology

The Gastrointestinal Physiology Section **Student Prize** is designed to challenge and reward students and postdoctoral fellows who are conducting their research efforts in gastrointestinal physiology. Two awards—one for work done while enrolled as a student for a doctoral degree and the other for work performed during the first through the third postdoctoral years—are presented at the spring APS/FASEB meeting. Applicants must be first author on abstracts submitted for the spring APS/FASEB meeting, which are accompanied by a letter from the applicant's advisor indicating whether the applicant is a graduate student or postdoctoral fellow. Each award consists of a certificate and $300. The Steering Committee chooses a senior physiologist as the recipient on the **Smith, Kline and French Prize** in Gastrointestinal Physiology. The awardee receives $500 and presents a lecture at the Section's annual meeting.

Renal Physiology

The Renal Physiology Section **Award for Excellence in Renal Research** is to promote and develop excellence in research related to molecular, cellular, and organ mechanisms expressed by the kidneys. Annual awards are presented to a graduate and a postdoctoral student with judging based on abstract submission (25%) and meeting presentation (75%). Papers are evaluated by three judges in renal hemodynamics, epithelial transport, and metabolism. A certificate and prize of $200 are presented to the recipients at the annual renal dinner.

G. Edgar Folk, Jr. Senior Physiologists Fund

The G. Edgar Folk, Jr., Senior Physiologists Fund has been set up through the generosity of family and former graduate students and postdocs to provide modest but helpful assistance to senior physiologists 70 years or older who no longer have grant funds available to them. The awards might be used for such purposes as attending an APS meeting to present a paper, engaging in a series of modest experiments, or completing a manuscript (paying for typists or perhaps for page charges). Recipients will be selected with the assistance of the Senior Physiologists Committee throughout the year. Names of awardees will not be made public. Mary Folk writes that the purpose of the fund is for the Senior Physiologists Committee "to have *fun* assisting colleagues and for Emeritus APS members to keep in closer touch with APS."

Inquiries concerning the G. Edgar Folk, Jr., Senior Physiologists Fund should be made to Martin Frank, Executive Director, APS.

Oklahoma Society of Physiologists

The ninth annual meeting of the Oklahoma Society of Physiologists was held on the campus of Central State University, Edmond, Oklahoma, Friday, June 1, 1990. President **Beverly L. Cox** called the meeting to order and introduced the Dean of College of Mathematics and Science, **G. Kay Owens.** The keynote address, "Animal Rights, Animal Wrongs, Animal Research," was delivered by Martin Frank, APS Executive Director.

Scientific papers and posters were presented by members and associate members from Oklahoma University Health Science Center; Oklahoma State University and its affiliate, the College of Osteopathic Medicine; Tusla University; and Central State University. At the business meeting, the Secretary-Treasurer, **William J. Radke,** summarized the minutes of the last annual meeting and reported on the monetary assets and liabilities.

New elected officers are President: **Barbara Shirley,** Tulsa University; President-Elect: **Roger Thies,** Oklahoma University; and Secretary-Treasurer: **Craig Clifford,** Northeastern State University, who will preside at the 1991 annual meeting at Tulsa University.

1991 APS Specialty Meeting

Interactions of the Endocrine and Cardiovascular Systems in Health and Disease

September 29-October 3 (Preliminary Program)

	SUNDAY SEPTEMBER 29	MONDAY SEPTEMBER 30	TUESDAY OCTOBER 1	WEDNESDAY OCTOBER 2	THURSDAY OCTOBER 3
MORNING		**SYMPOSIUM** HORMONE TRANSPORT IN BLOOD **SYMPOSIUM** MECHANISMS OF ENDOCRINE HYPERTENSION	**SYMPOSIUM** NEUROTRANSMITTER RELEASE IN BRAIN NUCLEI CONTROLLING CARDIOVASCULAR FUNCTION **SYMPOSIUM** VASCULAR SPECIALIZATIONS IN ENDOCRINE ORGANS	**SYMPOSIUM** ANF AND CARDIOVASCULAR REGULATION **SYMPOSIUM** TREATMENT OF CARDIOVASCULAR DISEASE IN DIABETES	**SYMPOSIUM** CALIOTROPIC HORMONES AND CARDIOVASCULAR FUNCTION **SYMPOSIUM** HORMONAL SIGNAL TRANSDUCTION AND REGULATION OF VASCULAR SMOOTH MUSCLE
AFTERNOON		**LECTURE** THYROID HORMONE AND CARDIAC FUNCTION	**SYMPOSIUM** NEUROPEPTIDES IN BLOOD FLOW REGULATION **SYMPOSIUM** REGULATION OF ANGIOGENESIS	**LECTURE** CARDIOVASCULAR AND ENDOCRINE ASPECTS OF AGING	**SYMPOSIUM** NEUROHUMORAL MECHANISMS IN BULBOSPINAL CONTROL OF THE CIRCULATION **SYMPOSIUM** INSULIN RESISTANCE AND HYPERTENSION
EVENING	**OPENING RECEPTION**		**TUTORIAL** SECOND MESSENGER SYSTMES IN VASCULAR SMOOTH MUSCLE **TUTORIAL** METHODS OF HORMONE MEASUREMENT	**SOCIETY DINNER** ISSUES IN ANIMAL EXPERIMENTATION	

1990-1991 Standing Committees and Sections

APS Council

Officers
Shu Chien, President (1992)
Vernon S. Bishop, Past President (1991)
Norman C. Staub, President-Elect (1993)

Councillors
Beverly Bishop (1991)
Allen W. Cowley, Jr. (1993)
Brian R. Duling (1992)
David J. Ramsay (1993)
Stanley G. Schultz (1992)
Peter D. Wagner (1991)

ex officio members
Norman R. Alpert, Finance (1991)
John S. Cook, Publications (1992)
Carl V. Gisolfi, Program (1991)
Leonard S. Jefferson, Sections (1993)
William S. Spielman, Education (1991)

Society Standing Committees

Animal Care and Experimentation

Maintains the APS "Guiding Principles in the Care and Use of Animals" updated; provides consultation regarding animal experimental procedures and care; and keep abreast of legislation and new developments in animal models for student teaching and alternatives for animal usage.

Virginia M. Miller, Chair (1992)
Kenneth M. Baldwin (1993)
Phyllis M. Gootman (1992)
Charles W. Leffler (1993)
Howard S. Lowensohn (1991)
Richard L. Malvin (1991)
Stephen F. Flaim, *ex officio* (1993)
William M. Samuels, *ex officio*

Committee Reports

Animal Care and Experimentation

The Animal Care and Experimentation (ACE) committee experienced one of its most active and, perhaps, most productive years (July 1989-June 1990).

Last summer, a working party composed of members from the ACE and the Governmental Relations Initiative Programs committees developed the Society's response to Parts I, II, and III of the Animal Welfare Act regulations being proposed by the US Department of Agriculture's Animal and Plant Health Inspection Service.

At its October meeting, the committee acted upon several projects that should be beneficial to the APS membership.

Development of a **Sourcebank**, which is a repository of informational materials on animal issues and available to members without charge.

Development of **model pound release bill**. The bill, for use by state and local governments, has incorporated provisions that attempt to assure the public-at-large that such a law would provide adequate protection against pet release by a pound or shelter. Copies of the bill are available to members without charge.

Actions by the ACE at its April meeting:

Development of **model animal facilities bill**. The bill proposes standards for the care and treatment of animals held by pounds, shelters, pet stores, kennels, animal clinics, and hospitals. The model bill is to be offered as an amendment to state or local legislative proposals seeking to restrict or regulate research or educational institutions use of animal models.

After reviewing two cases where Congressional actions **suspended research funding** because of charges of animal abuse by animal activists, ACE approved the following resolution:

> "In the absence of specific details, the committee believes that direct support to the investigators is unwarranted. However, the process leading to the suspension of these projects was clearly flawed in bypassing peer review and having a fair and open hearing for the investigators. Therefore, the ACE Committee unanimously recommends that APS initiate an investigation into the conduct of these two cases by the Government Accounting Office and related agencies."

Proposed a **survey of the membership** to determine what difficulties, if any, have been brought about by local institutional animal care committees concerning the use of animals; whether or not the use was challenged strictly for humane reasons; and, what routes of appeal are available to the investigators.

The ACE also approved the exploration of four areas as possible **new committee objectives:**

Determine whether there is a need for guidelines for the care and use of animals at science fairs.

Push for change in the Animal Welfare Act regulations to permit blanket approval for some standard procedures, thus eliminating the need for institutional animal care and use committee approval for changes in a research protocol.

Gain recognition by the Animal and Plant Health Inspection Service as an expert information source on issues of laboratory animal care and use.

Develop liaisons with other societies' animal care and experimentation committees.

Stephen M. Cain
Chair

Career Opportunities in Physiology

The primary objective of the committee for the past year has been to finalize and send to press a new APS **career opportunities brochure** targeted for high school and undergraduate students. The brochure answers the question "what is a physiologist" and goes on to describe the diversity of careers that are available to individuals with interest and training in physiology, in a fashion likely to capture the imagination. This years efforts have focused upon completing the design and collecting a series of photographs of physiologists at work that are representative of the diversities of people, equipment, research interests, and environments that characterize careers in physiology. The text of the brochure was re-edited to present, among other things a more proactive posture with respect to the necessary use of animals in physiological research. As of this writing, all the materials have been selected and the brochure is in final layout prior to printing. We anticipate that the final brochure will go to press this summer. The committee is looking for a corporate sponsor(s) to assist in the publication costs of the brochure.

At its spring meeting the committee discussed new objectives for 1990. It was decided that the committee would plan and present a workshop on **Career Opportunities in Physiology** for the 1991 APS/FASEB meeting. Paul Murray will coordinate the process of planning the program and will chair the workshop. It is currently anticipated that the workshop will feature four to five speakers representing the spectrum of careers in physiology. In order to bring focus to the workshop, the speakers will be asked to address several specific points during the course of their remarks. The program will be finalized this fall and the invitations to speakers made at that time.

The committee also addressed the outstanding issue of a mechanism to identify and track the diverse career opportunities for physiologists. The Association of Chairmen of Departments of Physiology publish the results of their annual survey each year, which pretty well covers the state of academic career opportunities. Sources for data on non-academic job openings for physiologists are not readily available. This is partly because physiologists working in non-academic environments are seldom labeled as physiologists. The job postings registered with the FASEB Placement Service can provide some insight as to the scope and number of non-academic jobs for which physiologists might apply; however, presently there is no way to match which applicants are finally accepted for which position. In a brief survey of other placement services within other societies, a handle with which to approach this problem was apparent. The issue was tabled in favor of focusing on the workshop.

The committee members remain aware of the need to foster good working relationships with the Education Committee and the Liaison with Industry Committee to enhance entry of women and minorities into careers in physiology. Members of the committee will be working with the Liaison with Industry Committee on areas of mutual interest.

The committee wishes to thank Martin Frank and the APS staff for their assistance with the brochure and other aspects of the committee's work during the past year.

Lewis B. Kinter
Chair

Committee on Committees

At the April APS/FASEB meeting the Committee on Committees (COC) completed its annual agenda and started its work for the upcoming year. This report describes the agenda and procedures by which new committee appointments were made, lists six topics proposed for Council's consideration (note 6 in particular,

Career Opportunities in Physiology

Provides Council with information regarding availability and needs for appropriately trained physiological personnel and recommends measures to assure proper balance in the supply and demand for physiologists.

Lewis B. Kinter, Chair (1991)
Nancy M. Coddington (1991)
Mary A. Frey (1993)
Ronald R. Geller (1993)
M. Harold Laughlin (1992)
Paul A. Murray (1992)
Mary Townsley (1991)

Committee on Committees

Serves as an advisory committee on Council to make recommendations for nominees to the standing committees and reviews charges of the various committees regarding overlapping responsibilities.

Beverly Bishop, Chair (1991)
Edward H. Blaine (1992)
Elsworth R. Buskirk (1992)
Stanley M. Cain (1993)
Brian R. Duling (1992)
Alan R. Hargens (1991)
Leonard R. Johnson (1991)
John T. Stitt (1993)

Ray G. Daggs Award

Annually selects a member of the Society to receive this award in recognition of distinguished service to the Society and to the science of physiology.

David F. Bohr, Chair (1991)
A. Clifford Barger (1993)
Walter C. Randall (1992)

Education

Provides leadership and guidance in the area of physiology education of undergraduate, graduate and professional students; recommends objectives for

graduate programs in physiology; and organizes workshops on the application of new techniques to physiological problems.

William S. Spielman, Chair (1991)
Mukul R. Banerjee (1992)
Francis L. Belloni (1993)
James P. Filkins (1991)
Lois J. Heller (1992)
Barbara A. Horwitz (1993)
Michael G. Levitzky (1991)
Lynne E. Olson (1993)
Allen A. Rovick *ex officio* (1991)

Finance

Reviews the proposed annual budget and fiscal plan for all Society activities and recommends a final budget and implementation plan to Council. Supervises the investment of the Society's financial resources subject to approval of Council.

Norman R. Alpert, Chair (1991)
Franklyn G. Knox (1992)
M. Ian Phillips (1993)
Norman C. Staub, *ex officio* (1991)
John S. Cook, *ex officio* (1992)
Martin Frank, *ex officio*
James C. Liakos, *ex officio*

Government Relations Initiative Program (ad hoc)

Develops short-term and long-term educational, informational, and political strategies for the Society to use to counter the challenge of antivivisectionists and recommends to Council policy statements and positions on legislation and regulatory proposals affecting the use of animals in research and teaching.

Allen J. Cowley, Jr., Chair (1991)
Thomas F. Burke (1991)
Arthur C. Guyton (1991)
Francis J. Haddy (1991)
Howard S. Lowensohn (1991)
Sidney Solomon (1991)
Fred W. Zechman (1991)
Virginia M. Miller, *ex officio* (1992)
Gabor Kaley, *ex officio* (1993)

for it describes the new **nomination form** which is to be used by all for making nominations for any committee appointment), and summarizes new committee appointments

The COC's agenda followed the procedures and timetable that Norman Staub had established during his tenure as chairman. To solicit nominations, a notice was published in the August 1989 issue of *The Physiologist* and letters were sent to members of Council and chairs of Sections, Committees, and Departments. The nominations submitted by these individuals and by members-at-large with brief descriptions of nominees were sorted, alphabetized, and forwarded to members of the Committee on Committees (COC).

Each COC member returned his votes to the chairman for preparation of a summary spreadsheet that was used during a 1½ hour conference call to prepare the recommendations made to Council at its spring meeting.

The following topics were proposed for Council's consideration:

Mechanisms for encouraging dialogue among committees

The June Council meetings were proposed as an ideal opportunity for committee chairs to meet and compare agenda items. In the meantime, Lorraine Tucker will send all committee reports to every committee chairman as a preliminary effort to encourage "cross talk" among committees.

Expanding and defining specific charges for each committee

The committee suggested to Council that individual COC members might be assigned the responsibility of serving as liaison to a particular committee as a mechanism for providing that committee with information and prompt feedback about Council's stand on issues. The COC suggested that perhaps individual Council members might assume such a responsibility. Council did not accept this offer. The COC may review and redefine the various committee charges, but it is Council's responsibility to see that committes carry out their charges.

Mechanisms for enhancing the efficiency and productivity of committees

Should committee members who cannot attend two consecutive committee meetings or conference calls be asked to resign—unless, of course, there are extenuating circumstances? Council would like to be informed of incidents as they arise.

Utilization of those individuals named as alternates for committee assignments

Individuals selected as "alternates" on the COC's voting sheets might be appointed to that committee whenever a vacancy occurs due to resignation, death, or some other eventuality or invited to meet with the committee. Council did not act on this item, but it was in favor of alternates filling interim vacancies.

Change in the appointment dates for committee assignments

Future committee apointments, accepted by Council, will begin on January 1 instead of July 1 when initiated in 1991. The COC will submit its slate at the October Council meeting. The new timetable is: January—committee appointments, April—committee meetings, June—committee chairs report to Council, and October—COC submits a slate of candidates to Council for the following year.

Introduction of a standardized nomination form

The standardized nomination form (page xxx) as accepted by Council will be published in *The Physiologist* with instructions for its use and an explanation for its need.

Beverly Bishop
Chair

Education

High school science teacher summer research program.

Last year the Education Committee recommended and Council approved APS support of a program for high school teachers to work in physiology laboratories for a summer. The program is designed to give high school science teachers an experiential education in modern physiology. Council approved support for 8 teachers at an annual cost of $50,000. Marty Frank was responsible for the announcement of the program in professional journals of high school science teachers, as well as communication with members of the APS. In response, the Education Committee received 30 applications for the program. Copies of each application were distributed to the Education Committee members in March 1990, who evaluated the applications and returned their rankings to be averaged by the APS office for discussion at the spring meeting of the Education Committee. Based on cost sharing by the sponsoring institutions and a grant from the NIDDK to support 2 awardees, the Education Committee recommended that council fund 12 awardees. At the APS Council meeting on April 4, 1990, Council approved that recommendation and approved $50,000 for a second year of support for the program.

Workshop/symposia.

In response to a charge from Council, the Education Committee will sponsor an annual symposium under the title "Contemporary Approaches to Physiological Research," to be offered on Sunday afternoon before the FASEB meeting each spring. In contrast to symposia organized by the various APS sections, it is the intent that these symposia be targeted at physiologists who are non-experts in the area, but who have an interest in learning about new technologies to implement in their individual research programs. Jerry Herlihy of the Education Committee, working with the help of Douglas Eaton, has organized the first symposium, entitled "Single Ion Channels," which was approved by the PAC for presentation at the 1991 FASEB meeting. The committee is working on the second annual symposium entitled "Quantitative Fluorescence Microscopy and Cellular Imaging" to be presented at the 1992 FASEB meeting. Lois Jane Heller agreed to organize and chair the symposium for the 1992 meeting.

Objectives/curriculum/standards for the PhD degree in physiology.

Progress on the development of a set of objectives and curricular guidelines continues, but at a slow pace. Written or telephone communication with representatives of each of the sections has provided the following summary on the status of the reports:

1) Completed reports have been submitted by the following sections: Comparative Physiology, Environmental, Thermal, Exercise Physiology, Neural Control and Autonomic Regulation, Respiratory, and Teaching.

2) The following sections have formed committees of identified individuals to assemble reports: Renal, Cell and General, Gastrointestinal, and Nervous Systems.

Ronald Carlin of the Teaching Section has expressed interest in starting to assemble the objectives into a single list. The reports that have been submitted will be sent to the Education Committee members and **Ronald Carlin** for their input.

In summary, the Education Comittee is especially pleased to see our efforts toward establishing the High School Teacher Summer Research Program and a Continuing Education Workshop/Symposia for the membership reach fruition. Although the establishment of a Curriculum/Objectives for the PhD in the area of physiology is proceeding more slowly than anticipated, we are hopeful that an initial version will be available during the next year.

William Spielman
Chair

Honorary Membership

Recommends to Council candidates for nomination to honorary membership, distinguished scientists who have contributed to the advancement of physiology.

Robert W. Berliner, Chair (1991)
William F. Ganong (1992)
Aubrey E. Taylor (1993)

International Physiology

Handles all matters pertaining to international physiological affairs, with an emphasis on developing countries; maintains a clearinghouse for linkages with developing countries; and recommends to Council, APS members to participate in the US/USSR Bilateral Exchange Program in Physiology.

Donald B. Jennings, Chair (1991)
Clark M. Blatteis (1991)
Phillip D. Gollnick (1993)
Dike N. Kalu (1992)
Daniel R. Richardson (1993)
C. Richard Taylor (1992)
Harvey V. Sparks, Jr., *ex officio* (1991)

Liaison with Industry

Fosters interactions and improved relations between the Society and industry; cooperates with the Career Opportunities in Physiology Committee to encourage high school and college students to choose a career in physiology.

Stephen F. Flaim, Chair (1993)
Mordecai P. Blaustein (1991)
David P. Brooks (1993)
Michael J. Cronin (1993)
John W. Fara (1991)
Lyle H. Hamilton (1991)
Carl V. Gisolfi, *ex officio* (1991)
Lewis B. Kinter, *ex officio* (1991)
Williams S. Spielman, *ex officio* (1991)

Long-Range Planning

Advises and reports annually to Council and interacts with the Section Advisory Committee; prepares systematic, periodic analyses and realistic

assessments of past and present societal performance and accomplishments; conducts periodic review of APS' relationship with other organizations; and devises specific goals and objectives pertinent to the future scientific mission of APS and American physiology.

Francis J. Haddy, Chair (1993)
Gerhard Giebisch (1991)
Joey P. Granger (1991)
John E. Hall (1993)
Ralph Lydic (1992)
Donald J. Marsh (1993)
Jere H. Mitchell (1991)
Jackie D. Wood (1992)

Membership

Considers all matters pertaining to membership; reviews and evaluates applications received from candidates for membership and recommends to Council the nominees for election to regular and corresponding membership.

Eugene M. Renkin, Chair (1992)
Frank P. Conte (1993)
Suzanne M. Fortney (1993)
James G. Dobson, Jr. (1992)
Ronald J. Korthius (1991)
Jay A. Nadel (1993)
Edward G. Schneider (1991)

Perkins Memorial Fellowship

Selects recipients for visiting scientist family support awards and supervises the administration of the Perkins Fund.

Harvey V. Sparks, Jr., Chair (1991)
Robert F. Grover (1992)
Charles V. Paganelli (1991)
Nicholas Sperelakis (1992)
Molly P. Hauck, *ex officio*

Porter Physiology Development

Selects recipients for visiting scientists and professorships; teaching and training fellowships, aimed at improving physiology departments of medical schools with predominantly minority enrollments. Counsels underdeveloped

Finance

The charge to the Finance Committee at its spring meeting is to review and modify the 1990 budget that was presented to Council in October 1989. With the Executive Director, the committee reviewed the Society's performance in 1989, revised the 1990 budget, and submitted it to the Council for revision and adoption. Based on the performance of the Society in 1989, the Finance Committee recommended an overall budget for fiscal year 1989 of $8,448,030.

During 1989, the Society's journal operations ended the year with income in excess of expenses in the amount of $404,887, a portion of which was directed to the Contingency and Reserve Account. The Society's operating fund, derived from direct membership activities ended the year with a deficit of $53,686. The Society's book operations ended the year with expenses in excess of income of $53,686.

The Finance Committee is also responsible for reviewing the performance accounts managed by Shearson Lehman Hutton. As of December 31, 1989, the accounts had the following market value: Operating Reserve Investment Account = $4,176,211; Publications Contingency and Reserve Account = $3,184,016; Caroline tum Suden Account = $290,748; IUPS Account = $195,719; Perkins Memorial Fund = $178,363.

The Publications Contingency and Reserve Fund is a long-term fund established by the publications trustees of which the income can be used by Council for emergencies of the Society including publications. Its utilization is determined each year at the spring meeting, keeping in mind that the primary goal is to return as much as possible to capital investment.

The Operating Reserve Investment Fund was authorized in 1976. These are funds derived primarily from advance subscription fees received for Society publications; hence, they are diverted from the current operating cash account in an attempt to generate capital gains. Our long-term goal is to have sufficient funds in properly managed accounts to underwrite the activities of APS for one to one-and-one-half years.

As a result of the review of the Society's finances and anticipated increases in expenses for 1991, the Council recommended that journal prices be adjusted to move toward a three-tiered system. Member rates will remain fixed at 1990 member rates. Non-member individual rates will remain fixed at 1990 institutional rates. The 1991 institutional rates will be increased by 12% above the 1990 rates. The adjustment of rates will produce a three-tiered schedule in which non-member individuals and members will ultimately pay two-thirds and one-third of the institutional rates, respectively. Page charges will also be increased from $30 to $40 per page, the first increase in over 20 years.

The Finance Committee is also planning to conduct a financial review of the Society and programs to develop a strategic plan for the organization. It is desirable to anticipate the financial needs of APS during the next five years so the Council can develop programs to benefit the members and the discipline of physiology. Initial aspects of the review resulted in Council's decision to fund the High School Science Teachers Summer Research Program in 1990 and 1991. In addition, it contributed to Council's decision to support, both financially and administratively, two specialty meetings a year starting in 1992.

The annual audit of APS by Coopers and Lybrand was received and reviewed by the Finance Committee as part of its responsibility. The audit found the operations of the Society to be "in conformity with generally accepted accounting principles" and the statements "present fairly, in all respects, the financial position of the American Physiological Society."

N. R. Alpert
Chair

APS Balance Sheet
December 31, 1989

Assets		Liabilities	
Cash, including savings accounts	$ 286,429	Accounts payable and accrued expenses including $57,347 in 1989 due FASEB	$ 503,229
Certificates of deposit	4,344,848	Unearned income	
	4,631,277	Subscriptions	3,766,262
US treasury bills, at cost which approximates market value	1,463,906	Dues	220,921
Marketable securities, at cost, market value: 1989, $7,360,227	6,839,146		3,987,183
Accounts receivable, including $20,000 in 1989 due from FASEB	615,099		4,490,412
Accrued interest receivable	97,072	Unexpended grants and programs	1,191,379
Advances to section editors	178,948		5,681,791
Inventories, net of inventory reserve of $300,000 in 1989	930,306	**Fund Balances**	
Prepaid expenses	13,302	Publications general fund	7,292,790
Furniture, fixtures and equipment, net of accumulated depreciation of $94,996 in 1989	103,521	Publications special fund	56,448
	14,872,577	Society general fund	56,359
Net assets restricted and allocated for unexpended grants and programs:		Publications contingency and reserve fund:	
Cash, including savings accounts; 1989, $55,954	345,553	Program Endowment Fund	500,000
Certificate of deposit	95,728	Principal	2,061,543
US treasury bills, at cost which approximates market value	96,333	Income	415,025
Marketable securities, at cost, market value: 1989, $664,830	618,177		10,382,165
Accounts receivable, net	35,588		$ 16,063,956
	1,191,379		
	$ 16,063,956		

physiology departments; assists in the selection of NIDDK minority fellowship awards; and supervises the administration of the Porter Fund.

H. Maurice Goodman, CoChair (1992)
Eleanor L. Ison-Franklin, CoChair (1993)
Douglas C. Eaton, (1993)
Richard M. Effros (1993)
Pamela Gunter-Smith (1993)
David E. Mohrman (1992)
L. Gabriel Navar (1991)
Fleur L. Strand (1993)
James G. Townsel (1991)

Program

Develops the scientific programs for the Society with the assistance of the Program Advisory Committee; assists Council in shaping policy for scientific programs and in the organization of fall specialty meetings.

Carl V. Gisolfi, Chair (1991)
Larry I. Crawshaw (1993)
James M. Downey (1992)
Robert D. Foreman (1991)
George A. Hedge (1992)
Heinz Valtin (1991)
Norman C. Staub, *ex officio* (1991)
Martin Frank, *ex officio*

Program Advisory

Recommends to the Program Committee scientific programs for APS meetings; organizes contributed abstracts into sessions, selects session chairs and introductory speakers.

Cardiovascular — Erik L. Ritman & Harris J. Granger (1991)
Cell and General Physiology — Peter M. Cala (1993)
Comparative Physiology — Jeff Hazel (1991)
Endocrinology and Metabolism — David Wasserman (1992)
Environmental, Thermal and Exercise Physiology — Charles M. Tipton
Gastrointestinal Physiology — Gilbert A. Castro (1993)
Nervous System — Ralph Lydic (1991)
Neural Control and Autonomic Regulation — M. Ian Phillips (1991)

Renal Physiology – Mark A. Knepper (1992) & Bruce M. Koeppen (1993)
Respiratory Physiology – Robert A. Klocke (1991)
Teaching of Physiology – Ronald Carlin (1991)
Water and Electrolyte Homeostasis – Gerald F. DiBona (1992)
Clinical Physiology Subcommittee – Julian F. Biebuyck (1992)
Epithelial Transport Group – Douglas C. Eaton (1991)
History of Physiology Group – Daniel Gilbert (1991)
Hypoxia Group – Hershel Raff (1992)
Liaison with Industry – Stephen F. Flaim (1993)
Education Committee – William S. Spielman (1991)

Public Affairs

Advises Council on all matters pertaining to public affairs that affect physiologists and implements public affairs activities in response to Council guidance.

Gabor Kaley, Chair (1993)
John R. Claybaugh (1992)
Claude Desjardins (1992)
Malcolm S. Gordon (1991)
Henry R. Hirsch (1991)
Virginia H. Huxley (1993)
Virginia M. Miller, *ex officio* (1992)
Stephen F. Flaim, *ex officio* (1993)
William M. Samuels, *ex officio*

Publications

Manages all Society publications including the appointment of editors and editorial boards; supervises the Book Advisory Committees (handbooks, technical, clinical series and history) to ensure timely publication.

John S. Cook, Chair (1992)
Melvin J. Fregly (1991)
Loring B. Rowell (1993)
James A. Schafer (1993)
Charles M. Tipton (1992)
Shu Chien, *ex officio* (1991)
Martin Frank, *ex officio*
Brenda Rauner, *ex officio*

Government Relations Initiative Programs

The Committee on Government Relations Initiative Programs (GRIP) has been involved in a variety of projects since last summer, when a working party composed of GRIP and Animal Care and Experimentation committee members developed the Society's response to Parts I, II, III of the Animal Welfare Act regulations being proposed by the US Department of Agriculture's Animal and Plant Health Inspection Service.

GRIP also developed the Society's response concerning conflict of interest guidelines proposed by the National Institutes of Health and the Alcohol, Drug Abuse, and Mental Health Administration. GRIP position was that the proposed guidelines, which later were withdrawn, were unwarranted and constituted an invasion into a scientist's freedom of action and expression, as well as placing undue burdens on both the researchers and their families.

For the spring APS/FASEB meeting in April, GRIP sponsored three workshop programs: an all-day program on "Media Training for the Scientist: How to Meet the Press"; a noon hour workshop on "New Animal Welfare Regulations. Are They Good or Are They Bad?"; and a late afternoon workshop on "How To Develop Grassroots Organizations in Support of Animal Research."

GRIP approved a statement calling for the federal government to consolidate all regulations, guidelines, and standards concerned with the care, treatment, and use of laboratory animals, thus enabling institutions to put in place a single set of policies independent of the agency that sponsored the research, and thereby minimizing the occurrence of noncompliance. If such a statement is approved by the APS Council, an effort will be made to gain cosponsorship of other societies and associations.

The committee also discussed what parameters APS should have in place when called upon to investigate issues involving laboratory animals. GRIP adopted the following statement:

> "The Animal Care and Experimentation Committee should review the procedures of each case to determine the merits of the case and then recommend to the APS Council as to what action, if any, is to be taken."

Allen W. Cowley, Jr.
Chair

International Physiology

The proceedings of the International Physiology Committee meeting were extremely educational and productive in helping define future directions of the committee and produced important suggestions for maintaining communication between the IPC and similar activities in the American Association for the Advancement of Science (AAAS) and the International Union of Physiological Sciences (IUPS).

US-USSR bilateral exchange program

During 1989, four visits of American scientists to the USSR and three exchange visits from Russian scientists were approved. The reports submitted from these visits indicate they have been quite successful. An important comment has been that future visits include young Soviet scientists, as well as senior scientists.

Bruce Stevens reviewed his exchange visit. From the discussion, it became apparent that communication can be a problem for these exchanges; for example, exchange of research information. It was suggested that it might be possible to establish better communication through intermediation of the Fogarty Institute

and the USSR Academy of Medical Sciences through OMNET, or, the Fax of the IUPS Paris office with a Fax relay to the APS office in Washington.

AAAS Sub-Saharan Africa journal distribution program

Lisbeth Levey, AAAS, provided the IPC with the distribution list for APS journals to institutions in developing countries. She also brought to the committee's attention a request from the Nigerian physiology departments for workshops for Nigerian teachers of physiology to update their knowledge of recent advances in research technology, as well as physiology curricula. The request is for 2 or 3 APS members to conduct a 1- to 2-week workshop for 20 Nigerians in the summer of 1991. The AAAS will attempt to raise travel funds, and the Nigerian institutions will cover in-country expenses. Pending the success in raising funds, the committee will proceed with identifying potential physiologists to participate in the workshops.

IUPS Commission on Teaching in Developing Countries

Accomplishments of the workshop, organized by Keith Cooper and George Somjen and held at the 1989 IUPS Meeting in Kuopio, Finland, included the organization of an African Association of Physiological Sciences and publication by IUPS of a handbook of student laboratory exercises using minimal equipment. A similar workshop is planned for the 1992 IUPS meeting in Scotland.

The IPC believes that a different thrust of the APS could be to emphasize activities focusing on physiological research in developing countries. As expressed by Cooper, "those who learn in an environment where there is research activity are exposed to a 'bubbling pool,' whereas those who learn in a non-research environment are exposed to a 'stagnant pond.' " Thus, the IPC and the Society could complement the activities of the IUPS with this somewhat different, but not necessarily exclusive, emphasis.

Clearinghouse for developing countries

Within the past year, the first twinning of North American scientists to individual scientists in some 16 foreign countries has been accomplished. This initiative of Harvey V. Sparks, Jr. resulted in the submission of names from 49 scientists from 30 countries. There is a need for more North Americans to participate in the program.

John F. Perkins Fellowship Committee

The Perkins Committee provides up to $15,000 of support to families of visiting physiologists. Because of the increasing number of applications, the sizes of the awards are decreasing to allow more scientists to receive some support. More funds are required for this purpose.

Distribution of APS journal

The IPC, which is responsible for recommending the award of up to 50 sets of APS journals to needy institutions, will establish guidelines to ensure fair distribution and optimal access.

1991 spring meeting activities

In consultation with Daniel Richardson, a poster-discussion session on Physiology in Developing Countries will be organized for the 1991 spring meetings. The session will focus on collaborative research programs carried out in developing countries with discussion on experiences of planning and organizing these projects and the problems involved. An important purpose will be to show others how it can be done. The 4:30-6:30 PM session will be followed by a reception for foreign students and scientists. Preliminary announcements will appear in NIPS and *The Physiologist* prior to distribution of the call for papers for the spring meeting.

NIPS Managing Board
John S. Cook (1992)
Howard E. Morgan (1993)

Section Advisory

Recommends to Council ways to strengthen the sections' roles in programs, public affairs, and governance of the Society; serves as a Nominating Committee to nominate Society officers; and nominates members as candidates for membership on Society committees.

Leonard S. Jefferson, Chair (1993)
Cardiovascular – Douglas Griggs (1992)
Cell and General Physiology – Paul J. DeWeer (1992)
Comparative Physiology – Albert F. Bennett (1991)
Endocrinology and Metabolism – Jack L. Kostyo (1993)
Environmental, Thermal and Exercise Physiology – Elsworth R. Buskirk (1991)
Gastrointestinal Physiology – John A. Williams (1991)
Nervous System – Ralph Lydic (1991)
Neural Control & Autonomic Regulation – Mark R. Kaufman (1993)
Renal Physiology – Walter F. Boron (1993)
Respiratory Physiology – Joe R. Rodarte (1993)
Teaching of Physiology – Daniel Richardson (1993)
Water and Electrolyte Homeostasis – Leonard Share (1991)

Senior Physiologists

Maintains liaison with senior and emeritus members and assists in the selection of recipients of the G. Edgar Folk, Jr. Awards.

David G. Greene, Chair (1992)
Horace W. Davenport (1992)
A. Pharo Gagge (1993)
Steven M. Horvath (1992)
John T. Reeves (1993)
Helen M. Tepperman (1993)

Women in Physiology

Deals with all issues pertaining to education, employment, and professional opportunities for women in physiology. Develops programs to provide incentives enabling graduate students to present their research work at APS meetings; coordinates activities with other committees on women in the FASEB organization; and administers the Caroline tum Suden Professional Opportunities Awards.

Hannah V. Carey, Chair (1993)
Helen J. Cooke (1991)
Andrea R. Gwosdow (1992)
John W. Manning (1993)
Jessica Schwartz (1992)
Barbara Vance (1993)
Susan A. Ward (1993)
Martin Frank, *ex officio*

Recommendations

The IPC received a mandate to re-examine the continuing need and role for this committee. As a result of a survey of the Society's past presidents, members of Council and its own members concerning the continuing need and potential role of the committee, the following recommendations have been made:

That the IPC be maintained and that it be encouraged to develop programs to enhance the role of the APS on the international scene, particularly with respect to developing countries.

That the IPC role be seen to be distinctly different from that of the representatives of APS to the US National Committee. The primary role of the IPC will be in establishing communication and facilitating interchange between the APS, other physiological societies and their individual members. In particular, the IPC will promote exchanges between physiologists of the APS and other countries for the purposes of research activity, education, and mutual development. If the IPC undertakes symposia or workshops for its special purposes, it will do so through the normal mechanisms of the Society.

Recognizing that other constituents of the Society are actively involved internationally, and for the purpose of optimizing communication, the IPC recommends that Council establish representation from other committees to the IPC, as deemed appropriate. In particular, it is recommended that the US representative to IUPS, who acts as treasurer to that organization, be made a member of the IPC and that it be arranged for that individual to be invited to liaise with the AAAS on behalf of the APS to ensure communication on international activities. It would also be useful for a representative from the Perkins Committee and from the Teaching Section of APS to be made ex officio members of the committee.

Donald B. Jennings
Chair

Society Representatives to Other Organizations

American Association for Accreditation of Laboratory Animal Care

Stephen M. Cain (1992)
Virginia M. Miller (1992)

American Association for the Advancement of Science

Robert L. DeHaan (1992)
M. Ian Phillips (1992)

American Institute of Biological Sciences

Martin Frank

Council of Academic Societies of the Association of American Colleges

Sarah D. Gray (1992)
George A. Hedge (1993)

Liaison with Industry

Minority Program Survey

The Liaison with Industry Committee (LWIC) made a commitment to initiate a unique program to stimulate the interest of minority youth to enter biomedical science careers, particularly, physiology. This interest of LWIC is a consequence of continuing concern that it continues to become increasingly difficult for departments of physiology to identify and recruit qualified graduate students; and a disproportionate small number of minorities are entering life science careers. The ultimate objective of LWIC is to: *1*) stimulate minority students to enter a professional scientific career and *2*) enlarge the pool of physiologists available to academe, industry and government.

LWIC members expressed a strong preference to develop local community programs that would identify college bound minority youth and offer them mentoring and opportunities to experience a "hands on" research environment. Accordingly, the committee conducted a survey among members of the Pharmaceutical Manufacturers Association (PMA) to become aware of extant minority programs that are currently cosponsored by representatives of the pharmaceutical industry and the local academic community.

The survey was intended to provide only an overview of the types of programs, conducted jointly by academe and industry, which are available to minority students. No attempt was made to quantitate the results, rather, the responses were evaluated qualitatively to determine the spectrum of programs sponsored by representative PMA firms. Sixteen of 52 companies surveyed responded. Survey results confirmed LWIC assumptions that most extant programs are aimed toward students already oriented toward careers in science and significantly less atten-

tion is paid to increasing the pool of minority students by stimulating their interest during their elementary school training.

It is apparent that among respondents there:

1) is an awareness and concern about the unavailability of minority students for training and ultimately employment in biomedical science positions.

2) are numerous extramural programs in support of high school, college and post-graduate students.

3) there are few intramural programs for minority students at all educational levels.

4) There are only a scattering of programs intended to stimulate the interest of minority high school students in biomedical science, generally. There are no extant programs reported that stimulate interest in physiology specifically.

Several examples of unique, successful industry/academic programs that provide enhanced scientific mentoring experiences for minorities were reported (vide infra).

American Chemical Society summer education experience for the disadvantaged (SEED). Project SEED enables disadvantaged high school students to spend 10 weeks conducting scientific research in academic, government and industrial laboratories across the country. Hoffman La Roche is one of many organizations that support this program.

Inroads is a national mentoring program that develops and places talented minority high school and college youth in business and industry. For high school students, it combines intensive instruction in basic academic skills (math, English, science) with career counselling. Sponsoring corporations pledge to develop a career opportunity for each intern. Searle, Schering-Plough, SmithKline, and McNeil are participants.

Prime is a Philadelphia-based pre-college program designed to increase the number of minority students entering careers in engineering, pharmacy, mathematics and science. Merck is a participant.

Kalamazoo area mathematics and science center (KAMSC) is a Kalamazoo-based unique, ongoing partnership between the public and private sectors. It provides accelerated instruction in mathematics and science to qualified students. Conceived and endowed initially by the Upjohn Company, it is administered by the Kalamazoo Public Schools. Although not specifically oriented toward minority students, the current enrollment includes 21 blacks, 14 Orientals and 2 Hispanics (total student population = 283).

Visiting scientist program is a corporate-specific program that encourages junior high school students who may be interested in science to pursue that interest and sign up for the right courses in high school. The program is sponsored by SmithKline.

Mentoring program is a corporate-specific program that provides scientists as role models to local high schools and encourages students to pursue scientific careers. Lilly and Upjohn sponsor mentoring programs.

Molecular biology enrichment for youth is a summer science camp at Iowa State University that is for junior high school students who have a strong record of science achievement. Minorities comprise 30% of the enrollment. Lilly is a participant; the program is funded by NSF.

Mathematics, engineering, science achievement (MESA) is a California-based program that is intended to stimulate the interest of under-represented ethnic groups in math, engineering, and the physical sciences. The program provides mentoring and technical exposure for high school students. Activities include organized study to develop academic skills required to enter college in addition to summer enrichment programs, academic advising, scholarship incentive awards, and carrer exploration. Syntex is one of the supporters of this project.

LWIC members elected to gather further information on the INROADS project to determine whether this could be of specific interest to APS. The committee

Federation of American Societies for Experimental Biology

Board
Vernon S. Bishop (1991)
Shu Chien (1992)
Norman C. Staub (1993)

Education Committee
Francis L. Belloni (1993)

Executive Committee
Vernon S. Bishop (1991)

Executive Officers Advisory Committee
Martin Frank

Finance Committee
Francis J. Haddy (1992)

Life Science Advisory Committee
Walter B. Severs (1991)

Meetings
Carl V. Gisolfi (1991)

Program Committee
Martin Frank

Public Affairs Committee
Richard L. Malvin (1991)

Public Information Committee
Marie M. Cassidy (1991)

Research Conference Advisory Committee
Frank Booth (1993)

3M Life Sciences Award Committee
Jerome A. Dempsey (1993)

National Association for Biomedical Research

Martin Frank

US National Committee for IUPS

Vernon S. Bishop (1991)
Shu Chien (1992)
Norman C. Staub (1993)

US National Committee on Biomechanics

Roger M. Glaser (1993)

Society Sections

How To Become Affiliated

In compliance with the Society's Bylaws, a number of sections have been organized encompassing various physiological specialty interests. These sections advise the Society on matters of interest to the specialty represented by the section, assist the Society in organizing scientific meetings, and nominate individuals to membership on Society committees.

Membership in the sections is open to all members of the Society. The Statement of Organization and Procedures for each section establishes specific requirements for membership. APS members who wish to become affiliated with one or more of the listed sections should contact APS Membership Services, 9650 Rockville Pike, Bethesda, Maryland 20814 (301-530-7171).

Cardiovascular

Allyn L. Mark, Chair (1991)
Douglas Griggs, Section Advisory Committee (1992)
James Covell, Secretary (1991)
Richard J. Traystman, Treasurer 1991
James Covell, Cardiac Mechanics Sub section (1991)
Albert P. Shepherd, Splanchnic Circulation Subsection (1991)
Harris J. Granger, Program Advisory Committee (1991)
Erik L. Ritman, Program Advisory Committee (1992)
James Bassingthwaighte (1991), James M. Downey (1992), & Kim Gallagher (1993), Nominating Committee

Cell and General Physiology

Paul J. DeWeer, Chair and Section Advisory Committee (1992)
Caroline S. Pace, Secretary-Treasurer (1992)
Peter M. Cala, Program Advisory Committee (1993)
Antonio Scarpa, Councillor (1993)
Nancy K. Wills, Councillor (1991)
Marion J. Siegman, MYOBIO (1991)

is convinced that it will be necessary for APS to engage in a sustained, long-term project in order to enlarge the minority pool of candidates for advanced degrees in physiology. It appears that it will be critical to form a consortium of student, parent, secondary school teacher, university, and industry to make an impact on the future number of minorities in physiology.

Special interest group: APS Industrial Physiologists will be contacted to determine level of interest in forming a special interest group for physiologists employed in industry. Eliminated from further consideration were an Industrial Research Section, a social group, and an Applied Physiology Section.

New chairman: Stephen Flaim has replaced Norman B. Marshall as LWIC chairman.

Norman B. Marshall
Chair

Porter Physiology Development

The activities of the Porter Physiology Development Committee during 1989-1990 continued its major emphasis on providing fellowship support to pre- and postdoctoral minority trainees. In addition, requests were approved for travel expense and stipends in support of summer research experiences in the laboratories of physiologists for undergraduate students. Funding was also renewed for enrichening courses in physiology at the Atlanta (GA) consortium and Dillard University in New Orleans (LA). The committee members have also served again as a review panel for applicants to the Travel Fellowships for Minority Physiologists, a program funded by the National Institute of Diabetes and Digestive and Kidney Diseases and awarded to the Society under the directorship of Martin Frank.

Six predoctoral fellowships were continued or initiated in 1989-90 and the status of each of these students is as follows:

J. Michael Gonzalez-Campoy, under the supervision of Franklyn Knox, has completed the requirements for the PhD in the Department of Physiology, the Mayo Graduate School of Medicine, as of February 1990. His studies in renal physiology have resulted in three publications, a chapter (in review) for the second edition of *The Kidney: Physiology and Pathophysiology,* and a fourth manuscript, which is in preparation. He will resume his medical education during the spring of 1990.

Alfredo Rego, has also completed his training leading to the PhD degree at Georgetown University under the guidance of Peter W. Ramwell. His dissertation involved studies on the immunosuppressant, Cyclosporin A, its effects on the vasculature, and the relationship of these effects to hypertension and myointimal hyperplasia following organ transplantation. The work has yielded two full manuscripts, one of which is in press, and the second is under review. Rego has received an NIH Minority Fellowship award to be undertaken for two years.

Cynthia A. Jackson, will be completing work for the PhD under the supervision of Lawrence Rabinowitz, Department of Human Physiology, School of Medicine, University of California/Davis near the end of August 1990. Her studies on renal rapid adaptation to potassium were reported, in part, at the 1989 fall meeting in Rochester, Minnesota. She has plans to extend her training in a postdoctoral program.

Maria Luisa Ruiz is completing the second year of graduate study in the Division of Medical Sciences at the Harvard Medical School. She has enjoyed laboratory rotations under Edward Mroz, Peter Hess, and Morris Birnbaum. She is interested in molecular biological approaches to physiological investigations and expects to begin her dissertation by fall 1990 and take the qualifying examination.

Evangeline Motley, a doctoral candidate in the Department of Physiology and Biophysics at Howard University, is in the terminal months of her training. Bernell Coleman serves as her thesis advisor, and he anticipates she will be eligible for graduation in May 1990. She has been a co-author on two published papers and five abstracts over the course of her studies, the final year of which has been supported by the Porter program. Her investigations into transduction mechanisms of alpha-1 adrenoceptors in the vasculature have produced three manuscripts that have either been submitted or are in preparation.

Pauline Washington entered the graduate studies program at the University of Western Ontario in 1988. After a brief leave of absence, she resumed her studies and the Porter Fellowship in fall 1989 where she is currently pursuing the Master of Science degree. She is very early in her laboratory studies at present, in which she hopes to investigate choline transport into nerve cells leading to acetylcholine synthesis. She has successfully completed her departmental written comprehensive examination.

Postdoctoral fellowships were awarded to the following persons:

Annabell Segarra, who was also predoctoral Porter Fellow, was granted an award to supplement her position in the neuroendocrine laboratory of Bruce McEwen, the Rockefeller University. She is successfully conducting three interrelated lines of experimentation involving neural ontogeny and sexual differentiation in male and female rats. Segarra notes seven manuscripts or papers that are related to her dissertation or current research. She has presented six papers during 1989 and 1990, one of which was given at the International Congress of Physiological Sciences, Helsinki.

W. Richard Campbell, a postdoctoral fellow in the laboratory of R. Clinton Webb, Department of Physiology at the University of Michigan Medical School, has spent the past year developing and learning techniques related to studies on vascular responsiveness to endothelin.

Jean A. King, received a full fellowship during 1989 for postdoctoral training in the laboratory of Eugene Emory, Department of Psychology, Emory University. King was also a predoctoral fellow under the auspices of the Porter Program and has now succeeded in obtaining a postdoctoral fellowship from NIH/NIMH in support of her work with Emory. Notably, King has participated in the Atlanta Consortium course and is exemplary of the potential effect of the Porter program in attracting more minorities into the discipline.

Darlene K. Racker, received support for publication costs for three manuscripts growing out of her dissertation. She is now completing her postdoctoral experience in the laboratory of Brian Hoffman, Department of Pharmacology, College of Physicians and Surgeons of Columbia University.

The Atlanta Consortium was again supported by the Porter Committee in enriching the mammalian physiology course through support of lecturers from nine institutions. This represents a broadening of exposure of the students to a variety of physiologist researchers and is directly resulting from the efforts of John C. S. Fray, a former Porter Fellow who coordinated the course. The effect of Fray's planning is seen in the significant increase in enrollment (over 40) and in the expressed interests by the students in research. On hearing their interests, Fray was prompted to submit a proposal to the Porter Committee to support six students in summer research fellowships. These were very successful, and the committee is pleased at this new thrust. Students were admitted to the laboratories of Pamela Gunter-Smith (a former Porter Fellow), Fleur Strand, Janice Douglas, and Eugene Emory. Fray will again be the course manager and resident physiologist at the consortium during spring 1990.

Winston A. Anderson, a professor of Zoology at Howard University, was again a faculty mentor for two summer students at the Marine Biological Laboratories at Woods Hole, Massachusetts. The students were supported by the Porter Physiology Development program, and their work earned co-authorship for them on papers published in the Journal of Submicroscopic Cytology and Pathology.

Comparative Physiology

Albert F. Bennett, Chair and Section Advisory Committee (1991)
Marvin H. Bernstein, Secretary (1992)
Stan L. Lindstedt, Treasurer (1992)
Jeff Hazel, Program Advisory Committee (1991)
Eldon J. Braun, Councillor (1994)

Endocrinology and Metabolism

Jack L. Kostyo, Chair (1991) and Section Advisory Committee (1993)
H. Maurice Goodman, Secretary-Treasurer (1992)
David Wasserman, Program Advisory Committee (1992)
John A. Resko, Councillor (1992)

Environmental and Exercise Physiology

Elsworth R. Buskirk, Chair and Section Advisory Committee (1991)
Charles Tipton, Secretary-Treasurer and Program Advisory Committee (1993)
Frank Booth, Steering Committee (1993)
Jerome A. Dempsey, Steering Committee (1991)
Kent B. Pandolf, Steering Committee (1991)
Hershel Raff, Hypoxia Group Subsection (1992)

Gastrointestinal Physiology

John A. Williams, Chair and Section Advisory Committee (1991)
Joseph Fondacaro, Secretary-Treasurer (1991)
Gilbet Castro, Program Advisory Committee (1993)
Terry Machen, Councillor (1993)
Phillip Rayford, Councillor (1991)
William A. Weems, Councillor (1992)

Nervous System

Ralph Lydic, Chair and Section Advisory Committee (1991)
Susan M. Barman, Treasurer (1991)
L. Arthur Campfield, Councillor (1991)
Lynn T. Landmesser, Councillor (1991)
Edward Taub, Councillor (1991)

Neural Control and Autonomic Regulation

Marc P. Kaufman, Chair and Section Advisory Committee (1993)
Cheryl M. Heesch, Secretary (1991)
M. Ian Phillips, Program Advisory Committee (1991)

Renal Physiology

Walter F. Boron, Chair and Section Advisory Committee (1993)
P. Darwin Bell, Secretary (1992)
Tomas C. Welbourne, Treasurer (1991)
Mark A. Knepper, Program Advisory Committee (1992)
Bruce M. Koeppen, Program Advisory Committee (1993)

Respiratory Physiology

Joe R. Rodarte, Chair and Section Advisory Committee (1993)
Michael P. Hlastala, Secretary (1991)
D. Eugene Rannels, Treasurer (1993)
Robert A. Klocke, Program Advisory Committee (1991)
Aron B. Fisher, Councillor (1991)

Teaching of Physiology

Daniel Richardson, Chair and Section Advisory Committee (1993)
Kathryn A. Taubert, Secretary (1992)
Nels C. Anderson, Treasurer (1992)
Ronald Carlin, Program Advisory Committee (1991)
Allen A. Rovick, Education Committee Liaison (1991)

The committee will continue to explore possibilities for enriching the science program at the Little Big Horn College, Crow Agency, Montana. Conversations have been on-going with Janine Pease-Windy Boy, President, members of the Agency, and Martin Frank regarding the best approach by which the Society and the Porter Program can be helpful in instituting a summer physiology lecture-demonstration experience in summer 1990 (see p. 77). The Porter Committee views this as an opportunity to extend its influence among a larger group of Native Americans than it has been able to accomplish to date.

We again express our appreciation to the Harvard Apparatus Foundation for its continuing support of the Porter Development Program, and the National Institute of Diabetes and Digestive and Kidney Diseases for the Travel Fellowship Award. We should also like to acknowledge gifts from the Lederle Laboratories of the American Cyanamid Company and individual members of the American Physiological Society.

Eleanor L. Ison-Franklin
H. Maurice Goodman
Co-Chairs

Publications

Journals

In 1989 the *American Journal of Physiology* and *Journal of Applied Physiology,* including the pages in the new *AJP: Lung Cellular and Molecular Physiology* and *Advances in Physiology Education,* published 20% more pages than in 1988; 123 (2%) more manuscripts were submitted.

The *Journal of Neurophysiology* and *Physiological Reviews* remained stable in 1989, although JN appeared thinner because of the change in page size. In the first half of 1990, however, JN published 20% more pages and received 8% more manuscripts. PRV has published three more reviews in its first two issues of 1990 to accommodate a backlog. PRV has also adopted the larger format for 1990, which will result in significant savings in printing costs. Even more significant savings are being effected by editing all manuscripts on disk. The Publications Department is prepared to receive accepted manuscripts for *all* its journals in the many formats listed in the Information for Authors. Submission on disk is encouraged because disk processing is proving more cost-effective than typesetting articles from typed manuscripts.

Dale J. Benos (Department of Physiology and Biophysics, University of Alabama at Birmingham) has been appointed editoir of *AJP: Cell Physiology* and succeeded P. A. Knauf on July 1. After interviews at the spring meeting in Washington, L. Reuss (Department of Physiology and Biophysics, Galveston) was appointed editor of *Physiological Reviews,* to succeed G. H. Giebisch on January 1, 1991. Reuss has chosen M. L. Jennings in the same department to be his associate editor. The European Committee of *Physiological Reviews,* which has been extremely active in obtaining articles, is now headed by R. Green (Manchester), having taken over this spring from B. R. Jewell (Leeds).

Candidates for editorships of *AJP: Endocrinology and Metabolism* and *AJP: Gastrointestinal and Liver Physiology* have been sought by consultation with the relevant sections of the Society, advertising in the journals, and mailings to current editors and associate editors. We expect to make appointments by January 1 with the new editors assuming their positions July 1, 1991.

To help balance the journals' budget for 1991, the Publications Committee recommended the page charges be increased from $30 to $40, the first increase in more than 20 years. The recommendation has been accepted by Council.

There was no increase in subscription rates (except for expedited mailing overseas) in 1990, but increases will certainly be required to support the expanding

number of pages, as well as increased printing and mailing costs. Council has decided to implement a three-tier price structure in the future. In 1991, institutional subscriptions will be increased by 12%, personal subscriptions for nonmembers will be at the 1990 institutional rate, and individual subscriptions for APS members will remain at the current 1990 member rate. Institutional subscription rates will continue to be adjusted while individual subscription rates will be held constant until the nonmember personal and member individual rates become two-thirds and one-third, respectively of the institutional rate.

The number of subscriptions to the consolidated *American Journal of Physiology: Journal of Applied Physiology, Physiological Reviews,* and the *Journal of Neurophysiology* continued to decline in 1989, averaging 3%, which is approximately the same figure as for most other professional journals. This net figure is the result of a fairly high turnover. In round numbers, these major journals suffered a net loss of about 10% of the old subscribers and gained 7-9% in new subscribers. The individual journals of the *American Journal of Physiology* experienced even greater activity but the net loss averaged only 1% for the 8 journals. We are continuing an active promotional campaign to win back old subscribers and attract new ones.

News in Physiological Sciences

With the approval of the International Union of Physiological Sciences, our copublisher of *News in Physiological Sciences,* we have initiated a program offering NIPS in 1991 at half-price ($25 per year) to any member of any society affiliated with IUPS. The participating societies will take responsibility for sending their members a brochure, prepared by our Publications Department, outlining the offer. The office in Bethesda will handle and analyze responses for forwarding to Williams & Wilkins, who handle NIPS subscription fulfillment.

Books

Since our last report in the February issue of *The Physiologist,* on the recommendation of the Handbook Advisory Committee and with the concurrence of Oxford University Press, the Publications Committee and Council approved new Handbooks on the Nervous System, Heart and Circulation, the Endocrine System, and Muscle and Motility. Editors have been proposed for each of the Handbooks and are currently being recruited. The Handbook Advisory Committee, chaired by D. G. Stuart, is at this time considering other series.

A new advisory committee to the Publications Committee, for the History of Physiology, was established at the spring meeting; J. B. West is its first chair.

Committee Appointments

On July 1 this year, J. A. Schafer (Alabama) and L. B. Rowell (University of Washington) joined the Publications Committee, and H. E. Morgan became the new member representing APS on the NIPS Joint Managing Board.

John Cook
Chair

CALL FOR PAPERS

Have you received your *Call for Papers?* Deadline for receipt of abstracts is *December 5, 1990.* **Contact** FASEB Meeting Office, 9650 Rockville Pike, Bethesda, Maryland 20814. Phone: (301) 530-7010.

Water and Electrolyte Homeostatis

Leonard Share, Chair and Section Advisory Committee (1991)
Ronald H. Freeman, Secretary-Treasurer (1993)
Gerald F. DiBona, Program Advisory Committee (1992)

Epithelial Transport Group

Douglas C. Eaton, Chair and Program Advisory Committee (1991)

History of Physiology Group

John B. West, Chair (1991)
Daniel Gilbert, Secretary-Treasurer and Program Advisory Committee (1991)
Ralph H. Kellogg, Steering Committee (1991)

Hypoxia Group

Reed W. Hoyt, Chair (1992)
Hershel Raff, Secretary and Program Advisory Committee (1992)

MYOBIO Group

Marion J. Siegman, Chair (1991)
Jack A. Rall, Program Advisory Committee (1991)
Robert S. Eisenberg, Steering Committee (1991)
Alexandre Fabiato, Steering Committee (1991)
Frederick S. Fay, Steering Committee (1991)
Allan W. Jones, Steering Committee (1991)
Melvyn Lieberman, Steering Committee (1991)
Richard L. Moss, Steering Committee (1991)
R. John Solaro, Steering Committee (1991)

Membership Status

(March 1990)

Regular	4,809
Emeritus	719
Honorary	25
Corresponding	356
Associate	826
Associate Corresponding	13
Student	248
Total	6,996

Newly Elected Members

The following, nominated by Council, were elected to membership in the Society at the Spring Business Meeting, 1990, Washington, DC.

Honorary

A. S. Paintal
V. Patel Inst, London

Jens Christian Skou
Aarhus, Denmark

Ian Glynn
Cambridge Univ, United Kingdom

Tomas Hokfelt
Karolinska Inst, Stockholm

Regular

Uwe Ackermann
Univ of Toronto

S. Lee Adamson
Mount Sinai Hosp, Toronto

Mujahid Anwar
St. Peter's Medical Ctr, New Jersey

Jeffrey Laurence Ardell
Univ of South Alabama

Robert Michael Aronson
Deerfield, Illinois

Kamal Fouad Badr
Vanderbilt Medical Ctr, Tennessee

Kenneth Melvin Baker
Geisinger Clinic, Pennsylvania

John Charles Baldwin
Yale Univ Sch of Medicine

Jaques Belik
Univ of Manitoba

Leonard Brooks Bell
V.A. Medical Ctr, Wisconsin

Theresa J. Berndt
Mayo Clinic

Section Advisory

The chair reported to SAC that as of Council's meeting on March 30, 1990, Statements of Organization and Procedures of the Cardiovascular and Neural Control and Autonomic Regulation Sections had been approved by Council. Of the current total of 12 Sections, 10 are now operating under Council approved SOPs. The Sections still lacking approved SOPs are Endocrinology and Metabolism and Nervous System.

Oral reports of current activities and status were received from all chairs present. Section chairs were asked to address three specific areas in their reports: programming, governance, and central APS support for Section activities. The following is the personal assessment of the SAC chair of the general tone and the level of satisfaction or dissatisfaction expressed in these three general areas.

Programming

All Sections currently report success and general satisfaction with their programming efforts. Articulation of Sections with the Program Committee through the Program Advisory Committee appears now well perceived. The long lead time required and the detailed advance planning sought by PAC has become accepted by Section programmers. Several Sections are training additional Steering Committee members in PAC procedures thereby assuring depth and continuity in program planning. The number and breadth of fall specialty meetings already approved or nearing review is impressive. If Sections are considered to be primarily concerned with enriched scientific communication among members, current programming activities bespeak healthy vigorous Sections.

Governance

Section chairs reviewed their activities this year such as holding Section meetings, communicating through newsletters, carrying out Section elections, and in participating through the Nominating Committee in election of APS officers. A broader spread of Section responses is found in this area. Most Sections have able scientists as committed leaders; these Sections appear to have strongly developing traditions. Other Sections report continued difficulty in achieving forward momentum; three Sections fall in this category: Endocrinology and Metabolism, Neural Control and Autonomic Regulation, and Nervous System.

A new complaint was echoed by several Section chairs. Current SOPs only allow primary members to vote for election of Section leaders. Several Sections would like to open Section participation more broadly and to have secondary members take part in all Section activities. Especially in those Sections like Comparative and Teaching where most of the membership are secondary members, a looser structure is seen as facilitating a more vigorous member participation.

A second area that troubles a broad cross section of Section chairs relates to the interface between SAC and Council. After the joint meeting last year of SAC with Council, a meeting widely perceived as a useful occasion, at which a decision was made to have annual SAC-Council joint meetings, no such meeting is planned thus far this year. This development, broadly looked upon as regressive, needs immediate corrective action. There is widely endorsed feeling among Section chairs that a continuing dialog relating to the composition of Council vis a vis Sections is in order.

Section support by APS

There exists broad approval among Section chairs for the current efforts by the APS central office to facilitate Section activities. The Section chairs all expressed satisfaction with the flexible budgeting procedures that Martin Frank has instigated. A few chairs have experience with American Heart Association staff support for AHA Sections in which a dedicated central staff person takes over a significant portion of the continuing functions like newsletters and elections and assures timely and orderly execution of Section function. These SAC mem-

bers suggest that APS central support of Sections should evolve in that direction. But until that apparatus comes into being, Section chairs are quite positive about the mechanisms that have been introduced and continue to function well.

Recommendations of SAC Chair for Council Action

1) Formal action is needed encouraging SAC to define further the nature of the problem concerning participation of secondary Section members in all Section affairs. A general survey of the problem encompassing possible solutions by a SAC committee is in order.

2) Action by Council to assure a joint meeting of SAC and Council in 1990 is needed. Advantage might well be taken at that time to have SAC briefed by the chairs of the Finance and Publications Committees, principal areas in which Section leaders perceive a need for better communication.

R. B. Reeves
Chair

Senior Physiologists

Physiologists who during the course of their professional life have passed the customary landmarks of name-on-the-door, rug-on-the-floor, responsibilities galore and much much more become at age 70 seniors by official designation. This happens irrespective of whether they are still competing at the forefronts, tapering off, or by unlikelihood superannuated. It is with this group that the APS Committee on Senior Physiologists maintains postal contact, however intermittent, via an approved form letter that may be demeaning to some (but is a practical necessity) or an attractively engraved Beaumont House card. These mailings convey birthday greetings, often some warm personal comments and an invitation to inform Society members about their current activities and interests. Many are touched by being thus remembered and respond. Others simply keep mum, including many whose reflections on life as a physiologist would be of wide interest to readers of *The Physiologist.* The line between undue modesty and unbecoming reticence is indeed fine.

During the past year, 110 APS members turned 70 years of age bringing the total number of physiologists in the senior category of 996. This number has been increasing by leaps and bounds over the past few years due in part perphaps to man's and woman's ever-increasing longevity. The printout of seniors in 1989 lists 79 physiologists who are at least 85 years of age and 27 who are in their 90s. 27 who are in their 90s.

Considering there are only six members on this committee, the task of maintaining any kind of liaison with such a large contingent of members may seem an onerous assignment. Actually correspondence with septugenarians who do not respond to two or more contacts is suspended. Those aged 80 and above usually receive a Beaumont House card annually, but this is at the discretion of committee members. Thus 33 responses obtained in 1988-1989 represent perhaps 15% of our mailings. This is less than desired. We would appreciate greater openness in our relations with the seniors with whom we are fellow members.

This committee also reviews applications submitted to the APS G. Edgar Folk, Jr. Senior Physiologists Fund. During the past year four applications were reviewed, approved, and funded.

It is with deep regret that we note the death of a new member of the committee, Fred S. Grodins.

Roy O. Greep
Chair

Katryna Bogovich
Univ of South Carolina

Charles Ronald Bowden
Janssen Research Fndn, Pennsylvania

Nigel William Bunnett
Univ of Califiornia, San Francisco

Michael A. Castellini
Univ of Alaska

Peter Chung-Yick Chen
Del Mar, California

Daniel Paul Costa
Santa Cruz, California

Bryan F. Cox
Rorer Ctl Research, Pennsylvania

Michael Cutaia
V.A. Medical Ctr, Rhode Island

Daniel Norman Darlington
Univ of Maryland

Pamela Bowes Davis
Rainbow Babies & Children's Hosp, Ohio

M. Joan Dawson
Univ of Illinois

Dennis Anthony Diederich
Univ of Kansas Medical Ctr

Stanley Bruce Digerness
Univ of Alabama at Birmingham

Roderic G. Eckenhoff
Univ of Pennsylvania

Mary Litchfield Ellsworth
St. Louis Univ Sch of Medicine

Anthony Peter Farrell
Simon Fraser Univ, Canada

Michael Francis Flessner
Natl Institutes of Health

John Fox
Tulane Univ Medical Sch

Mitchell Friedman
Univ of North Carolina at Chapel Hill

Lawrence P. Garetto
Indiana Univ Sch of Dentistry

Dorothy Winter Gietzen
Univ of California, Davis

Dennis I. Goldberg
Pfizer Inc., Connecticut

Paul D. Graf
San Francisco, California

Steven Miller Grassl
SUNY Health Science Ctr

Kathy Kaiser Griendling
Emory Univ, Georgia

Michael Douglas Hammond
James A. Haley V.A. Hosp

Steven Curtis Hempleman
Univ of California, San Diego

Robert L. Hester
Univ of Mississippi Medical Ctr

Carmen Hinojosa-Laborde
Medical Col of Wisconsin

Carl E. Hock
UMD-New Jersey Sch of Medicine

Charles Walter Holliday
Lafayette Col

Christopher N. Honda
Univ of Minnesota

Francis A. Hopp
V.A. Medical Ctr, Wisconsin

Peter J. Hornsby
Medical Col of Georgia

John Walter Hubbard
Hoechst-Roussel Pharmaceuticals, Inc.

Florence Niles Hutchison
V.A. Medical Ctr, South Carolina

Mary Brewer Jones
Univ of Texas at San Antonio

Richard Lee Jones
Univ of Alberta

Michael Donald Karlstad
Univ of Tennessee Medical Ctr

Susan R. Kayar
UMDNJ Robert W. Johnson Medical Sch

Joan Alexis Keiser
Ann Arbor, Michigan

Patricia Ann King
Univ of Vermont

Jack G. Kleinman
V.A. Medical Ctr, Wisconsin

Kevin C. Kregel
Univ of Arizona

Keith Kroll
Univ of Washington

Women in Physiology

This past year the Women in Physiology Committee (WPC) has initiated the development of a data base of information on the **employment status of women in physiology.** With the assistance of Linda Buckler of the APS staff and advice from Martin Frank, the WPC developed a short, but fairly comprehensive, questionnaire that was distributed to all women on the APS mailing list.

The questionnaire was designed to determine present rank and position, areas of research training, interest and expertise, funding status, scientific productivity as indicated by number of publications, peer recognition as indicated by membership on journal editorial boards, and study sections. Respondents were also asked to indicate whether or not they were actively or potentially seeking employment and, if so, the type of position sought. Finally, respondents were asked if information provided in the questionnaire could be shared with potential employers. The first mailing of the questionnaire has been completed. From a total of 714 questionnaires sent out, 348 responses were received. Tables I and II summarize major information acquired from the initial questionnaire. The majority of these respondents held PhDs (304). Other degrees included MDs (44), and Masters (21). 12 had no higher degree. A total of 97 professors, 77 associate professors, 63 assistant professors, and 9 postdoctoral fellows responded. 102 respondents did not fit into these standard academic categories. The types of positions that respondents are seeking are indicated in Table II. The relatively small percentage of postdoctoral fellows (3%) responding to the questionnaire is not surprising considering that relatively fewer postdoctoral fellows are APS members. However, the WPC would like to receive information from this group. In the next questionnaire, senior APS members will be encouraged to distribute copies to junior colleagues. Based on information provided in our first questionnaire, it appears this group of women is fairing quite well in terms of research funding and professional service. Also, 135 women indicated they had more than 30 publications in peer-reviewed journals. It will be important to increase our sample size to determine whether those who responded to the initial questionnaire represented the most successful women and whether the responses accurately reflect the status of women in scientific careers in physiology.

The committee is presently working with Linda Buckler to develop a computer-based system in which relevant information can be retrieved rapidly upon request. A letter informing chairs of physiology departments of the availability of information on female physiologists seeking employment was distributed in January 1990. A number of chairs seeking to fill academic positions in their departments have subsequently requested this information. The questionnaire is expected to be distributed annually in order to keep the data base current. Anyone who did not receive a questionnaire last year is encouraged to request one from the APS. It should be emphasized that information provided by respondents will not only

Table I. Summary of Major Information acquired from 1989 WPC Questionnaire on Employment Status of Women in

	Career Status		Type of Position Sought				Source of Grant Support					
							NIH				NSF	Other
Present Position	Active Srch	Would move	M/D/V*	Indust.	U/G**	Pvt. Fnd.	R01	RCDA	First	Fellow		
Professor	0	35	26	3	12	6	50	13	1	3	15	34
Assoc. Professor	5	47	42	11	21	13	33	8	3	14	5	42
Ass't. Professor	5	33	33	14	13	19	13	5	14	7	6	27
Postdoctoral	3	6	7	5	6	5	–	–	–	7	–	2
Other	18	36	27	24	20	18	8	1	3	11	3	33
Totals	32	157	135	57	72	61	104	27	21	43	29	138

*Medical/Dental/Veterinary Schools; **Undergraduate/Graduate; + Non-Medical School

Table II. Areas of Specialization of respondents to 1989 WPC Questionnaire

Present Position	CV*	Cellular	Endocrine	G.I.	Neural	Pulmonary	Renal	Other
Professor	23	13	26	5	26	9	3	28
Assoc. Professor	25	18	16	7	10	9	6	17
Ass't. Professor	25	10	10	4	7	10	9	15
Postdoctoral	2	1	2	0	1	2	1	2
Other	33	8	7	4	12	3	11	43
Totals	108	50	61	20	56	33	30	105

help women to find suitable employment, but will also help the WPC monitor the progress of women in their scientific careers.

The second major activity of the WPC was to distribute six **Caroline tum Suden travel awards** to deserving graduate students and postdoctoral fellows. Awards were based on the quality of competing abstracts submitted. A total of 76 abstracts were received and evaluated by the committee. The general areas of scientific emphasis and number of awards in each area are indicated in Table III. Areas were identified based on primary categories indicated on abstract forms. It should be emphasized that there was considerable overlap in these areas and categories were quite generalized. Individual awardees, abstract titles and institutional affiliations were as follows.

Top six abstracts

Kay K. Azuma, C. B. Hensley, D. S. Putnam, and A. A. McDonough. Differential regulation of Na,K-ATPase $\alpha 1$ and $\alpha 2$ mRNA levels and peptide abundance in hypokalemic rats. USC School of Medicine, Los Angeles.

Najia Jin, C. S. Packer, and R. A. Rhoades. Acute oleic acid injury alters pulmonary arterial smooth muscle contractility but not endothelial function. Indiana University School of Medicine, Department of Physiology.

Li Lu and C. D. Logsdon. CCK, bombesin and carbachol stimulate oncogene expression in rat pancreatic acini. University of Michigan, Department of Physiology.

Lawrence C. Starke and T. J. McManus. Intracellular free magnesium determines the volume set point in duck red cells. Duke University, Department of Cell Biology.

Xaio-Ping Sun, E. A. Mayer, F. Shanahan, P. Anton, and A. Kodner. Regulation of intracellular Ca^{++} in molt-4B lymphoblasts by VIP. UCLA Medical Center, Department of Medicine.

Jun Yu, R. Bose, S. Mink, W. Kepron, and E. J. Cragoe. Mechanism of blocking effect of amiloride on ragweed-induced tracheal smooth muscle contraction in dogs. University of Manitoba, Department of Pharmacology.

Joseph Charles LaManna
Univ Hospitals of Cleveland

Gary Henry Laverty
Univ of Delaware

William Ronald Law
Natl Navy Medical Ctr

Jack Randall Layne
Nazareth Col, New York

Richard Michael Lewis
Univ of Texas Medical Sch

Isabella Yee-Shan Liang
NHLBI, Natl Institutes of Health

Martin J. Lipton
Univ of Chicago

J. Antonio G. Lopez
Univ of Iowa Hospitals

Victor Winslow Macdonald
Letterman Army Inst Research, California

Richard John Martin
Cleveland, Ohio

Leslie Claire McKinney
Natl Navy Medical Ctr

Denis J. Meerdink
Univ of Massachusetts Medical Ctr

Mark Alan Milanick
Univ of Missouri

Kenneth D. Mitchell
Tulane Univ Sch of Medicine

Aaron Jay Moe
Washington Univ Sch of Medicine

Marshall Henry Montrose
Johns Hopkins Univ, Maryland

Adonis Konstantine Moschovakis
Natl Institutes of Health

James M. Mullin
Lankenau Medical Research Ctr, Pa

Paul Alan Murray
Johns Hopkins Univ, Maryland

Physiology

Professional Service						Teaching Experience			
Study Section	Journal Editor	Editorial Board	Natl'. Comm. Member	Officer Sci. Soc.	Ad Hoc Reviewer	M/D/V*	Grad,NM +	Undergrad	Other
46	13	49	30	33	76	52	27	25	7
14	5	24	9	8	54	61	50	40	4
3	2	5	4	1	39	52	27	25	7
—	—	—	—	—	—	4	1	7	1
14	3	16	10	11	43	60	42	58	14
77	23	94	53	53	212	229	147	155	33

Yasushi Nakagawa
Univ of Chicago

Thomas E. Nelson
Univ of Texas Health Science Ctr

Donal Sean O'Leary
Wayne State Univ

E. Christopher Ortin
Colorado State Univ

Mary D. Osbakken
Philadelphia, Pennsylvania

Daniel E. Peavy
Indiana Univ Sch of Medicine

David H. Petzel
Creighton Univ, Nebraska

Grant N. Pierce
St. Boniface Hosp Research Ctr, Canada

David Mark Pollock
Abbott Laboratories, Illinois

Andre Joseph Premen
USUHS, Maryland

Kenneth Gordon Proctor
Univ of Tennessee Health Science Ctr

Edmond W. Quillen
Royal Victoria Hosp, Canada

Fred Daniel Romano
Univ of Massachusetts Medical Sch

Michael Glenn Ross
Harbor-UCLA Medical Ctr

Jonathan Sack
Univ of Alabama at Birmingham

Jeanne L. Seagard
V.A. Medical Ctr, Wisconsin

Paul Edward Segall
Berkeley, California

William Lawrence Sexton
Kirksville Col of Osteopathic Medicine, Missouri

Machiko Shirahata
Johns Hopkins Univ, Maryland

Eric Edward Simon
Jewish Hosp, Missouri

Richard H. Simon
Ann Arbor, Michigan

Edward F. Smith III
SmithKline Beecham Pharmaceuticals, Pennsylvania

Edward E. Soltis
Univ of Kentucky

D. Lowell Stacy
Glaxo Inc., North Carolina

Dimitrije Stamenovic
Boston Univ

Awards were presented to these individuals at the APS business meeting at the spring FASEB meeting by the chair of the WPC.

Another activity of the committee was to organize a **women scientists' mixer** (open to all interested scientists), which was held at the spring FASEB meeting. The organization of this event was through the efforts of Hannah Carey, a WPC member. The social was a well-attended event that allowed women of varied scientific backgrounds and professional ranking to interact in a positive fashion. The WPC is presently considering whether or not to continue to host similar functions at future FASEB meetings. Comments and/or suggestions from interested APS members is welcomed. These should be addressed to **Hannah Carey**, Department of Comparative Biosciences, School of Veterinary Medicine, University of Wisconsin, 2015 Linden Dr. West, Madison, WI 53706 or BITNET: HCAREY@WISCMACC or INTERNET: HCAREY@VMS.MACC.WISC.EDU.

The WPC also met at the spring FASEB meeting to discuss the APS nomination process and future directions of the committee. Beverly Bishop, chair of the Committee on Committees and member of the APS Council, spoke to the WPC on the APS nomination process. Bishop stressed the importance of seeking detailed information regarding functions of various committees before proceeding. Also stressed was the importance of indicating the contributions the nominee is expected to make to the committee and why the nominee is particularly suited for the committee in question. A report from WPC member, Jessica Schwartz, on the Endocrine Women's Society was presented in absentia. This committee has been quite successful in placing women on Endocrine Society ballots and has developed an extensive network that has helped to identify qualified women who can be nominated for different committees. The WPC discussed a variety of possible networking mechanisms and welcomes suggestions from APS members on how best to establish a functioning network within this society. Prior to adjourning, the WPC voted unanimously to bestow an honorary membership to Bishop who has taken a personal interest in the committee and its goals. Bishop's considerable experience in the function of APS committees in general will be a valuable asset to the WPC.

The outgoing chair of the WPC, Catherine Chew, offers thanks to all the members for their efforts on behalf of the committee this past year and wishes the new chair, Hannah Carey, best regards for the coming year.

Catherine Chew
Chair

Table III. Caroline tum Suden (CTS) Travel Awards. General scientific areas represented and numbers of awards made in different areas.

	Total Abstracts	CTS Awards
Cardiovascular	16	
Muscle (Smooth/Skeletal)	11	1
Pulmonary	11	1
Neural Control	10	1
Cellular	9	1
Endocrine	5	
Gastrointestinal	3	1
Ion Transport/Pumps	3	1
Renal	2	
Exercise	2	
Temperature Regulation	2	
Metabolism	1	
Teeth/Bones	1	

Renal Section Awards

The Renal Section selected winners for the Excellence in Renal Research Award at the 1990 APS/FASEB spring meeting, in Washington, DC. The winners in the pre-doctoral category were: **J. Michael Gonzalez-Campoy** for his study of the effect of low dose infusions of prostaglandins PGI_2 and PGE_2 during changes in renal perfusion pressure. He performed this work with Franklyn G. Knox at the Mayo Clinic, Rochester, MN.

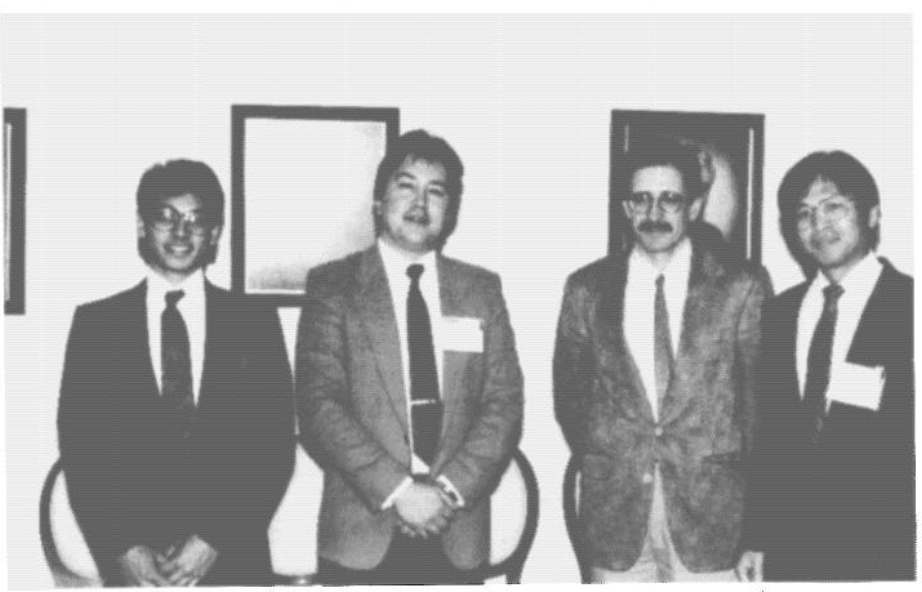
Shashank Desai for a study on the regulation of countercurrent multiplication of ammonium in the rat renal medulla. He was sponsored by Mark. A. Knepper at the Laboratory of Kidney and Electrolyte Metabolism, National Institutes of Health, Bethesda, MD.

The winners in the post-doctoral category were:

Christos Chatziantoniou for his report on the differences in renal vascular response to angiotensin II and thromboxane A_2 between young SHR and WKY rats. He preformed his work in collaboration with William J. Arendshorst at the University of North Carolina at Chapel Hill, Department of Physiology, Chapel Hill, North Carolina.

Ming Jer Tang for his work on Na,K-ATPase beta mRNA that is preferentially stimulated by low K^+ in cultured rat proximal tubules. His work was directed by Alicia McDonough, at the University of Southern California, Department of Physiology, 1333 San Pablo St., Los Angeles, California.

William B. Guggino, Chair
Selection Committee



Renal Section winners of the Excellence in Renal Research Award are (L-R) Sashank Desai, Christos Chatziantonion, William Guggino, and Meng Ter Tang.

Robert A. Star
Univ of Texas Southwestern Medical Ctr

Michael A. Steinmetz
Johns Hopkins Univ, Maryland

Michael Stephen Sturek
Univ of Missouri

David Philip Swain
Marshall Univ, West Virginia

Patricia Carol Szlyk
USARIEM

Denham Salisbury Ward
Univ of California, Los Angeles

James Woodrow Weiss
Beth Israel Hosp, Massachusetts

Laurel Wiegand
Hershey, Pennsylvania

Carole Ann Williams
East Tennessee State Univ

Gary L. Williams
Texas A&M Univ

M. Michael Wolfe
Brigham & Women's Hosp, Massachusetts

Michael R. Yelich
Loyola Univ Medical Ctr

Corresponding

Hubert Josef Bardenheuer
Univ of Munich, West Germany

Franz Xaver Beck
Univ of Munich, West Germany

John Michael Davis
Univ of Munich, West Germany

Gerard J. Huchon
Hosp Ambroise Pare, France

Wolfgang Ernst Jelkmann
Univ of Bonn, West Germany

Tokihisa Kimura
Tohoku Univ Sch of Medicine

Mary A. Lung
Univ of Hong Kong

Masanobu Maeda
UMD-New Jersey Medical Sch

Tetsuji Miura
Sapporo Medical Col, Japan

Heinrich Ulrich Paul Murer
Univ of Zurich, Switzerland

Ivan Sabolic
Massachusetts General Hosp

Joaquin Sanchis
Univ of Barcelona, Spain

Associate Corresponding

Juan Hidalgo
Univ of Barcelona, Spain

Koichi Tsukimoto
Univ of California, San Diego

Xiaojian Yuan
Univ of Maryland

Associate

Bonnie Lucille Blazer-Yost
Philadelphia, Pennsylvania

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New Instructions for Making Committee Nominations

The Society's work gets done by its committees. Therefore, the "best" people should get appointed to committees. To help in this important task, Council solicits recommendations from the Committee on Committees (COC). The COC, in turn, each year asks *all* society members, councillors, and heads of sections, committees, and departments to nominate individuals to fill vacant committee slots. To facilitate their task, COC prepared, with Council's approval, a new Nomination form. The advantages of such a form are that each nomination will be submitted in a standardized format and contain the relevant information on which COC can base its selection when preparing a slate of candidates.

Nominations submitted by letter in 1989 will be retained for consideration in 1990. However, all new nominations (including self-nominations) are to be submitted on the new nomination form included on page 137 in this issue of *The Physiologist*. Use xerox copies for multilple nominations or obtain additional forms from the APS office in Bethesda. The COC will welcome your comments on this innovation.

Beverly Bishop, Chair
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Physiology and FASEB 1990

The 1990 FASEB Meeting in Washington, DC was a joint meeting of four FASEB member societies and three guest societies. Over all, 5673 abstracts of volunteered papers were submitted. Of this total, 2461 papers were submitted by the APS membership and two APS guest societies [Society of Experimental Biology and Medicine (SEBM) and the Biomedical Engineering Society (BMES)]. The physiology component of FASEB 90 represented 43% of the short communications presented by APS members and guests.

Of the APS-sponsored papers, 21% (518) represented women physiologists as first authors, and 4% (105) were by members from outside the Americas. In addition, 6% (136) were received from physiologists employed by industry. Table 1 provides information on the various departmental abstracts received by APS, of which 26% (648) were received from departments of physiology and 4% (98) were received from departments of physiology and biophysics.

Of the 2,461 APS member-sponsored abstracts, 25% (631) were designated by authors for inclusion in topics programmed by other FASEB societies (Table 2).

Table 3 displays the distribution of volunteered papers, programmed by APS and its guest societies, in relation to society sections. Of the 2,267 papers programmed by the Program Advisory Committee, 1,521 (67%) were scheduled as poster presentations, 624 (28%) as slide presentations, and 122 (5%) as poster-discussion presentations. Overall, there were a total of 93 poster sessions, 63 slide sessions, 38 symposia/invited sessions, and 6 poster-discussion sessions. A total of 200 physiology sessions were scheduled during FASEB 90.

Table 4 displays the total number of abstracts programmed by each section. The Cardiovascular Section programmed 631 abstracts (28%), followed by the Respiration Section that programmed 449 abstracts (20%).

TABLE 1. **Author Affiliations of Programmed Volunteered Papers**

Department	No. of Papers	% Total
Physiology	648	26
Physiology & Biophysics	98	4
Medicine	88	3
Pharmacology	106	4
Biology	118	5
Surgery	104	4
Anesthesiology	73	3
Pediatrics	55	2
Biochemistry	17	1
Anatomy	19	1
Pathology	33	1
Other	355	14

TABLE 2. **Volunteered Papers Sponsored by APS, BMES, and SEBM for FASEB 90**

Society	Total Received	FASEB Program Designation				Total
		APS	ASPET	AAP	AIN	
APS	2,318 (94%)	1,687 (69%)	197 (8%)	328 (13%)	106 (4%)	2,318
BMES	52	43	1	6	2	52
SEBM	91	32	19	28	12	91
Total	2,461	1,762	217	362	120	2,461

TABLE 3. **APS Scientific Sessions at FASEB 90**

Section	Slide	Poster	Poster Discuss	Symposia/ Invited	Total
Cardiovascular	18	18		5	41
Cell & general	0	6	1	3	10
Comparative	2	4		2	8
Endocrinol & metabolism	7	9		2	18
Environmental & exercise	4	6		1	11
Epithelial	2	2		0	4
Gastrointestinal	1	8		0	9
History	0	1		1	2
Muscle	3	4		2	9
Nervous system	0	3		0	3
Neural control and autonomic regulation	3	6		1	10
Renal	5	2	1	2	10
Respiration	9	12	3	1	25
Teaching	0	1	1	3	5
Water & electrolyte	7	4		0	11
BMES	2	4		3	9
SEBM	0	0		1	1
Clinical	0	0		3	3
Theme	0	3		5	8
Public Affairs/GRIP	0	0		3	3
Total	63	93	6	38	200

*Includes five debates and one tutorial

TABLE 4. **Programming of Volunteered Papers by Sections/Groups**

Section	Number of Abstracts
Cardiovascular	631
Cell & general	81
Comparative	35
Endocrinol & metabolism	195
Environmental & exercise	139
Epithelial	82
Gastrointestinal	70
History	2
Muscle	105
Nervous system	68
Neural control and autonomic regulation	101
Renal	105
Respiration	449
Teaching	18
Water & electrolyte	101
BMES	47
Theme	37
Non-conforming	1
Total	2,267

News from Senior Physiologists

Letters to Horace Davenport

"I have not yet begun to decrease my level of activities," writes **Leonard Malis.** "I am still professor and chairman of the department of neurological surgery at the Mount Sinai School of Medicine with an extremely active operative and teaching schedule. My laboratory physiological work is now limited pretty much to discussion with and supervision of my younger colleagues. I still do a great deal of instrument design and construction.

"All and all, I would say that I am about 95 percent neurosurgeon and only still, perhaps, five percent a physiologist. This rather considerable change in my career occurred about 1967 with the advent of clinical microneurosurgery when I began to devote virtually all of my energies to that field and rather stopped wet lab research."

At a luncheon celebrating his 80th birthday **Charlie Code** said in part:

It all started 61 years ago when I took a year out between 1st and 2nd year medicine to complete a bachelor's degree in science and to do medical research. Upon its completion, I decided research would be my goal. I soon learned that "only truth will serve." No substitute would do. My father had earlier told me: "Charlie, always tell the truth but sometimes keep your damn mouth shut." The latter has been hard for me. But I learned you must choose the right time to tell it as it is; tell it when the telling will do most good, for at the wrong time it can *collapse* the very structure you are trying to assemble.

But in science truth is not enough, you have to be able to put it all together in a concept. Sir Henry Dale with whom I worked did this best. At a histamine symposium in his honor in London in 1954, Feldberg who had worked with him longer than I, turned and said: "Charlie, who is the most flexible in his ideas amongst the 100 or so of us here?" I replied: "Sir Henry Dale." If the data presented were nearer the truth than those upon which he had based his ideas he switched—bang!—just like that. He was devoid of affectionate affiliations with his own ideas.

While discussing such qualities later with Frank C. Mann at Mayo he said: "You know, Charlie, a man or woman of genius is one who sees relations or correlations between things which the rest of us identify as unrelated." I thought that over and discussed it with him again: "Dr. Mann, I would like to add to your definition." He asked: "What is that?" I said: "A person of genius is one who sees relationships or correlations between facts which the rest of us see as unrelated, and is right!" Mann accepted that.

By then I had seen some of my friends in science drift off into that nether-netherland of unsupported ideas. With some, one idea was pursued from graduate student days to their death, when the idea from the beginning was wrong! Others like butterflies or hummingbirds had gone from blossom to blossom, going from one beautiful idea to another without ever developing a theme that would tie it all together. As Sir Henry once said, "By all means, if you see a good short cut, take it, but don't spend your life on it."

Letters to Roy O. Greep

Sir John Eccles, writing from Switzerland, says he continues to maintain an intensely active life, "working 80 hours a week. I have no grant support since retiring in 1975, but I work as scientists did before they were deluded by grants. I have help from Frankfort MPI for illustrations and from McGeer's Institute at the University of British Columbia.

My last book, *Evolution of the Brain: Creation of the Self* is of course Darwinist for the first section. The second part is concerned with the human self, continuing from the Popper, Eccles book, *The Self and Its Brain.* This present book is coming out simultaneously in six languages. In November, I will be the first Ideas Lecturer at Oxford Farmington Institute.

This year my wife and I have been around the world for conferences and lectures, and in October-November we go to Tokyo and London. Meanwhile, in September we go to the FWA meeting in Stockholm and then to Oslo. So you can see that I do rather well for 87 years.

I think I have told you enough to illustrate how the human brain can perform when it is kept active at a high level."

James Irving, living in Manchester, MA, reports that he has had a hip operation that went wrong and is now unable to walk unaccompanied. "However, that (the operation) has not prevented me from keeping up with the literature in my field, calcification, which has made most interesting advances." He adds that he regrets he is unable to attend conferences, especially the Gordon Conferences (of which he once was chairman).

"I am retired with my wife in the countryside, where I have a small study equipped with a microscope," writes **Louis Poirier** from Montpellier, Quebec, Canada. "In addition to some scientific activities, I contribute to the improvement of the quality of life in this area. To this end, I take part in local organizations involved in ecology, urbanism, etc. I also go for more personal activities such as bird feeding and bird watching and gardening vegetables and flowers, having a good size kitchen-garden and a greenhouse. In harmony with my environmental interests, weed killers and insecticides are prohibited.

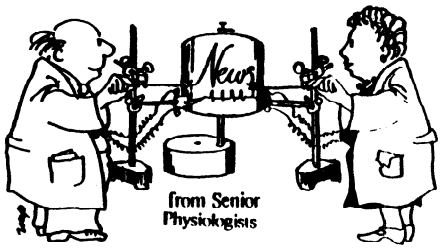
Carl Bunde writes from Cincinnati that he has been doing "a lot of visiting and some tourists trips" since his wife, Wilma, died in September 1988. "I was gone 93 days in 1989 and 31 days already in 1990.

"I still work some. Almost fulltime in 1988, almost halftime in 1989, and about one-fifth time this year. My main job is chairman of the institutional review board at Hill Top Research." He added that he plans to attend the FASEB spring meeting in Atlanta.

"Since the publication of the fifth edition of my text book I have not been engaged in physiological activities," writes **Ewald Selkurt.** "For several years following my retirement, I spent considerable time in the department participating in seminars and graduate teaching. But I have done no research since my retirement in 1980.

"In 1989 I moved to Summer Trace Retirement Center in Carmel, IN, and my opportunities for scientific interplay were abrogated. I have become involved in painting (watercolor, acrylic, oil), and until recently, I enjoyed singing with several choruses."

Paul MacLean reports from his laboratory at Poolesville, MD, where he is a senior research scientist for the National Institute of Mental Health, "Old age, it would seem, is in large part a sociogenic disease. When one reaches a particular age, one is expected to 'roll over'! If the Chinese are still respected in old age, is it possibly because they still have a brain to communicate with? Could this in any way reflect their diet of 15 percent fat, as opposed to the Western diet of 40 percent fat?



"Does the amount of fat in the diet affect the rate of accumulation of lipofuscin, which accumulates in cells somewhat like garbage bags in New York City when collectors go on strike. Having no way of disposing of lipofuscin, nerve cells fill up somewhat like seed pods and pop open.

"On a just-sufficient diet, animals can be maintained in good health for as long as 30 percent beyond life expectancy. Since people are just beginning to know something about the time nature knocks them off, perhaps the next step in human evolution will come when it is learned how to extend a healthful existence. The hopeful thing about healthful aging is people become progressively nicer mammals."

Elinor Bodian writes from Baltimore than **Dave Bodian** has Parkinson's disease and is in a nursing home where he is recovering from a broken collar bone. He has no vision in one eye and the vision is distorted in the other eye. He is unable to write, but enjoys hearing from friends.

Unique Materials

Work published in the Society's journals must necessarily be independently verifiable. Authors describing results derived from the use of antibodies, recombinant plasmids and cloned DNAs, mutant cell lines or viruses, and other similarly unique materials are expected to make such materials available to qualified investigators on request. Authors should also submit published nucleic acid/amino acid sequences to a widely accessible data bank. Sequence data submission forms for the National Biomedical Research Foundation—Protein Identification Resource Database (NBRF-PIR) are available from the APS Publications Office, 9650 Rockville Pike, Bethesda, MD 20814 (301-530-7186).

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Nathan W. Shock, Baltimore, MD (11-12-89)

Willie W. Smith, Bethesda, MD (09-08-89)*

Dorothy R. Stewart, Carrboro, NC (03-05-90)*

** indicates date notified of death.*

24,000 Animal Activists March on Washington in Demonstration Against All Uses of Animals

Animal activists conducted a march on Washington this summer, which played to mixed reviews.

The activists claimed that "the animal rights movement has arrived; and, we're not going away." But those who look at the numbers think, perhaps, the movement has plateaued.

The much ballyhooed march attracted 24,000 demonstrators, a figure significantly less than that of other highly publicized marches on Washington in recent times.

Moreover, the number of demonstrators may even be of greater significance in gauging the popularity of the animal rights movement when considering the march—designed to be a public outcry against all animal uses, such as food, clothing, product-safety testing, utilitarian purposes, and entertainment, as well as biomedical research—attracted less than two percent of the combined reported memberships of the six sponsoring organizations. The sponsors were the American Antivivisection Society, American Society for the Prevention of Cruelty to Animals, Doris Day Animal League, Humane Society of the United States, New England Antivivisection Society, and People for the Ethical Treatment of Animals. They report a combined membership of 1,500,000 people.

The day-long demonstration that followed the march attracted generally negative coverage from the press, noting the demonstrators booed Superman (actor Christopher Reeves) when he encouraged moderation by saying some animals are needed in research, such as the research seeking a cure for AIDS. When Reeves was booed a second time for saying not everyone who uses animals in research is a villian, he left the podium.

A George Washington University undergraduate student sought a police escort from the scene when he was threatened by the demonstrators for attempting to hand out literature about responsible animal research.

Apparently there was some confusion about what the demonstration was about because one woman thought it was a place to find a good home for her cat. She carried the gray cat in a box with the sign, "I need a good home." She was surrounded by about 20 people, and 1 demonstrator played tug-of-war with the woman with the cat as the rope.

When a police officer intervened and let the woman leave with the cat, some of the group insulted him, saying he didn't care about animals. The woman said, "I don't understand it. I just wanted to find a home for the cat. I don't want him to go to the shelter."

Several women were quoted about the makeup of the demonstration, one citing her disappointment that demonstrators were almost exclusively white. Another, who said she had been an animal activist for 20 years, criticized the organizers for allowing only three women to speak. "Women have done all of the work in the animal rights movement," she said. "The spirit of animal rights is a female perspective. But men really run it, and they have for years."

W. M. Samuels

Model Animal Facilities Bill Developed by APS

A model bill that proposes standards for the care and treatment of animals held by pounds, shelters, pet stores, kennels, animal clinics, and hospitals has been developed by the APS Committee on Animal Care and Experimentation.

The model animal facilities bill is designed to be offered as an amendment to state and local legislative proposals seeking to restrict or regulate research or educational institutions use of animal models. In most locations there are no standards relating to the care and treatment of animals not housed in research and educational institutions.

The model animal facilities bill is the second model bill developed by the committee. In January, the committee announced the development of a model pound release bill.

Copies of the bill are available to APS members by writing to the APS national office, 9650 Rockville Pike, Bethesda, MD 20814.

Animal Groups Oppose the Use of Monkeys to Assist Disabled

Several animal groups are opposing a program that trains capuchin monkeys to assist handicapped individuals, charging the monkeys are transformed into slaves for the disabled.

Helping Hands: Simian Aides for the Disabled, Inc., of Boston, trains the monkeys to retrieve food and other objects, dispose of trash, turn appliances on and off, and perform other tasks for quadriplegics. It has placed 16 monkeys with quadriplegics. Commands are given to the monkeys by electrical impulses from a radio device.

The monkeys are housed in a colony at no charge in a zoological park at Walt Disney World.

HHS Secretary Sullivan Now Animal Activists Target for His "Terrorist" Remarks

The Secretary of the US Department of Health and Human Services has become the target for animal activists since calling them terrorists.

Louis W. Sullivan, speaking at a press conference three days prior to the animal activists' march on Washington, said, "I am saddened and a bit angry myself that we have to put up with major disruptions to science by so-called animal rights activists who are, in fact, nothing more than animal rights terrorists.

"In the past they (activists) have tried to foster a siege mentality among our scientists and at our nation's laboratories. They have tried to put us on the defensive through intimidation and even violence. They will not succeed, because they are on the wrong side of morality."

Sullivan's remarks were made at a press conference sponsored by the incurably ill for Animal Research, Association of American Medical Colleges, and the Foundation for Biomedical Research.

Activists at the Washington march blasted Sullivan for his position and one congressman who supports animal rights called for the secretary to make a public apology for his remarks. Since the march, activists have condemned Sullivan in letters to the editors of major newspapers.

Sullivan noted an irony of the activists' Washington "March for the Animals" in that some of those marching would likely not be able to walk without animal research. "A cure for polio would never have been found, and thousands who can today walk, run, and jump would have been crippled."

As to the animal rights philosophy, Sullivan said, "The questions involved in this debate—questions about personhood, rights, responsibilities, and ethics—are open questions. One of the greatest threats of the animal activists lies in their bold claim to have correctly and definitely decided these questions and that each of us must be forced to agree."

•

" 'Animal rights people may be going too far' with ever more aggressive protests of hunting. 'One of the protestors down in Beeville (TX) when we went quail hunting last year had bright orange hair. She drove up in a big Mercedes with leather seat.' "

—President George Bush
in conversation while fishing
as reported in The Washington
Post in April 1990.

AAMC Survey Indicates Millions Being Spent to Counter Activists

Medical schools are now spending more than $6.3 million annually in countering animal activists.

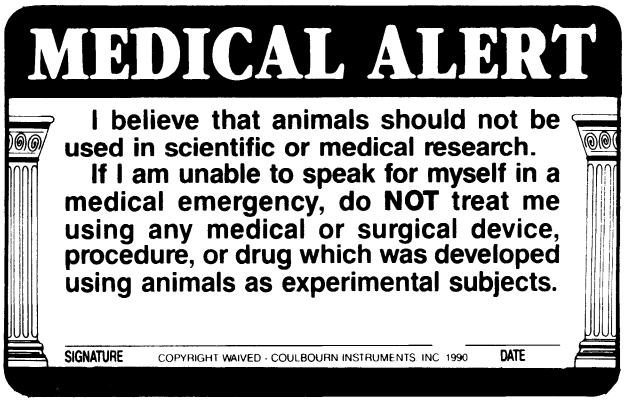
In a survey by the Association of American Medical Colleges of all 126 US medical schools, it was found that the schools also have added 30,000 working hours in addition to the new annual costs for legal expenses, security personnel, media efforts, and the purchase of specially bred animals to replace previously available pound animals.

In the past five years, the schools spent more than $11 million and 33,000 hours as a result of incidents initiated by animal activists and another $11 million and 140,000 hours in upgrading and maintaining animal facilities to new standards.

The survey also reported more than 3,800 incidents of harassment to faculty and staff in the last five years.

The costs cited do not include independent laboratories, research foundations, federal and state facilities, pharmaceutical companies, and universities and colleges without medical schools, as well as the other branches of universities and colleges with medical schools.

For Animal Rights Activists



Carry a few of these cards to pass out to activists on the picket line, in the classroom, or at cocktail parties, where you would rather not be more vocal. They are free for the asking. Contact: Colbourn Instruments, Inc., P O Box 2551, Lehigh Valley, PA 18001. Tel: (215) 395-3771, FAX: (215) 391-1333

Future Meetings

1990	
APS Fall Meeting	October 6-10, Orlando, FL
1991	
FASEB Annual Meeting	April 21-25, Atlanta, GA
APS Fall Meeting	September 29-October 3, San Antonio, TX
1992	
FASEB Annual Meeting	April 5-10, Anaheim, CA
1993	
FASEB Annual Meeting	March 28-April 1, New Orleans, LA
1994	
FASEB Annual Meeting	April 24-29, Anaheim, CA
1995	
FASEB Annual Meeting	April 9-14, Atlanta, GA

Scientific Program Committee XXXII IUPS Congress

The Scientific Program Committee for the XXXII IUPS Congress will be meeting in October or November 1990. The US National Committee representatives (Alfred P. Fishman, Andrew P. Somlyo, and Richard W. Tsien) will be offering suggestions for scientific program. If you have specific recommendations regarding topics or speakers, please send them to Donna Gerardi, Staff Officer, USNC/IUPS, National Research Council, Commission on Life Sciences, 2101 Constitution Avenue, NW, Washington, DC 20418 (202-334-2236).

First Announcement

XXXII International Congress of Physiological Sciences

August 1-6, 1993

Glasgow, Scotland

It is a great pleasure for the British National Committee for Physiology to invite physiologists to the XXXII International Congress of Physiological Sciences to be held in the Glasgow, Scotland, July 25-30, 1993.

This Congress will follow the conventional format and continue the rejuvenation of the spirit of congress by addressing the question of fractionation of scientific endeavour by including a part of most, if not all, satellite symposia within a central meeting. The main congress will include some special review lectures to highlight the development of ideas and new achievements in various areas of physiology, as well as symposia to encourage the free dissemination of ideas, techniques and progress in all areas of physiology. Oral and poster communications will be accepted to either complement symposia or as free communications. A vital part of the congress will be the organization of workshops to help teachers in third world countries to provide a more effective education for their students.

A number of satellite symposia are expected to take place in the British Isles and discussions will take place to try to bring the basic review and controversial components of these satellites into the framework of the congress as a whole.

National societies of physiology and corresponding organizations, as well as IUPS Commissions, will be kept informed of progress and developments and will be asked to contribute ideas both for congress symposia and associated satellites.

A Trade Exhibition will be held in concert with the Congress to provide information on developments of technology for research and teaching. A full and varied program will be offered to delegates and accompanying guests. This will include a welcoming reception, the conference dinner and a concluding reception.

Accompanying guests will be invited to join delegates for all social functions. In addition, a program of tours and excursions will be offered.

Accommodations have been reserved in many residence halls of Glasgow's two Universities and a number of hotels in several price categories. All accommodations are within easy travelling distance of the Conference Centre, but a shuttle bus service will be provided from the residence halls and hotels.

The official carrier for the Congress will be British Airways. All inquiries should be addressed to your local British Airways Office.

The Scottish Exhibition and Conference Centre occupies a superb landscaped site of 64 acres (26 hectares) beside the River Clyde. The surrounding skyline bears witness to the river's changing history, with cranes and modern offices silhouetted against the western sky. The landscaped river walkways and indeed the design of the Centre itself is a tribute to the changes that have taken place since the great liners made their maiden voyages from Clydeside.

Address all correspondence to: **IUPS 1993, CEP Consultants Ltd, 26-28 Albany Street, EDINBURGH EH1 3QH, U.K.**

Preliminary Registration

I plan to participate in the 1993 IUPS Congress July 25-30 in Glasgow.

Name: _____ Title _____

Position: _____

Address: _____

_____

Town: _____ Postcode: _____

Country: _____

My main area of interest is: _____

_____

Role of Integrative Physiology in Research Programs of Modern Physiology Departments

L. Gabriel Navar, PhD
Department of Physiology,
Tulane University School of Medicine
New Orleans, Louisiana

As one reads about the exciting developments in many areas of molecular biology and recombinant DNA biochemistry, it is quite difficult not to be completely overwhelmed. There are so many examples of major breakthroughs.

A recent report in the *Journal of NIH Research* that discusses the recent identification of the "Cystic Fibrosis gene" is an excellent example that may be particularly interesting to many physiologists. Investigations have identified a defect in the protein that may be responsible for regulating the transmembrane chloride conductance—either directly as a channel or by regulating the incorporation of the proteins that serve as channels. But, in spite of this great enthusiasm and without taking away any of the credit that is due to investigators in this area, it is important and worthwhile to remember a few facts.

First of all, this work was not done in a vacuum. To a very large extent, its completion was dependent on the revolution we have had over the last one or two decades in fields of computer science, bioengineering, and biotechnology. In a generic sense, all the folks that helped to make those laboratories productive and efficient should share in the credit, and many, in fact, most, were not molecular biologists, or biologists of any kind.

Second, who pointed to the need for looking at a possible gene defect related to proteins involved in chloride channels? What about the many clinicians and physiologists who carried out the detailed studies that led the way? One must wonder where we would be if all of these would have also opted to be gene jockeys instead of transporters.

Third, these findings are particularly important in the context of how they help understand the big problem, and to do this will require the cooperation of many different scientists with many different spheres of expertise. For what is clearer than ever in this day and age of modern biotechnology is that the day of the "all american" scientist or physician who can be an expert in all things is gone forever.

Importantly, this same article points out explicitly that other researchers, primarily physiologists, will now have to conduct "the experiments that will reveal exactly how and why the flawed protein fails to perform its function properly." In effect, the subtitle states "Physiologists see a wealth of research questions ahead," but, and I ask this very seriously, Will physiologists, properly trained to conduct these sort of studies, be available?? With the present pseudo elitist's academic environment that exists at so many institutions *it is not likely.* Indeed, this attitude is best exemplified by the comments of a chairman of a department of medicine at a well known academic institution. During the course of a faculty meeting, he strongly emphasized to all the division chiefs that the "tide was very strong and, everyone should channel *all* their scientific interests, training programs, and young, good talent to molecular biology." At which point my good friend of many years was prompted to say "do you mean to say that all those other problems *that were so important* only a few months or years ago have now all been solved?" At this, the chairman was compelled to respond "no, no, that certainly isn't true, but unless you are working on a very important problem, you should really think seriously about switching over to molecular biology."

Well, that wasn't quite good enough for the questioner. He had to retort "then, does that mean that if you choose to work in molecular biology, then you are free to work on any old problem, important or not?" We can only surmise that the conversation deteriorated. Nevertheless, the point was made. Do we choose our areas of endeavors based on current fads or on our notions of relevant and important issues?

This brings to mind another recent article that appeared in *Science,* it had nothing to do with biology, but it did emphasize how Raymond Jeonloz was making tremendous advances in understanding the physics of earth's internal core. What struck me was the short legend under his picture that read "Thomas Ahrens of CalTech was quoted as saying about Jeonloz, "He's very bright, but a lot of people are bright! His most important attribute is that he picks *very important problems and works on them very hard.*"

Isn't this, after all, the real bottom line. Let's all work toward that most important motto for all our students. "Within your domain of interest and expertise, choose the most *important* problem and work on it very, very hard! And, if you use the very best tools and approaches that have been made available by modern science, then that is all *that anyone can ask or expect.* And, it's *o.k.* if everyone isn't a molecular biologist."

Most importantly, we should not attempt to mold all

Presented at The Association of Chairman of Departments of Physiology, San Juan, Puerto Rico, December 1989.

faculty, all physician scientists, and all fellows and graduate students into one pattern. It can't be done, and we will fail miserably. On the one hand we will discourage and disenchant many bright, young minds that simply have inclinations in other directions. Furthermore, we will be irresponsible by failing to provide the balanced scientific pool capable of solving problems at many different levels. Perhaps the most unfortunate consequence is that many bright, talented individuals, especially the physician scientists, will simply bow out of scientific endeavors all together. For if the greatest freedom of the scientist, the freedom to work on problems that are most intriguing, is taken away, then one might as well go make more money doing something else. That is already happening now. And, if it continues, *we* are to blame for the absence of well-trained physiologists in the 21st century.

These considerations raise important issues we as individuals, as chairpersons, and as an organization must address.

Are we physiology chairpersons prepared to be "trend setters" or will we be content to be "camp followers?" Are we going to follow the developing patterns and simply establish made-over departments of biochemistry, or do we want to subserve a unique role in the overall research sector? The unique role of being able to emphasize functional biology that, by any other name, is still *physiology.*

Are we preparing to forge ahead into those biotechnological areas that others do not want or that may not be in vogue right now?

So, in essence, it is *not* a controversy of integrative versus reductionist's approaches to science. After all, we as scientists, in general, and physiologists in particular, are supposed to be characterized by independent thinking, healthy skepticism, and logical approaches to the scientific issues.

These attributes flourish in an environment characterized by modern scientific approaches using the best technology available.

Thus, it seems we should refocus our attention on the fundamental issues such as understanding the importance of the problem and determing the most direct manner of addressing the issues. The malady that is attempting to infect our scientific community is that there are those that *insist* you *must* address the issue—any issue—with the techniques and approaches *they* deem most important and innovative. Yet surely we all know that all questions and issues are not created equal or alike. What works for one problem may not work for the other. So, ultimately, we must be creative enough to recognize, just as always, it takes many different investigators working on multiple facets of the problem, at several levels, to provide a better understanding of the questions and, indeed, to provide the answers.

Let us all work together to establish an ambience of cooperation and mutual respect for one another's strengths and viewpoints, so we can enter this next decade with a more mature attitude about the role of the physiological sciences in this universe of scientific inquiry.

People and Places notices come almost exclusively from information provided by members and interested institutions. To ensure timely publication, announcements must be received at least *three months* (by the 5th of the month) before the desired publication date. Send all information to Martin Frank, Editor, *The Physiologist,* APS, 9650 Rockville Pike, Bethesda, MD 20814.

Stephen Flaim has been named Division Director, Department of Pharmacology and Toxicology, Alliance Pharmaceutical Corporation. An active member of the Society since 1975, Flaim is chair of the APS Liaison with Industry Committee.

Formerly at the New England Medical Center in Boston, **Howard L. Corwin** has moved to the Dartmouth Hitchcock Center, School of Nephrology, Hanover, NH.

Formerly at the University of Pennsylvania, **James C. Reynolds** has taken a position as Chief, Division of Gastroenterology and Hepatology at the Presbyterian University Hospital in Pittsburgh, PA.

Recent elections of the Institute of Medicine included APS members **Joseph C. Greenfield, Jr.** Duke University Medical Center, Durham, as an active member and **Thomas P. Almy** Dartmouth Medical School, Etna, as a senior member.

So They Say . . .

"Those opposed to research with animals have seldom stood on principle and instructed their physicians not to use the results of biomedical research on animals when it would benefit their loved ones or themselves. Nor have they been willing to foreswear for themselves the advantages of any future advances from animal research."

-John Kaplan, Standford University Law Professor, in an article in *Science.*

Bristol-Myers Squibb Award

Erwin Neher Director, Membrane Biophysics Department, Max-Planck Institut, received the Bristol-Myers Squibb Award for Distinguished Achievement in Neuroscience Research at the third annual presentation in New York, NY, June 28, 1990. Neher, elected to honorary membership in the Society in 1988, is a renowned physiologist. He has received world acclaim for his development of the "patch clamp" technique that has had enormous impact on the understanding of bioelectric phenomena of individual cells and represents one of those giant methodologic steps forward in the history of physioloy.

New FASEB Director

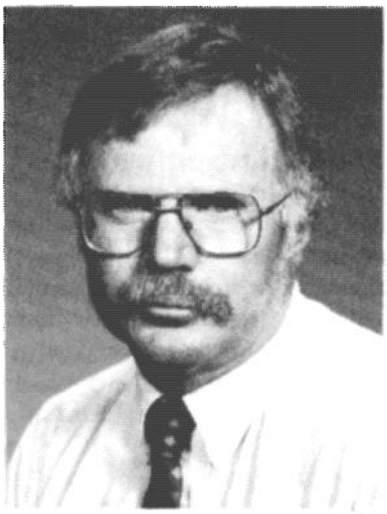
Michael J. Jackson has accepted the position of Executive Director of the Federation of American Societies for Experimental Biology (FASEB). He will officially begin his new duties on September 1, 1990.

Jackson is currently Dean for Research and professor of physiology at The George Washington University Medical Center, Washington, DC. He has over 20 years experience as an investigator working on the development of a model for gastrointestinal absorption and secretion of pharmaceutical agents.

Jackson said he envisions a new facilitating role for FASEB to develop consensus among biomedical science societies on national policies that relate to research. "We need to develop channels of access that allow scientists' views to become influential at the national policy level," he said.

Jackson received his BSc at the University of London and PhD at the University of Sheffield in 1966. He has been at The George Washington University since 1967. Jackson has served the University in a variety of capacities during his 23 years there as a professor of physiology and has served as an administrator of research since 1985. He has been active on university committees dealing with education, research, radiation safety, human experimentation, animal care, and conflict of interest. An APS member since 1970, Jackson has served as associate editor of the *American Journal of Physiology: Gastrointestinal and Liver Physiology* and as chairman of the Program Committee.

Outstanding Basic Science Faculty Award



James A. McMillan, Professor of Physiology at Montana State University, received the Outstanding Basic Science Faculty Award from the 1990 graduating class of the University of Washington School of Medicine. McMillan teaches physiology to 20 Montanans who are enrolled in the University of Washington School of Medicine and take their first year of medical school at Montana State University as part of the WAMI Regional Medical Education Program. He is the first basic science faculty member not based in Seattle to be selected for the award. Gregory Grose, a Montana member of the graduating class, presented the award to McMillan during the medical school's hooding ceremony. "Dr. McMillan taught us a lot in our first year, including a little physiology," said Grose. "But the most important thing he taught us was to be comfortable in saying 'I don't know'."

Academy Taps APS Member

Min Chueh Chang, who has been a member of the American Physiological Society since 1946, is one of 60 newly elected members of the National Academy of Sciences. Chang is principal scientist emeritus at the Worcester Foundation for Experimental Biology at Shrewsburg, MA. He spent his career in reproductive biology and has received many awards for his work. At present millions of women around the world are using various types of pills originated by Chang and his colleagues for contraception.

Election to the Academy's membership is considered to be one of the highest honors accorded to a United States scientist. Currently, there are 1,601 Academy members.

Bozler Honored

In celebration of **Emil Bozler's** 89th birthday, the Department of Physiology, Ohio State University, opened a display of memorabilia from his career. The display is in the lobby of the Graves Hall Basic Science Building. Bozler is recognized for his contributions to muscle physiology. Congratulating Bozler on the exhibit is Jackie D. Wood, Chairman, Department of Physiology.

Know Your Sustaining Associates

Abbott Laboratories

Abbott Laboratories is a worldwide company devoted to the discovery, development, manufacture and sale of a broad and diversified line of human health care products and services. Abbott innovations include *Nembutal* and *Pentothal* anesthetics, the *Erythrocin* line of antibiotics, the *Ausria* and *Auszyme* diagnostic kits for hepatitis B, the first US licensed AIDs virus antibody detection kit, *Similac* and *Isomil* infant formula, the *TDx* drug detection system, and the *ADD-Vantage* drug delivery system. Abbott's commitment to the future is evident in its $500 million dollars spent on research and development in 1989 and an annual compound growth rate in R&D spending over the past 5 years of 20%.

American Medical Association

The American Medical Association promotes the art and science of medicine and the betterment of public health. The AMA accomplishes this mission by advancing standards of medical education, promoting support for biomedical research, representing the medical profession, providing information about medical matters, and upholding professional conduct and performance.

Beckman Instruments, Inc.

Beckman Instruments, Inc. is a major international manufacturer of bioanalytical and diagnostic instruments and related products for science and medicine. The company was founded in 1935 by Arnold Beckman, who was inducted into the National Inventors Hall of Fame on Feb. 8, 1987. In 1982, the Orange County–based company merged with Smith Kline in Philadelphia to form SmithKline Beckman Corporation, a leading health care and life sciences company recognized worldwide.

Beckman's business is to combine chemistry and engineering. Its product lines include hundreds of instruments and related products. For the life sciences, Beckman manufactures centrifuges, liquid scintillation counters, spectrophotometers, and pH meters. For health care, the company produces clinical systems, diagnostic kits, reagents, and quality controls. A complete sales and service force supports Beckman customers.

Berlex Laboratories

Berlex Laboratories is a US subsidiary of the multinational pharmaceutical and chemical firm Schering AG West Germany (not connected with Schering-Plough Corp. or Schering Corp. of New Jersey). It conducts research and markets prescription drug products primarily for cardiovascular, diagnostic imaging, metabolic, endocrine, and central nervous system uses.

Coulbourn Instruments, Inc.

Coulbourn Instruments, Inc. manufactures electronic instruments for in vivo life science applications. Products include the LabLinc Modular Instrument System for physiological signal conditioning, experiment control, and data acquisition, featuring over 100 modules, including computer interface ports, signal conditioning and processing, and counting and timing modules for chart and computer-based polygraphs.

The company also produces transducers, biotelemetry, signal processors, stimulators, and auditory and animal behavior test equipment.

Major markets include pharmaceutical, chemical, and biotechnological firms, universities, research hospitals, and government laboratories.

Dagan Corporation

Dagan Corporation manufacturers electronic instruments used in electrophysiology. Dagan offers a full line of analog and digital products, including preamplifiers for use in intracellular and extracellular recording, single and two electrode voltage/current clamps, patch clamps/whole-cell clamps, signal averagers, programmable multichannel stimulators, and iontophoresis generators.

Glaxo, Inc.

Glaxo Inc., a leading research-based pharmaceutical company headquartered in Research Triangle Park, North Carolina, manufactures and markets prescription medicines including treatment for respiratory ailments, ulcers, hypertension, infectious diseases, and diseases of the skin. Glaxo is a wholly owned subsidiary of Glaxo Holdings p.l.c.

Grass Foundation

The Grass Foundation underwrites the annual Walter B. Cannon Lectureship given at the spring meeting of the American Physiological Society. The naming of this lectureship serves two functions: to commemorate the enormous contribution of Cannon to the growth of knowledge of physiology and to pay a tribute to Cannon on behalf of many of the founding trustees of the Grass Foundation who were members of his research group at Harvard Medical School early in their careers.

This lectureship is in accordance with the Grass Foundation's charter mandate to support research and education in neurophysiology. Other programs include funding for other annual and visiting lectureships, summer fellowship support for young students, and occasional relevant course support.

Harvard Apparatus

Harvard Apparatus, since its inception in 1904 at the Harvard Medical School, continues to design, develop, and supply the unique apparatus that has shaped the development of teaching and research in physiology and allied science, including syringe peristaltic and respiration pumps, recording systems, and research accessories.

ICI Pharmaceuticals Group

The ICI Pharmaceuticals Group R&D facility is based in Wilmington, Delaware. It consists of about 700 staff, of whom about 170 are in drug discovery. Within ICI, the US drug discovery function has sole responsibility for discovering new drugs in the pulmonary and CNS therapeutic areas. Current CNS targets are nondyskinetic antipsychotic drugs, disease-modifying drugs for Alzheimer's disease, and drugs for cerebral stroke and ischemia. The entire gamut of experimental approaches is available, including biochemical, neurochemical, electrophysiological, histochemical, and behavioral. Subserving the discovery efforts are a Molecular Pharmacology Unit at Wilmington and a Biotechnology Department in ICI-UK.

Jandel Scientific

Jandel Scientific designs and sells IBM-compatible software for scientific research. Products include Sigma-Plot for publication-quality scientific graphs (with automatic error bars, regression lines, and many other scientific graphing options); Sigma-Scan for *x-y* digitizing, morphometric measurement, and analysis; and PC3D for generating three-dimensional reconstructions of objects from serial sections. JAVA, the latest product, is a video analysis system capable of image processing, densitometry, automatic object counting and edge tracking, and morphometric measurement. JAVA works with a video digitizing board and input from a video camera, VCR, or other video source.

Janssen Pharmaceutica

Janssen Pharmaceutica was founded in Belgium in 1953 by Paul Janssen. It is now an international company built on the foundation of research and a bedrock of innovation. The company remains under the direction of Janssen and has an unparalleled record in the successful development and marketing of new pharmaceutical products. According to the Japan Drug Research studies, Janssen was responsible for more significant new drug discoveries during the period 1970–1983 than any pharmaceutical company in the world.

The company currently has approximately 6,000 employees worldwide. It is a world leader in medication used in the treatment of allergies, mental disorders, digestive and intestinal problems, cardiovascular conditions, and worm and fungal infections. Janssen's compounds have also enabled major advances in anesthesia and immunology. In addition, Janssen has also discovered many chemical compounds to identify and characterize receptors in the brain and the periphery that have played a prominent role in advancing our knowledge about neurotransmitters.

R. W. Johnson Pharmaceutical Research Institute

Ortho Pharmaceutical Corporation is now a part of the R. W. Johnson Pharmaceutical Research Institute. It is headquartered in Raritan, New Jersey and is a research-based pharmaceutical company engaged in the development and manufacture of a wide range of health care products marketed in more than 60 countries around the world. A wholly owned subsidiary of Johnson & Johnson, R. W. Johnson Pharmaceutical's operating divisions produce a variety of contraceptives, gynecological therapeutics, prescription and proprietary skin-care products, self-care diagnostics, and a growing number of biotechnology-derived pharmaceuticals, including immunomodulators and monoclonal antibodies.

With more than 4,000 trademark registrations worldwide, R. W. Johnson Pharmaceutical continues its commitment to an intensive research and development program to ensure tomorrow's innovative health care products in the areas of conception control, immunobiology, and the treatment of gastrointestinal disorders and cardiovascular disease.

Narco Bio-Systems

Narco Bio-Systems designs, manufactures, and distributes the Physiograph® physiological recording systems for use in clinical, research, and teaching applications. A selection of multichannel chart recorders are available with a complete line of modular input preamplifiers, signal conditioners, transducers, and accessories. This allows maximum flexibility for designing systems for recording physiological functions.

Pennwalt Pharmaceuticals

Pennwalt Pharmaceuticals Division, based in Rochester, New York since 1886, has continually been committed to provide physicians and consumers with excellent products. In addition to providing fine pharmaceuticals, Pennwalt has become a leader in the technology of controlled drug delivery systems. Existing or imminent consumer and prescription products include agents to treat cardiovascular and neurological diseases, pain, infections, immunological disturbances, eating disorders, colds, and allergy. Current research promises to yield additional products targeted for these therapeutic areas.

Moving?

If you change your address or telephone number, please notify the APS office (301-530-7171) as soon as possible.

Pharmacia

Pharmacia is the world's leading supplier of separation and purification products for the biotechnology industry, as well as a research-intensive international manufacturer of products for use in areas of medicine, including gastroenterology, rheumatology, oncology, ophthalmology, blood volume replacement, allergy, and dermatology.

Procter & Gamble Company

Procter & Gamble is a multinational, technically based consumer products corporation with operations in 28 states and 36 foreign countries. It has four technical centers, and its world headquarters are in Cincinnati, Ohio. Technical centers are also located in Egham and Newcastle, England; Brussels, Belgium; Schwalbach, Germany; and Osaka, Japan.

The worldwide PhD population of Procter & Gamble is ~850, divided equally between chemists and life scientists, and total employees number 75,000.

Sales in the paper, soap and detergent, health care, personal care, pharmaceutical, beverage, and food categories make Procter & Gamble one of the largest US corporations. *Fortune* magazine has named Procter & Gamble as one of the most admired corporations in the United States.

Schering-Plough

Born out of a 1971 consolidation of two companies—Plough, Inc. and the Schering Corporation—Schering-Plough is dedicated to the discovery, development, and marketing of novel therapeutic entities. The company focused its research in the fields of anti-inflammatory, antiallergic, cardiovascular, and anti-infective disorders. The company has also attained a leading position in immunology and recombinant DNA technology.

SmithKline Beecham

A division of Smith Kline Beckman Corporation, Smith Kline & French Laboratories is a technology-intensive, worldwide health care company. Smith Kline & French is a leading supplier of pharmaceuticals to treat infectious, gastrointestinal, cardiovascular, and arthritic diseases and a leader in research, development, and marketing of innovative medicines.

Squibb Corporation

Squibb Corporation, a leading worldwide developer, manufacturer, and marketer of pharmaceutical and allied health care products, is organized into the Squibb Operating Group and the Science and Technology Group.

The Squibb Operating Group is responsible for the manufacturing, marketing, and distribution of products and services. Squibb's pharmaceutical products are marketed by Squibb International and Squibb United States. The Medical Products segment consists of ConvaTec and the companies of Edward Weck Incorporated.

The Squibb Science and Technology Group is composed of The Squibb Institute for Medical Research, Worldwide Regulatory Affairs and Licensing. Celebrating its 50th anniversary in 1988, The Squibb Institute is among the nation's first industry-sponsored research centers. In recent years, it has focused on four main areas: *1*) cardiovascular disease, *2*) infectious disease, *3*) diagnostics, and *4*) inflammatory disease. It has recently broadened into molecular biology, the neurosciences, and metabolic disorders.

The Upjohn Company

The Upjohn Company, a multinational corporation headquartered in Kalamazoo, Michigan, has celebrated its centennial year as a maker of fine pharmaceuticals. It is one of the 15 largest research-based pharmaceutical manufacturers in the world. It has research, production, and warehousing facilities in more than 45 countries and its products are sold in more than 150 countries.

Upjohn has long been committed to the research, development, manufacture, and marketing of pharmaceuticals. Human health care is the heart of Upjohn's endeavors.

Waverly Press

Approaching its 100th anniversary, Waverly Press is a full-service publication printer specializing in journals and other periodicals.

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Waverly practices team concept management. Both client and staff are part of the team. Through this management concept, each publication receives close personal attention.

Striving for excellence in the graphic arts industry is a tradition at Waverly Press—one that continues. Waverly believes in quality products and service through quality people.

Otto Folin: America's First Clinical Biochemist
Samuel Meites
Washington, DC: American Association for Clinical Chemistry, Inc., 1989, 428 pp., illus., $55.00.

For more than 30 years at the beginning of this century the analytical methods devised by Otto Folin (1867-1937) were used by every chemically minded physiologist and clinician, and they were the mainstay of the clinical chemistry laboratories that were becoming essential in every accredited hospital. Folin himself helped to set the standards of accuracy in those laboratories. Now Samuel Meites, the archivist of the American Association for Clinical Chemistry, has produced this hagiography to commemorate Folin's achievements. The first 361 pages are a biography crammed with trivialities including the problem of selecting the wallpaper for Folins' Cambridge home. Sixty pages would have been adequate to record Folin's growth and accomplishments as a scientist. The last pages contain abstracts of Folin's major papers. The book has no indexes.

As a boy Folin escaped to the United States from the proverty-stricken Smaland district of Sweden, and he was taken in by relatives in Minnesota. Thanks to his native ability, hard work, and loans from relatives and friends he was able to take advantage of the educational opportunities offered by the New World. After graduating from the University of Minnesota, Folin earned a PhD at the University of Chicago on the chemistry of urethane. During the obligatory trip to Europe where Folin worked briefly with Olof Hammarsten, Ernst Salkowski, and Albrecht Kossel his interests turned to the chemistry of natural products. There was as desperate period when Folin returned to the United States and hunted for a job, but after working at first for a commercial laboratory and then as half the chemistry faculty at the University of West Virginia, Folin was offered the directorship of a new chemistry laboratory at the McLean Hospital for mental diseases in Waverly, Massachusetts. Seeing that neuropathology had contributed little to the understanding of the cause of mental disease, the hospital's progressive director hired Folin and gave him a chemical laboratory to see what he could do about the problem. Folin soon discarded a search for a specific neurotoxin, and he undertook to modify analytical methods or to invent new ones that would enable him to describe completely, accurately, and quantitatively the composition of urine of normal persons. Once that was done, Folin intended to look for differences in the urine of the hospital's patients that might explain their condition.

Charles Eliot, the president of Harvard, made Folin head of the department of biochemistry in Harvard Medical School in 1907. There Folin endlessly improved and applied his analytical methods. His department was always a small one, and he forced L. J. Henderson out of it, because Henderson's interests were too broad to fit into Folin's plans. Folin had few graduate students, but among them were James B. Sumner and Edward A. Doisy who in their subsequent distinguished careers did not follow the path laid out by Folin. The most notable accomplishment in the department during Folin's tenure was the identification of phosphocreatin by Cyrus Fiske and Yellapragada Subbarow. That depended, at least, on Folin's method for determination of phosphate.

Meites overestimates the quality and significance of Folin's own application of his methods. When Folin was able to make a reasonably complete analysis of 24-hour urine collections, he saw that the daily output of creatinine is nearly constant for a particular individual but that the output of urea is proportional to the quantity of protein in the diet. On the basis of these facts Folin erected his theory of the distinction between endogenous and exogenous metabolism. Endogenous metabolism is the turn-over in tissues that results from the daily "wear and tear" of living, and its endproduct is the creatinine in the urine. Exogenous metabolism is that occurring in the breakdown of dietary protein, and it results in the urinary excretion of urea whose daily quantity reflects the daily input of protein. This idea was expounded in textbooks until it was decisively destroyed by the isotope experiments of Rudolf Schoenheimer and David Rittenberg. Those who took Folin's idea seriously were led astray. For example, H. B. Lewis's belief that there is endogenous metabolism of cystine distinct from cystine's exogenous metabolism prevented him for more than 20 years from making the imaginative leap that would have explained the large excretion of cystine in cystinurea. Fortunately, the majority of American physiological chemists including Henderson, Sumner, and Doisy paid no attention to the theory when they formulated their own research programs, and the mainstream of American physiological chemistry flowed past Folin.

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The Regulation of Sodium and Chloride Balance.
Donald W. Seldin and Gerhard Giebisch (editors)
New York: Raven Press, 1990, 532 pp., $69.00.

This book is one of a series by these editors on electrolyte and water metabolism. The chapters in this volume are organized around the normal and abnormal processes involved in sodium and chloride balance. They integrate the enormous information regarding membrane transport processes and renal mechanisms for sodium and chloride transport and excretion with the latest theories and data regarding regulation of NaCl balance and edema formation.

The book is directed at students rather than scientists. As is the case for the other books in this series, statements in the text are not referenced directly, but general references and pertinent reviews are listed at the end of each chapter for those interested in pursuing questions in greater detail. Thus, as an introductory text for students and physicians, the book meets the objectives of providing a thorough review of the fundamental processes of salt and fluid balance. In addition, chapters devoted to abnormal NaCl balance also include some guidelines on the approach to the therapy of the disorders.

The text has many strong features. One of the most obvious is the strong chapters on the distribution of sodium and chloride across cell membranes and the mechanisms of segmental sodium and chloride reabsorption. These reviews provide a solid, yet not overwhelming, introduction to renal mechanisms of NaCl excretion. Another strong aspect are the chapters on the regulation of electrolyte balance by the renin angiotensin system in normal and in abnormal conditions. Perhaps not all investigators will agree with the conclusions of the authors of these chapters. However, as an introduction of the subject for students, the complexities of the system are sufficiently simplified so that one comes away with a strong framework from which to view additional experimental data and from which one can begin to interpret pathological conditions in humans.

Perhaps the strongest area of the book involves the discussion of the edematous states. There is a generous introduction to the

pathophysiology of edema, and the specific edematous states of congestive heart failure, nephrotic syndrome, and hepatic cirrhosis. The pathophysiology of idiopathic edema (such as it is known) is articulated in a balanced and clear exposition. Additional chapters on NaCl loosing states and hyponatremia and sodium handling in the hypertensive states round out the presentation of abnormal NaCl balance in disease.

There are few weaknesses in the text, and there are surprisingly few redundancies. The reader should be aware of a few areas where the exposition is incomplete or incorrect. The discussion of abnormalities in ion transport and red cells in the hypertensive state reflects our understanding of this system many years ago, but does not reflect its current status. In the chapter on pharmacokinetics of diuretics, the mechanism of action of metalazone is presented as being that exclusively of the proximal tubule. As described in the chapter on primary and secondary effects of diuretics, metalazone exerts its primary action in the distal convoluted tubule and has only minor effects in the proximal tubule.

The editors have done an excellent job in coordinating the compilation of information on NaCl balance in a fashion that is readily understandable. The text is appropriate for students and physicians who wish to have an introduction and reference to integrated systems of NaCl handling and the pathophysiology of the edematous states.

John B. Stokes III
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Structure and Function of the Kidney
R. K. H. Kinne, E. Kinne-Saffran and K. W. Beyenbach (editors)
Basel: Karger, 1989, 200 pp., illus., tables, index, $110

Kidneys appear to have originally evolved as a device for excreting metabolic waste and, perhaps, excess water and, during vertebrate evolution, obtained more important roles in the control of fluid and mineral balance to maintain volume and osmotic homeostasis. It is an extremely difficult task to comprehend the diverse morphology and function of kidneys of a variety of species from phylogenetically different vertebrate classes that live in different environments. This book accomplishes this ambitious task rather well by focusing on structure and function of primitive kidneys on tissue, cellular, and some molecular bases to define basic functional and organizational patterns that may underlie all kidneys in various taxonomical stages of vertebrates. This book, a first volume on cellular and molecular aspects of comparative physiology series, consists of four chapters: *1*) Morphology of glomerular and aglomerular kidnesy (H. Hentschel and M. Elger); *2*) The archinephron of *Myxine glutinosa L.* (L. M. Fels, G., Rause-Degener, and H. Stolte); *3*) Comparative physiology of the proximal tubule (K. W. Beyenbach and M. D. Baustian); and *4*) The nephron in reptiles (W. H. Dantzler).

The first chapter involves comparative anatomy and cellular structures of renal vascular systems, corpuscles, and tubules and structure-function relationships in glomerular and aglomerular kidneys. Although the tetrapod kidneys are also briefly discussed, major emphasis is on the renal organs of cartilaginous and bony fishes. The author states that in contrast to the diversity of nephron types and terminologies among various vertebrates' kidneys, the fine structure and cytological organization of glomerular and tubular cells are quite similar. This indicates that diversity of nephron functions may in large part be due to structural organization and interrelationships among nephron components that may have developed in response to unique needs of animals rather than to differences in basic function of filtering vascular capillary cells or transporting epithelial cells.

The second chapter focuses on morphology, function, and regulation of renal glomeruli and archinephric ducts of hagfish (*Myxinoidea*), which are considered the most primitive living vertebrates. The authors precisely review all available literature on hagfish kidneys, including that from their laboratories, and suggest that the archinephron of *M. glutinosa* is primarily a volume-regulating device. Although the single nephron glomerular filtration rate of the hagfish is high, the glomerulus appears to filter only when intravascular volume pressure rises. There is no net fluid or sodium reabsorption in archinephric ducts, and their osmotic water permeability is low.

The third chapter compares structure and function of proximal tubules that are invariably present in all vertebrate kidneys and play a major role in transport of organic solute, fluid, and electrolytes and in the maintenance of body fluid homeostasis. The authors intend to show similarities in urine formation between glomerular and aglomerular fish kidneys, focusing on NaCl and water transport in proximal tubules. The authors make unique observations on fluid and NaCl secretion in isolated proximal tubules from both freshwater and marine fishes that may be modulated by cAMP-stimulated apical membrane Cl conductance and/or basolateral membrane NaCl cotransport. Although it appears obvious that proximal secretion of NaCl and water plays a critical role in urine formation in aglomerular kidneys, a question remains as to its physiological significance in renal function of freshwater teleosts and amphilbians and of terrestrial vertebrates.

The fourth chapter is a comprehensive review, much of which is derived from the author's group, of morphology, glomerular filtration, tubule transport and their regulation in reptilian kidneys. Although the trend of thought from the earlier three chapters, which mainly concentrated on renal functions in fishes, is somewhat disrupted here, the author states that reptiles are adapted to a wide range of environments, including freshwater, marine, and arid terrestrial, in which kidneys play a significant role in volume and osmoregulation. This chapter is focused on the regulation of glomerular filtration rate and direction, magnitude and site, as well as cellular and molecular mechanisms of tubular transport (if known) of major organic and inorganic substances. In reptiles, differing from mammals, the proximal tubule is not the primary nephron segment for the bulk of NaCl absorption. As much as 50-70% of the filtered NaCl is apparently absorbed along the distal and collecting tubules or ducts. This is in contrast to cartilaginous and bony fishes, in which proximal tubules appear more dominant in terms of nephron organization and contribution to urine formation.

In summary, this book consists of a unique selection of topics focusing on the evolution of renal function and structure-function relationships at tissue and cellular levels of vertebrate kidneys. Readers will find discussions of information on basic organizational, cellular, and functional similarities among phylogenetically diverse animal species as well as unique features and developments perhaps necessitated by adaptation to a variety of changing environments.

Hiroko Nishimura
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University of Tennessee

The Animal Rights Controversy

Laurence Pringle
New York: Harcourt-Brace-Jovanovich, 1989, 103 pp., illus., index, $16.95

The Animal Rights Controversy is an excellent primer for those who are new to the issues raised by the philosophies embraced by the advocates of animal rights. It also is a good refresher course to those who are not so new to the moral and ethical questions of animal rights.

In a relatively few pages Laurence Pringle, who has written no less than 17 books about nature, ecological processes, and controversial issues, has put into focus the animal rights issues involving the use of animals by humans for purposes of food, clothing, sport, scientific research, zoo, and pets. And in each case he explores fairly both sides of the issue as well as provides the reader with the philosophical and historical aspects of the issue at hand.

Pringle's writing is easy reading, with the issues presented in a straight-forward, objective style that allows readers to make their own judgments.

The Animal Rights Controversy is a book that should be read by all physiologists regardless of personal views on the subject. Moreover, it is a book that should be read by those willing to think carefully about complex questions. However, it is not a book for those zealots who are not willing to consider both sides of an issue.

William M. Samuels

Airway Smooth Muscle in Health and Disease

Ronald F. Coburn (editor)
New York: Plenum Press, 1989, 318 pp., illus., index, $59.50

Advances in airway smooth muscle biology seem to have lagged somewhat behind those of other smooth muscle tissues and cardiac muscle. Because smooth muscle physiology was the theme of the recent combined meetings of the American Physiological Society and American Thoracic Society, Dr. Coburn's monograph is both timely and well timed.

This is not a primer for the uninintiated, but rather a well-coordinated series of state-of-the-art essays that addresses some difficult and important topics. As might be expected from a monograph edited by Dr. Coburn, the preponderance of material addresses basic mechanisms of the cell biology of airway smooth muscle, and there is especially strong emphasis on electrophysiology. In large part, the chapters are well coordinated for a multi-authored text. While certain themes (neuropeptides, stimulus-transduction, epithelial-smooth muscle interactions) are repeated within the various chapters, this does not exceed that which is necessary to address the important mandate for this sort of text that each chapter serve as a free-standing review.

A recurrent weakness in many state-of-the-art texts is the failure to define the limitations of technology and to state clearly what is *not* known in the field. A particular strength of this monograph is the recurrent clear statements by the contributors of these limitations. Thus, the reader may find both consolation and affirmation in ascertaining what is not known in some vital areas of airway smooth muscle physiology.

There are some particularly strong chapters, which in themselves justify the purchase of this textbook. These include a clear and elucidative discussion by de Lanerolle of the relationship between myosin phosphorylation and force generation, a basic, easily understood elucidation by Tomita of the mechanism of voltage- and receptor-mediated activation, and an essay by Kotlikoff on the application of patch clamping in airway smooth muscle.

It is regretable that the chapters on the applied science of airway reactivity generally are not of comparable quality to those chapters addressing the basic science. In part, this may be the result of assigning only about one third of the text to these topics, thus necessitating rather superficial treatment of the clinical applications. The gap between knowledge of basic mechanisms and our understanding of the clinical phenomenon of airway hyperreactivity/asthma cannot be closed by this text or any other, and it may have been a mistake to attempt to address both ends of the spectrum in a single, abbreviated book. This probably was unavoidable, because publishers' marketing divisions remain ever vigilent about books that address physiological function in deference to the disease state. The decision to limit the text to ~300 pages also may explain some omissions from the basic science component of the text. A somewhat more detailed discussion of airway smooth muscle morphometry and airway smooth muscle mechanics (ala' Stephens and Fay) and a more basic description of airway immunological mechanisms (which are addressed almost exclusively by Kaliner in the "clinical section" of the book) would have been useful. An annoying number of typographical errors and misspellings, including investigators' names, does little to inspire faith that attention to more important editorial aspects of the text have been treated impeccibly by the publisher.

Who should purchase this book? In general, anyone who reads *The Physiologist* with an interest in airway smooth muscle biology. This includes senior investigators, fellows, and doctoral and post-doctoral students in the field. In spite of its minor omissions, this is a generally well-edited text, consisting of thoughtful essays by some excellent scientists. Even for those who may not be ready for a state-of-the-art text on airway smooth muscle, it may be worth tackling this text on a word-for-word basis. Indeed, at $59.50, one can hardly afford to do otherwise.

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APS Membership Applications

Membership applications may be obtained from APS Membership Services, 9650 Rockville Pike, Bethesda, MD 20814. Applications received between February 1 and July 1 are considered for nomination by Council at the Fall Meeting, and those received between July 1 and February 1 are considered for nomination at the Spring Meeting of the Society.

(see p. 143)

The EEG Handbook. Frances M. Dyro. Boston, MA: Little, Brown and Company, 99 pp., illus., index, $21.00.

Electromyography of Jaw Reflexes in Man. D. van Steenberghe and A. Delaat. (Leuven, Belgium: Leuven University Press, 451 pp., illus., index, $45.00. (Proc. of the IADR Satellite Symposium, Catholic University, Leuven, Belgium, 1989).

Comparative Physiology. R. K. H. Kinne, E. Kinne-Saffran, K. W. Beyenbach (editor). *Structure and Function of the Kidney* (series, vol. 1). R. K. H. Kinne (editor). Basel: Karger, 1989, 200 pp., illus., index, $110.00.

The Control of the Hypothalamo-Pituitary-Adrenocortical Axis. F. Clifford Rose (editor). Madison, CT: International Universities Press, Inc., 458 pp., illus., index, $65.00.

The Animal Rights Controversy. Laurence Pringle. New York, NY: Harcourt Brace Jovanovich, 103 pp., illus., index, $16.95.

*Biologic Markers in Reproductive Toxicology.*Norman Grossblatt and Lee R. Paulson (editors). Washington, DC: National Academy Press, 395 pp., illus., index, $27.95.

Physiological Processes: An Introduction to Mammalian Physiology. Margaret Stanier and Mary Forsling. New York, NY: McGraw-Hill Book Company, 438 pp., illus., index, $35.00.

The Science of Mind. Kenneth Klivington. Cambridge, MA: The MIT Press, 239 pp., illus., index, $39.95.

Comparative Physiology. R. K. H. Kinne, E. Kinne-Saffran, K. W. Beyenbach (editors). *Urinary Concentrating Mechanisms* (Series, Vol. 2). R. K. H. Kinne (editor). Basel: Karger, 1989, 148 pp., illus., index, $88.00.

Atlas of Electroencephalography. Alan Guberman and Madeleine Couture. Boston, MA: Little Brown and Company, 220 pp., illus., index, $145.00.

Spontaneous Alternation Behavior. W. N. Dember and C. L. Richman (editors). New York: Springer-Verlag, 1989 211 pp., illus., index, $39.00.

Microvascular Mechanics: Hemodynamics of Systemic and Pulmonary Microcirculation. Jen-Shih Lee and Thomas C. Skalak (editors). New York: Springer-Verlag, 1989, 222 pp., illus., index, $59.00.

Animal Models of Depression. George F. Koob, Cindy L. Ehlers, and David J. Kupfer (editors). New York: Birkhauser Boston Inc., 1989, 295 pp., illus., index, $55.00.

New Trends in Lipid Mediators Research. Series Editors: P. Braquet Vol. 3: Leukotrienes and Prostanoids in Health and Disease. U. Zor, N. Naor, and A. Danon (editors). New York: Karger, 1989, 345 pp., illus., index, $213.50.

Contributions to Nephrology. Series Editors: G. M. Berlyne and S. Giovannetti Vol. 73: Diabetes and the Kidney. A. Heidland, K. M. Koch, and E. Heidbreder (editors). New York: Karger, 1989, 232 pp., illus., index, $112.75.

Microcognition: Philosophy, Cognitive Science, and Parallel Distributed Processing. Andy Clark. Cambridge, MA: The MIT Press, 1989, 226 pp., illus., index, $19.95.

The Regulation of Sodium and Chloride Balance. Donald W. Seldin and Gerhard Giebisch (editors). New York: Raven Press, 1990, 532 pp., illus., index, $69.00.

Fundamentals of Human Neuropsychology. Third Edition. Bryan Kolb and Ian Q. Whishaw. New York: W. H. Freeman and Company, 1990, 910 pp., illus., index.

Oxygen Radicals: Systemic Events and Disease Processes. Dipak K. Das and Walter B. Essman (Editors). Basel: Karger, 1990, 196 pp., illus., index, $116.

Adaptation and Development of Gastrointestinal Function. M. W. Smith and F. V. Sepulveda (Editors). Manchester, UK: St. Martin's Press, 1989, 168 pp., illus., index, $60.00 hardcover; $19.95 paperback.

James Parkinson: His Life and Times. F. Clifford Rose (Editor). A. D. Morris. Boston: Birkhauser, 1989, 207 pp., illus., index, $59.00.

From Reading to Neurons. Albert M. Galaburda (Editor). Cambridge, MA: The MIT Press, 1990, 545., illus., index, $45.00.

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Contributions to *News in Physiological Sciences*

Articles for *News in Physiological Sciences* are usually invited, but appropriate unsolicited contributions will be considered. Guidelines for writing and requirements as to style and format are available. Published items, including letters, will be edited as needed.

Send to: Dr. John T. Shepherd, Department of Physiology and Biophysics, Plummer 1043, Mayo Foundation, Rochester, MN 55905, USA.

American Physiological Society Centennial Collection

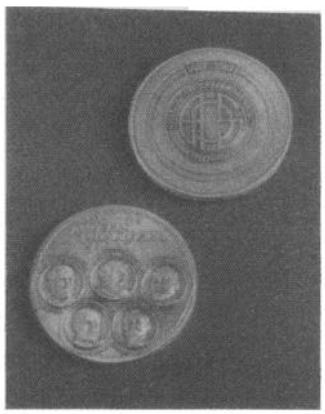
The Centennial Founders Set

The Centennial Founders Set is a limited production of ceramicware commemorating the 100th anniversary of the founding of the American Physiological Society. Each piece—plate, cup, and tile—is fired in a radiant cobalt blue porcelain and etched in 23-carat gold. The face of the 10-inch plate features a reproduction in gold of the Centennial portraits of the five founders and inscribed on the back is a brief history of APS. The tile features a gold reproduction of the Centennial Seal and the cup has both the founders' portraits and Centennial Seal embossed on the sides. A Founders Plate is to be donated to the White House Collection of Commemorative Plates in Washington, D.C.

The cost of the Centennial Founders Set is $45.00. Individual pieces are priced as follows: $35.00 for the plate; $10.00 for the cup; and $6.00 for the tile.

The Centennial Coffee Mug

Centennial Coffee Mug is a replica of the Founders Cup with the Centennial Seal imprinted in white on a radiant cobalt blue mug. The cost for the coffee mug is $7.50.



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Life Sciences Research Office Report

Under the terms of a contract with the Food and Drug Administration (FDA), the Life Sciences Research Office (LSRO), Federation of American Societies for Experimental Biology (FASEB) has completed a study examining the issues related to the development of medical foods for dietary management of diseases with orphan status. The report entitled, "Evaluation of Incentives for Development of Orphan Medical Foods," presents an overview of the current status of an evaluation of the incentives for the development of medical foods for orphan diseases. Specifically, this report addresses the identification of human diseases that may benefit from orphan medical foods, criteria to define orphan status for medical foods, identification of incentives that would benefit further development of orphan medical foods, the scope of research and development efforts that are necessary prior to the use of an orphan medical food, the impact of noneconomic barriers on product development, and a comparison of US and foreign development of orphan medical foods.

Copies of the report may be purchased ($18 per copy, prepaid) from the FASEB Special Publications Office, 9650 Rockville Pike, Bethesda, MD 20814. (Maryland residents must add 5% sales tax with order.)

Bachelor's Degrees in Natural Sciences and Engineering Declined 9 Percent in 2 Years

The number of bachelor's degrees awarded in engineering and the natural sciences has declined, in contrast to the growth in bachelor's degrees in nonscience fields, according to a new National Science Foundation report.

The report, *Science and Engineering Degrees: 1966-88, A Source Book,* shows the declines found in engineering and the natural sciences occurred among both men and women. For women, this decline was the first ever; for men, this decline reversed the increases evident since 1980.

Among women baccalaureates in 1988, 23 percent earned their degrees in science/engineering fields; among men, the comparable figure was 39 percent.

At the masters and doctoral degree levels, the number of awards in science and engineering continues to increase, reflecting the growth in baccalaureates in the early 1980s.

The NSF Division of Science Resources Studies has analyzed this data according to NSF catagories of science and engineering fields. The period 1986 to 1988 has been highlighted here because 1986 represents the turning point for the decline in bachelors' degrees. More detailed data on bachelors, masters, and doctorates, by more specific fields, are available for the period 1966-88 from the Division of Science Resources Studies.

To obtain a copy of the report, contact: Elizabeth Michael, Division of Science Resources Studies, Room L-611, National Science Foundation, 1800 G Street, NW, Washington, DC 20550, (202) 634-4284.

Scientific Meetings and Congresses

30th Annual ASCB Meeting, San Diego, CA, December 9-13, 1990. *Information:* American Society for Cell Biology, 9650 Rockville Pike, Bethesda, MD 20814. Tel: 301-530-7153, Fax: 301-530-7139.

Seventh International Hypoxia Symposium, "High Altitude Physiology and Medicine," Lake Louise, February 26-March 2, 1991. *Information:* Ingrid Ellis, Hypoxia '91, Conference Coordinator 1M10, McMaster University, 1200 Main Street West, Hamilton, Ontario, Canada. L8N 3Z5. Tel: 416-525-9140, ext 2182.

Second International Conference on The Sodium/Calcium Exchange, Baltimore Marriott Inner Harbor, MD, April 8-10, 1991. *Information:* Conference Department, New York Academy of Sciences, 2 East 63rd Street, New York, NY 10021, Tel: 212-838-0230, Fax: 212-888-2894.

IX International Congress of Electromyography and Clinical Neuro-Physiology, Jerusalem, Israel, June 2-6, 1991. *Information:* Arieb N. Gilai, Convener, EMG - CN - IX Congress, P. O. Box 29334, Tel Aviv 61292. Tel: 972-3-5102542, Fax: 972-3-660604.

Fourth International Reinhardsbrunn Symposium on Circumventricular Organs, "Circumventricular Organs and Brain Fluid Environment: Molecular and Functional Aspects," German Democratic Republic, March 24-29, 1991. *Information:* Professor A. Ermisch, Section of Biosciences, Karl Marx University Leipzig, Talstr. 33, DDR - 7010 Leipzig, German Democratic Republic.

Plenary Lectures And Symposia

Sunday

Monday

Tuesday

Wednesday

Poster And Slide Sessions

Sunday

Monday

Tuesday

Wednesday

1.1

APPLYING THE TECHNIQUES OF MOLECULAR BIOLOGY TO PHYSIOLOGICAL RESEARCH. S. Chien. Univ. of California, San Diego, La Jolla, CA

Most physiological functions are carried out by proteins, which are genetically coded as DNA in cell nuclei. The transcription of DNA to RNA and the translation of RNA to proteins provide the flow of genetic information, and the regulation of these processes lead to the control of gene expression and physiological functions. Molecular cloning techniques have led to the establishment of the amino acid sequence, the prediction of the secondary structure, and the correlation of molecular structure with physiological function of the protein. Comparisons of proteins with structural homologies have generated new insights into their tissue specificity, developmental differentiation, and evolutional changes. Techniques of molecular manipulations such as site-specific mutagenesis and transgenic mice have led to the identification of known functions with specific sites on a given protein molecule. The applications of these molecular biological techniques have also helped to elucidate the molecular basis of pathophysiological functions in disease states.

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COMPARATIVE INTESTINAL NUTRIENT TRANSPORT

5.1

VERTEBRATE INTESTINE APICAL MEMBRANE MECHANISMS OF ORGANIC SOLUTE TRANSPORT. Bruce R. Stevens, Dept. of Physiology, Coll. of Med., Univ. of Florida, Gainesville, FL USA 32610.

The intestinal epithelium apical membrane serves as the major interface between the environment and blood, controlling the net absorption of organic nutrients. Mechanisms of amino acid and sugar transport include un-regulated simple passive diffusion and regulated transporter (carrier) proteins. Transporter activities have been shown [1] to be regulated locally in enterocyte membranes at several levels: (*a*) ion and substrate kinetic activation and binding order, (*b*) membrane electrical potential modulation, (*c*) interactions among transporter protein subunits, and (*d*) intracellular phosphorylation events associated with enterocyte differentiation, as recently demonstrated in my laboratory. Organic nutrient accumulation occurs in enterocytes by energetic coupling to the electrochemical gradient associated with 2 Na^+ ions [2]. The use of high-energy electron radiation inactivation experiments and kinetic modeling has revealed that the sodium-activated glucose transporter, and also the proline transporter, each behaves *in situ* in the apical membrane as a tetramer of four subunits [3]. Inasmuch as intestinal transporter characteristics are shared among the vertebrate species studied, there may exist a universal vertebrate intestinal apical membrane mechanism of ion-activated organic solute transport.

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Intestinal brush border membrane Na+/glucose cotransporter functions in situ as a homotetramer.
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5.2

ARE INVERTEBRATE GUT DIVERTICULA NUTRIENT ABSORPTIVE ORGANS? G. A. Ahearn, G. A. Gerencser, M. Thamotharan, & R. D. Behnke Dept. of Zoology, Univ. of Hawaii, Honolulu, Hi 96822 and Dept. of Physiol., Univ. of Florida, Gainesville, Fl 32610.

Physiological mechanisms of gastrointestinal nutrient absorption among invertebrates remain severely underinvestigated. We briefly review some of the biochemical and biophysical forces affecting nutrient transfer across epithelial cells and membranes of vertebrate and invertebrate absorptive organs. Next, we present some of the described processes for sugar and amino acid transport in the tubular portion of the gastrointestinal tracts of three major invertebrate groups: echinoderms, molluscs, and arthropods. We then discuss in detail recent nutrient transport studies using purified epithelial brush border membrane vesicles of two invertebrate gut diverticula, the crustacean hepatopancreas and the starfish pyloric caecum. Lastly, transepithelial nutrient transport studies of crustacean hepatopancreatic epithelial cell monolayers grown in primary culture and mounted in flux chambers are used to demonstrate the applicability of these methods to structurally complex invertebrate organs as well as to characterize the cellular mechanisms responsible for movements of solutes across these cell layers. It is concluded that invertebrate gut diverticula may make a significant contribution to total nutrient absorption. Supported by NSF grant no. DCB89-03614.

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Proline transport by brush border membrane vesicles of lobster antennal glands.
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5.3

ROLE OF THE BASOLATERAL MEMBRANE IN INTESTINAL NUTRIENT TRANSPORT. Chris I. Cheeseman. Univ. of Alberta, Edmonton, Alta, Canada, T6G 2H7.

In the past when considering the absorption of organic solutes by the intestinal epithelium little emphasis has been placed on the exit across the basolateral membrane (BLM). However kinetic parameters for glucose *transport* into purified BLM vesicles show the carrier(s) responsible to have a very high turnover number indicating a very efficient clearance from the cell. In addition this carrier system can be modulated so that transport capacity is augmented within 30 minutes by elevated blood glucose concentrations. Dietary manipulations can also change the BLM glucose carrying capacity and chronic elevation of plasma glucose levels in diabetic animals increases BLM glucose transport. These observations indicate that the exit of glucose from the enterocyte can be altered in response to a variety of conditions. In contrast, *in vitro* lysine transport across the intestine is very slow in a variety of avian, anuran and mammalian species and the amino acid is accumulated within the enterocytes , *i.e.* exit is rate limiting. However transport of lysine across the BLM is greatly increased by the presence of some neutral amino acids including leucine (in the micromolar to millimolar concentration range). Investigation of the possible role of second messengers in this response show that diesterase inhibitors can augment the effect of leucine while forskolin on its own can produce a similar stimulation. To date it is not possible to conclude that cAMP is a direct mediator of the leucine effect but this second messenger does at least modulate the behaviour of the lysine transporter. The fact that at least two intestinal BLM transport systems can adapt or be regulated strongly suggest that this membrane plays an important role in the absorption of nutrients.

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5.4

COMPARATIVE ASPECTS OF LIPID DIGESTION AND ABSORPTION. A.R. Place. Center of Marine Biotechnology University of Maryland, Baltimore, MD.

Fat digestion and absorption for most animals is extremely efficient (>85%) yet inherently complex process. In the gastrointestinal lumen of an animal, bulk fat globules are dispersed into finely divided emulsion particles allowing the fatty acid esters to be enzymatically hydrolyzed at the emulsion-water interface. The insoluble lipid hydrolysis products are rendered absorbable by endogenous and exogenous detergents and transported across the epithelial layer of the gastrointestinal lumen. In the enterocyte, the hydrolysis products are repackaged for transport to other parts of the body. While we know a great deal about fat digestion and absorption in mammals, much less is known about these processes in birds, fishes, and invertebrates. Our current understanding of lipid digestion and absorption in these major taxa will be presented and contrasted with the mammalian systems. Specific adaptations and constraints in the lipid absorption machinery will be highlighted, especially as it relates to environmental temperature, physical properties of dietary lipids and the dietary intake levels of fats.

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A paper which quantitates, using chemical balance studies, lipid assimilation in a small oceanic crustacean. Up to 97% of ingested algal fatty acids are removed by the copepod, with a preference towards removal of polyunsaturated acids.

5.5

ONTOGENY OF INTESTINAL SOLUTE TRANSPORT. R.K. Buddington. Biol. Sci., Mississippi State University, Mississippi State, MS 39762-5759.

The intestines of developing animals are faced with two dramatic changes in functional demands. The first occurs at birth or hatch when the intestine assumes full responsibility for the provision of nutrients. To prepare for this and the high metabolic rate of neonates, many nutrient transporters, notably those for amino acids and some sugars, appear prenatally with rates of transport higher at birth than at later ages. Hence, the intestines of neonates are able to "take off running." The second functional change occurs at weaning when dietary composition shifts from one of stability, such as milk, to one of greater complexity and variability. Coinciding with the dietary shifts there are changes in the relative activities of different solute transporters. The best example is provided by the monosaccharide transporters of mammalian herbivores and omnivores. Whereas rates of aldohexose transport decline postnatally, even more so for galactose relative to glucose, at weaning transport of the ketohexose fructose increases relative to glucose. Changes in monosaccharide transport coincide with the loss of galactose and appearance of fructose in the diet. Curiously, even though fat intake is generally highest during suckling, the bile acid transporters do not appear until weaning. By manipulating the diet it has been possible to demonstrate the changes in transporter activity during early suckling are triggered by genetically hard-wired signals. Only just prior to weaning do mammals acquire the ability to regulate transporter activity in response to dietary changes. However, the identities of the specific signals remain uncertain. Postnatal declines in rates of amino acid and sugar transport are compensated for by increases in the amount of intestinal tissue. As a result, transport capacities of the entire intestine increase throughout development in proportion to increases in metabolic rate. Furthermore, recent finding disprove the fallacy that transport capacities are in great excess of intake. Instead, in some species transport capacities may pose a "digestive bottleneck" which could limit growth.

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5.6

DIETARY REGULATION OF INTESTINAL NUTRIENT TRANSPORT. W.H. Karasov. Dept. of Wildlife Ecology, University of Wisconsin, Madison, WI 53706.

Intestinal nutrient absorption rates are altered in response to changes in dietary levels of substrates and changes in daily food intake. Evidence for specific regulation of glucose transporters by dietary levels of carbohydrate exists for some mammals and fish, but evidence is negative for some other species including the single avian and reptilian species that have been studied. In mammals, many other intestinal nutrient transporters (e.g., those for amino acids, minerals, and vitamins) are also specifically regulated by dietary levels of their substrates. Nonspecific increases in absorption rates of all these classes of nutrients occur when feeding rate increases during acclimation to low temperatures, during lactation, and sometimes in response to dietary dilution with indigestible or nonmetabolizable substrates. Whether the observed regulatory changes are critical to whole-animal nutrition and adaptation depends on their direction and magnitude, and whether normal rates of enterocyte nutrient transport greately exceed, barely satisfy, or fall short of normal nutrient demands.

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5.7

Molecular biology approaches to comparative intestinal Na/glucose cotransport. A.M. Pajor, B.A. Hirayama, M.J. Coady, and E.M. Wright. Department of Physiology, UCLA School of Medicine, Los Angeles, CA 90024-1751.

The rabbit intestinal Na/glucose cotransporter has been cloned and sequenced, and used to study the expression of Na/glucose cotransporter genes and the species distribution of the cotransporter. Two directions have been followed. One of these used the predicted primary sequence of the cDNA clone for the design of synthetic peptides, and subsequent production of antibodies to those peptides. The antibodies were then used in Western blots of brush border membranes. The second approach used the cDNA sequence directly, both to isolate clones by hybridization and to examine the size of transcripts encoding the cotransporter in different species. The results suggest that the Na/glucose cotransporter cloned from rabbit intestine has structural and sequence homology to the intestinal Na/glucose cotransporters in species ranging from trout to man.

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COMPARATIVE ASPECTS OF FUNCTIONAL MORPHOLOGY OF THE RESPIRATORY SYSTEM

6.1

THREE-DIMENSIONAL IMAGING OF THE LUNG AND ITS TISSUES. W.S. Tyler, VM:Anatomy, Univ. of California, Davis, CA 95616.

Three-dimensional imaging of the lung and its tissues is a useful approach to functional comparative morphology of the respiratory system at the gross, light microscopic and electron microscopic levels of examination. Examples of several three-dimensional techniques for relating morphology to function will be demonstrated and the advantages and disadvantages of each discussed. Three-dimensional reconstructions of distal airways made from serial paraffin sections using an elaborate set of computer programs with automated digitization will be demonstrated[1]. Another example will demonstrate the usefulness of three-dimensional visualization of pulmonary artery blood flow in anesthetized ponies using simpler computer programs which require hand digitization[2]. The same computer programs will be used to demonstrate reconstruction of gross body slices. Examples of three-dimensional reconstructions made using the confocal light microscope to produce optical, rathan than physical, sections will also be demonstrated[3]. The use of high resolution computed tomography to resolve a problem concerning the subgross morphology of sheep lungs with possible functional significance will be discussed. The usefulness of stero paris of scanning electron micrographs to provide three-dimensional information will be demonstrated and discussed.

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6.5

MORPHOMETRY AND IMAGING OF LUNG INJURY. James D. Crapo, M.D. Duke University Medical Center, Durham, North Carolina 27710.

The lung undergoes a variety of different responses to injury after exposure to oxidants and inhaled pollutants. Hyperoxic exposure causes a diffuse injury to the alveolar septum involving both epithelial and endothelial cell injury and both interstitial and alveolar edema. Exposure to more highly reactive oxidants that occur in lower concentrations as air pollutants, such as ozone or NO_2, causes a more focal injury which is localized predominantly to small airways and the proximal portions of the gas exchange region. This injury predominantly involves the airway and alveolar epithelium but may be associated with significant effects on the alveolar interstitium leading to alterations in interstitial matrix proteins. The micromechanics of the gas exchange region of the lung are highly dependent upon the organization of matrix protein elements. Both collagen and elastin are highly ordered requiring either spatially oriented two-dimensional imaging or three-dimensional reconstructions to optimally localize and characterize focal injury to these tissue proteins. Morphometric analysis of lung tissue provides one of the most reliable means to define and compare different types of injury to an organ such as the lung which contains a highly patterned three-dimensional structure.

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COPING WITH EXTREME CONDITIONS: ADAPTATIONS OF METABOLISM AND EPITHELIAL TRANSPORT MECHANISMS IN INVERTEBRATES

7.1

Extremely alkaline conditions and electrogenic K^+ transport in the midgut of the tobacco hornworm

Julian A.T. Dow
Dept. of Cell Biology, University of Glasgow, Glasgow G12 8QQ, Scotland, UK.

Lepidopteran larvae demonstrate several remarkable digestive specialisations. Midguts of lepidopteran larvae transport potassium electrogenically from blood-side to lumen with an unprecedented electrical signature. Historically believed to represent an excretory specialisation to a diet dangerously high in potassium, the pump is now thought to serve multiple roles: the regulation of both blood and luminal [K]; the generation of an electrogenic K gradient for nutrient uptake (driven by a K/nutrient cotransport in Lepidoptera); and the generation of high luminal pH by Nernstian equilibration across the gut epithelium. The magnitude of the pH gradient is also exceptional: whereas the blood pH is 6.7, and that of the midgut epithelium 7.0, the luminal pH rises as high as 12.0. This again may serve several roles: at high pH, digestive hydrolysis is favoured; certain pathogenic bacteria might be killed; and the digestibility of tannin-containing diets might be increased. A model for the indirect generation of the pH gradient via electrogenic K transport has been proposed (1), and recent pH microelectrode evidence (3) shows that the midgut itself is the site of generation of the pH gradient. Under double perfusion *in vitro*, a symmetrical pH gradient of 2 units is observed across the anterior and middle, but not posterior, midgut regions. The gradient collapses under anoxia, but recovers on restoration of oxygen. Estimates for the energy requirements for this K pump, and also indirectly for the pH gradient, at 10% of the larva's total ATP production, suggest that it may be the dominant component of the larva's energy budget (2); so an understanding of these transport processes in the growing larva is important.

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7.2

NUTRIENT UPTAKE AGAINST EXTREME CONCENTRATION GRADIENTS BY MARINE INVERTEBRATES. S.H. Wright. Department of Physiology, College of Medicine, University of Arizona, Tucson, AZ 85724

Soft-bodied marine invertebrates (i.e., all but the crustaceans) accumulate dissolved organic material (DOM) from sea water directly into epithelial cells of the general integument at rates which can support tissue and whole animal nutrition. Best characterized are the several transport processes specific for free amino acids (FAAs). FAAs in the tissues of marine invertebrates often exceed 0.2-0.5 M, whereas the concentrations of individual FAAs in near shore waters are <100 nM; i.e., net accumulation of these nutrients occurs against chemical gradients that can exceed 10^6 to 1! Studies with intact tissues and epithelial plasma membranes isolated from the mussel, *Mytilus*, revealed transport to involve a direct coupling between fluxes of amino acid and Na. Thus, the mechanism of this process follows the paradigm that has proven to be a general strategy used by animal cells to concentrate organic molecules: secondary active Na-cotransport. Nevertheless, integumental transport processes are unique, not in kind, but in the conditions under which they must normally work: they must sustain organic solute gradients that are more extreme than any other reported in the animal kingdom. The bases for this extreme behavior are kinetic characteristics (for Na and for organic substrate) that also represent extremes: the highest affinity for amino acid (K_t's for FAAs of 1-10 μM) *vs.* the lowest affinity for Na (K_{50}'s of 300 mM). These transport processes are uniquely suited to make efficient use of a scarce nutritional resource, DOM, while sustaining the cellular FAA pools required for the maintenance of normal cell volume. (supported by NSF award DCB88 19367)

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7.3

Natriuresis and diuresis in blood-feeders: coping with massive fluid loads in mosquitoes. K.W. Beyenbach, Sect. Physiology, Cornell Univ., Ithaca, NY 14853.

Maturation of the oocytes of the female mosquito Aedes aegypti requires the consumption of a blood meal. In taking this blood meal the female consumes twice her body weight in fluid. This creates a weight problem, a water problem, and a salt problem. The diuretic hormone is part of an endocrine system that deals with these problems. In Aedes aegypti this hormone appears to be a 1800 MW peptide that works via cAMP stimulation of NaCl and water secretion across Malpighian tubules (1,2). This provides for the rapid excretion of the unwanted salt and water fraction of the meal. Recent studies have shown that the peptide is also present in male mosquitoes which do not feed on blood, and that Malpighian tubules of males and females appear to share the same ion transport mechanisms as well as similar diuretic hormones and receptors (3). Hence diuretic peptides in the mosquitoe are not sex-linked and they may be useful in meeting a variety of salt and water challenges.

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7.5

THE "DIURETIC HORMONE" OF A DESERT BEETLE: ELECTROPHYSIOLOGICAL EFFECTS ON MALPIGHIAN TUBULES. Susan W Nicolson. University of Cape Town, Rondebosch 7700, South Africa.

Fluid secretion by Malpighian tubules of Namib Desert tenebrionid beetles, Onymacris plana and O. rugatipennis, is dramatically stimulated by homogenates of the corpora cardiaca (CCH)[1]. This "diuretic hormone" results in rapid clearance of the haemolymph, but no diuresis. Addition of CCH or adenosine 3',5'-cyclic monophosphate (cAMP) to the medium bathing isolated tubules has no effect on basal membrane potential, but opposing effects on transepithelial potential[2]. Perfused Malpighian tubules of O. plana were subjected to cable analysis before and during stimulation by CCH, cAMP and high ambient K^+. Responses to these stimulants were consistent with increased fluid secretion but were apparently mediated by different mechanisms[3]. Changing perfusate composition has almost no effect, whereas there is a high basal permeability to K^+ and Cl^-ions. The patch clamp technique has been applied to O. rugatipennis tubules, access to the basal membrane being achieved by a new method of stripping tubules of their surrounding connective tissue.

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7.6

TRANSPORT MECHANISMS AND THEIR CONTROL IN LOCUST HINDGUT IN RELATION TO EXTREME ENVIRONMENT. J.E. Phillips, B. Thomson, R. Lechleitner, M. Chamberlin and J. Harrison. U.B.C., Vancouver, B.C., V6T 2A9.

The desert locust may experience either water excess or severe dehydration, low Na^+ intake, and changes in acidosis during feeding cycles. We have demonstrated that the hindgut possesses transport mechanisms contributing to homeostasis in the face of these external challenges. In this regard, this insect organ appears to play a role analogous to mammalian kidney tubules. Amino acids are the major respiratory substrates in locust hindgut, thereby providing ammonium which is exchanged for luminal Na^+. Nitrogen and acid excretion are simultaneously achieved. An apical electrogenic pump also secretes proton leading to OH^- and bicarbonate addition to the hemolymph. Besides acting as a major respiratory substrate, proline is actively transported at high rates in the rectum and drives substantial water reabsorption against large osmotic gradients. Three of the four major active transport mechanisms in these epithelia (i.e. for Cl^-, H^+ and proline) are all largely Na-independent. Most of these hindgut transfer mechanisms for ions and fluid are controlled by neuropeptide factors, one of which we recently purified.

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7.7

PRODUCTION OF HIGH SALT CONCENTRATIONS IN INSECT EXCRETORY SYSTEMS: ABSORPTION OF WATER FROM THE GUT CONTENTS AND THE ATMOSPHERE J. Machin and M.J. O'Donnell, Dept. Zoology, Toronto, and Dept. Biology, McMaster U., Hamilton, L8S 4K1.
The capacity for absorption of atmospheric water vapour has evolved repeatedly in the terrestrial arthropods (1). There are at least 9 distinct physiological mechanisms, involving modified salivary or silk glands, hydrophillic cuticular surfaces of specialized mouthparts, rectal epithelia or complexes of Malpighian tubules and rectal epithelia, and even the pleopods of terrestrial isopods (2). Vapour uptake entails movement of water against gradients as high as 70 osmol kg^{-1} by production of localized sites of reduced water activity that must be isolated from the body fluids. In the mealworm rectal complex, water activity is reduced by accumulation of KCl and to a lesser extent NaCl by Malpighian tubules which are applied to the surface of the hindgut and are enveloped by the perinephric membrane. Recent studies using double-barrelled ion-selective microelectrodes have revealed activities of K^+ and Na^+ as high as 2700 and 400 mM, respectively, in the Malpighian tubule lumen. In the presence of comparable chloride activities, these values are sufficient to account for much of the elevated osmolality (> 6.8 osmol kg^{-1}) which drives vapour uptake and recovery of water from the hindgut (3). Electrochemical gradients indicate active accumulation of K^+, Na^+ and also H^+, whereas Cl^- activity is near equilibrium with the positive lumen PD of about 50 mV.

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MONDAY PLENARY LECTURE

31.1

ADAPTATION THRESHOLDS: WHEN DO ENVIRONMENTAL CHANGES SET SELECTION IN MOTION? George N. Somero. Scripps Inst. of Oceanography, Univ. of Calif. San Diego, La Jolla, CA 92093.

Adaptive differences in the physiological and biochemical systems of organisms from widely different environments are well known, but adaptations that distinguish species adapted to only moderately different environmental conditions, e.g., of temperature, hydrostatic pressure or O_2 content, are not well understood. The minimal ("threshold") changes in temperature, pressure, or O_2 content that are sufficient to select for adaptive differences also remain largely undetermined. In this lecture, several physiological and biochemical systems are examined to discern when perturbation is sufficient to favor selection, how environmental sensitivity differs among systems, what properties of the systems are strongly conserved as a result of these fine-scale adaptations, and what types of amino acid substitutions are needed to restore appropriate protein structure and function. Perturbation thresholds are shown to vary among systems; some properties, e.g., protein-ligand interactions, are much more sensitive to thermal and pressure perturbation than other traits, e.g., protein polymerization equilibria. The role of fine-scale adaptations to temperature and pressure in establishing species' distribution patterns is emphasized, as are the advantages of studying closely related congeneric species from different environments to delineate threshold-level adaptations.

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THE ORGANIZATION AND MODULATION OF HOMEOSTATIC SYSTEMS

34.1

SLEEP, RHYTHMS, AND HIBERNATION. Craig Heller, Dennis Grahn, Lorenz Trachsel, Beverly Krilowicz, Joseph Miller. Stanford University, Stanford, CA 94305

Hibernation involves extreme adjustments of physiological regulatory systems. The hibernator is seasonally hypersomnic, and most of a bout of hibernation appears to behomologous to NREM sleep with REM sleep absent. Body temperature of the hibernator is regulated close to 0°C. The periodicity of arousal from torpor may be days to weeks. Because of the extreme ranges of arousal states, body temperature, and behavioral rhythms in the hibernator, it is an excellent model system for studies of the underlying neural control mechanisms. Single unit recordings from arousal state selective neurons throughout bouts of hibernation confirm and extend to lower body temperatures the conclusions based on EEG that hibernation consists mostly of a state homologous to NREM sleep. However, continuous EEG recordings during euthermic interbout periods suggest that the restorative function of NREM sleep is not accomplished during hibernation. Between bouts of hibernation animals mostly sleep with greater total sleep time after long hibernation bouts than after short ones. The power density of the EEG in the delta band is greater after long than after short bouts. The circadian system is involved in the timing of arousals from hibernation. A bout may consist of multiple circadian cycles. During hibernation in constant dark the circadian clock free runs with a temperature compensated periodicity. It can be entrained by a light/dark cycle. The temperature compensation of the circadian clock is not due to temperature insensitivity of suprachiasmatic nucleus neurons. In vitro, they are highly temperature sensitive and cease to fire action potentials at temperatures above the brain temperatures of deep hibernation. (Research supported by a grant from the Upjohn Co.).

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34.2

THE CIRCADIAN CONTROL OF SLEEP, WAKEFULNESS AND ACTIVITY.

Dale M. Edgar and William C. Dement. Sleep Research Center, Stanford University School of Medicine, Stanford, CA 94305.

The circadian timekeeping system governs the timing of virtually all physiological functions and behaviors in mammals. Daily oscillations in body temperature, and regular intervals of activity behavior and sleep-wakefulness are characteristic of this endogenous temporal regulatory process. Although destruction of the suprachiasmatic nucleus (SCN) of the hypothalamus is known to abolish circadian oscillations, the effects of such lesions as well as the fundamental role of the SCN in the regulation of sleep-wakefulness is less clear. Furthermore it is unclear whether the circadian control of homeostatic systems (e.g. sleep) is governed by physiological feedback pathways associated with voluntary activity behaviors.

To investigate these issues we have examined the regulated levels of sleep-wakefulness in intact and SCN-lesioned (SCNx) rodents, and have assessed whether scheduled opportunities for otherwise voluntary exercise influences circadian timing. In rats, precise SCN-lesions increase total sleep time approx. 1 hr and render animals chronically sleep satiated, suggesting that the SCN functions to potentiate vigilant wakefulness during the active portion of the circadian day. Scheduled daily exercise afforded by restricted running wheel access in otherwise free-running mice entrains sleep-wake circadian rhythms. Taken together, these data suggest that the circadian clock actively influences levels of wakeful vigilance and adjusts timing in response to feedback resulting from waking behavior.

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34.3

RESPIRATORY CONTROL IS ALTERED BY CHOLINERGIC PONTINE RETICULAR MECHANISMS. R. Lydic and H.A. Baghdoyan, Department of Anesthesia, The Pennsylvania State University, College of Medicine, Hershey, PA 17033.

Rapid eye movement (REM) sleep occurs in all placental, terrestrial mammals. REM sleep is known to alter homeostatic control but the specific cellular and receptor-level mechanisms causing sleep-dependent changes in breathing are incompletely understood. We are testing the hypothesis that cholinoceptive mechanisms localized to the medial pontine reticular formation (mPRF) can cause state-dependent changes in respiration. Microinjection of cholinergic agents into specific regions of the mPRF produces the only pharmacological model of REM sleep. We have applied this model to intact, unanesthetized cats chronically implanted for studying both respiration and levels of arousal. Our results show for the first time that non-respiratory regions of the mPRF -known to regulate states of consciousness- can also cause state-dependent changes in upper airway muscle activity (Lydic et al *FASEB J.* 3:1625, 1989), ventilation (Lydic and Baghdoyan *Neurosci. Lett. 102:*211, 1989), and the ventilatory response to hypercapnic stimuli (Lydic et al *FASEB J.* 3:A404, 1989). Extracellular recordings of parabrachial neurons across states of consciousness reveal a close correspondence between firing rates during REM sleep and during the cholinergically induced REM sleep-like state (Gilbert and Lydic, 1990). Considered together, these results support the hypothesis that cholinergic mechanisms in the mPRF can causally contribute to state-dependent changes in respiratory control.

Supported by: HL-40881(RL) and MH-45361(HAB).

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34.4

ADAPTIVE ADJUSTMENTS OF THE THERMOREGULATORY SYSTEM. L.I.Crawshaw. Department of Biology, Portland State Univ., Portland, OR 97207.

Under appropriate conditions, most vertebrate ecotherms are capable of accurately regulating body temperature. The actual regulated temperature differs widely across species, and presumably reflects the particular thermal environment present during the evolutionary development. Within a species, the regulated temperature can change following challenges involving temperature, microorganisms, and energy intake. Recently, several additional conditions have been shown to alter the regulated temperature. These include the lack of environmental oxygen in numerous species, the presence of very low levels of ethanol in goldfish, and the developmental state of amphibian larvae. In each case, the relationships have been quantified and the resulting physiological benefits clarified. Neuronal mechanisms that might underly the changes in regulated temperature brought about by these conditions will be discussed. (NIAAA Grant AA07592)

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34.5

The Role of Neurohypophysial Blood Flow in the Control of Neurohormone Release. R.M. Bryan, Jr., Dept. of Surgery, Division of Neurosurgery, M.S. Hershey Medical Center of The Pennsylvania State University, Hershey, PA 17033.

The adenohypophysis (AD) secretes hormones which have homeostatic functions. Hypophysiotropic hormones (HPHs) which are released into the blood in the neurohypophysis (NH) control hormone secretion by the AD. The concentration of HPHs in blood perfusing the AD is an important aspect of hormone release. Changes in the concentration of HPHs in the blood can be achieved (a) by altering the rate of release of the HPHs in the NH or (b) by altering the rate of blood flowing through the NH. Therefore blood flow in the NH was studied to determine how it is controlled.

During hypoglycemia (plasma glucose = 1.7 umol/ml) and hypercapnia (PCO_2 = 63 mm Hg), blood flow to most brain regions doubled (1,2). However, blood flow to the NH was not changed during the above conditions. Although elevated CO_2 produced a vasodilation in the neurohypophysial vascular bed, it was offset by a vasoconstriction produced by stimulation of alpha adrenergic receptors. I conclude that neurohypophysial blood flow is regulated differently than in other brain regions. The unique regulation may be for the purpose of controlling the concentration of HPHs in blood.

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3.

NMR SPECTROSCOPY: A NEW TECHNOLOGY IS HELPING TO SOLVE OLD PROBLEMS

35.1

^{31}P NMR INVESTIGATION OF SKELETAL MUSCLE METABOLISM IN DIVING DUCKS. Richard Stephenson* and David R. Jones. Departments of Zoology, University of Toronto* and University of British Columbia, Canada.

The effect of forced submergence on energy metabolism in birds has been controversial for more than a century. Specifically, it has not been conclusively shown whether anaerobic ATP production is effective in fully compensating for the observed reduction in oxidative phosphorylation, and/or whether there are any widespread decreases in ATPase activity ("metabolic arrest") during submergence. We measured indirectly the rate of ATP turnover in non-contracting pectoral muscle of the anaesthetised Pekin duck to provide a baseline by which we could interpret the changes seen during forced dives. We developed a method for simulating forced dives in ducks held immobile within a 30 cm bore 2.35T magnet. A typical cardiovascular response was observed under these conditions: marked bradycardia with maintained arterial blood pressure. Whole animal metabolism was estimated by the traditional methods of respiratory oxygen uptake and plasma lactate measurements. The concentrations of phosphorylated metabolites and intracellular pH were also measured before, during and following dives using ^{31}P nmr spectroscopy. This technology enabled us to discover that ATP concentration is maintained in muscle during dives and that creatine phosphate is an important source of this ATP. Anaerobic metabolism can maintain a resting metabolic rate, and the hypothesis that non-perfused tissues experience metabolic depression during forced dives is, therefore, not supported by this work. Financed by NSERC, BC Heart Foundation and BC Health Care Research Foundation.

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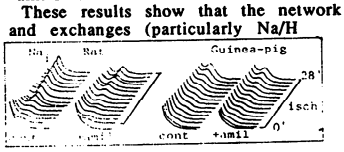
35.2

Species Differences in Sodium Accumulation During Ischemic Challenge in the Heart: A ^{23}Na NMR Study.
Joanne S. Ingwall and Monique Bernard, Brigham & Women's Hospital, Boston, MA

The membrane composition of ion pumps and exchanges in hearts of different species may not be alike and could result in differences in resting Na content and in the rate and extent of Na accumulation during ischemic challenge. Accordingly, we used ^{23}Na NMR with the shift reagent Dy(TTHA)3- in buffer-perfused hearts isolated from guinea pig and rat to identify whether there are species differences in the mechanisms responsible for intracellular Na^+ (Na_i^+) accumulation during ischemia. By 28 min of global total ischemia (37°) Na_i^+ accumulation in guinea pig was 50% less than in the rat (see Figure). Supplying amiloride (1mM) before ischemia delayed and reduced by 50% the accumulation of Na_i^+ during ischemia in the rat but had no effect in the guinea pig (see Figure). Thus amiloride abolishes the differences between these two species. These results show that the network of sarcolemmal ion pumps and exchanges (particularly Na/H exchange) differs in rat and guinea pig hearts and that these differences lead to altered Na handling upon ischemic challenge.



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35.3

THE EFFECTS OF BLOOD FLOW, GROWTH AND HYPOXIA ON TUMOR METABOLISM AS DETERINED BY NMR.

P. Okunieff. Massachusetts General Hospital, Dept. of Radiation Medicine, Boston, MA 02114.

Tumor pathophysiological factors are the key determinants of the success of most non-surgical treatment modalities. Under conditions of hypoxia, that commonly exist in tumors due to a disordered and insufficient vascular supply, cellular viability is often maintained while the effectiveness of radiation and various chemotherapeutic drugs are reduced. Likewise, with poor delivery of drugs in such areas, successful response to chemotherapy is prevented. Using ^{31}P NMR spectroscopy it is now possible to indirectly and non-invasively measure tissue oxygenation. New methods using ^{2}H NMR should permit blood flow measurements with the resolution of positron emission tomography. Ultimately, serial studies of a patient's tumor after various pharmacological alterations of physiology, should result in more efficacious and less toxic individually tailored treatment regimen.

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35.4

NMR SPECTROSCOPIC STUDIES OF ENERGY METABOLISM AND ACID-BASE BALANCE IN INVERTEBRATES. W. Ross Ellington, Florida State University, Tallahassee 32306.

Our group utilizes phosphorus NMR spectroscopic techniques to probe various aspects of energetics and regulation of intracellular pH (pH_i) in muscles from a variety of marine invertebrates. In this presentation we will briefly discuss three examples of the kinds of information that can be derived from such NMR studies-- (1) evaluation of the thermodynamic properties of the various phosphagen kinase reactions, (2) estimation of the apparent association constants for MgATP formation and the free Mg^{2+} concentrations in muscle cells under a variety of physiological circumstances, and (3) measurement of the non-bicarbonate buffering capacity and pH_i in isolated muscle preparations. The discussion will focus on the inherent limitations of the NMR approach (such as time resolution, sensitivity and digital resolution of chemical shift) as well as the underlying assumptions in the use of these methods. (Research supported by NSF grants DCB-8401258 and DCB-8710108)

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35.5

DIRECT MEASUREMENT OF THE FRACTIONAL DISSOCIATION OF IMIDAZOLE IN INTACT UNANESTHETIZED ANIMALS BY 1H NMR. B. M. Hitzig, Pulmonary Unit, Depts of Medicine and Physiology, Harvard Med. Sch. & Mass. Gen. Hosp. Boston, MA.

Regulation of the fractional dissociation of protein imidazole (Alpha Im) has been advanced as the regulatory scheme involved in acid-base homeostasis of animal body fluids and tissues. Until now, it has been impossible to test this hypothesis because there was no method for direct measurement of Alpha Im. We have devised a method of directly measuring Alpha Im in the cells of white skeletal muscle of Eastern Newts (*Notophthalmus viridescens*, n=12) using ^{1}H NMR spectroscopy. By measuring the chemical shift of the imidazole group of carnosine (15-20 mM in amphibian white skeletal muscle) we have determined that Alpha Im remained constant at 0.56 (±0.01) over a body temperature range of 20°C (10, 20 and 30°C). We were able to calculate intracellular pH (pHi) using our previous measurements of the pK of carnosine. pHi was 7.19 (±0.02) at 10°, 7.05 (±0.02) at 20°, and 6.90 (±0.02) at 30°C. This resulted in a dpHi/dT of 0.016 units/°C. These results compare favorably with direct measurement of pHi by ^{31}P NMR (7.22 ±0.06 at 10°C, 7.04 ±0.04 at 20°C, and 6.90 ±0.04 at 30°C). Our results support the Alpha Im hypothesis of Reeves. To the best of our knowledge, this study represents the first direct measurement of Alpha Im in the tissues of intact, unanesthetized animals. Supported by Am. Ht. Assoc. Grant-In-Aid 861030.

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36.1

RENIN-ANGIOTENSIN SYSTEM IN CARDIOVASCULAR HOMEOSTASIS: USE OF NONMAMMALIAN MODELS. Hiroko Nishimura. Univ. of Tennessee, Memphis, TN 38163

I will present two nonmammalian models investigating the role of the renin-angiotensin system (RAS) in cardiovascular homeostasis and discuss their biomedical implications. The first model, the aglomerular toadfish (*Opsanus tau*) kidney, is for determining the signals for cellular control of renin release. This model offers 1) an anatomically simpler juxtaglomerular apparatus, and 2) a baroreceptor or stretch receptor for control of renin release. Renin release from toadfish renal slices is suppressed by treatments that increase Ca^{2+} influx or cytosol Ca^{2+} levels, whereas cyclic AMP has no stimulatory effect. Protein kinase C and calmodulin may be involved in cellular signal transduction. Thus, in this model, we can elucidate the role of the Ca signal pathway in the control of renin release that may underlie the renal arterial baroreceptor. The second model, fowl arteries that exhibit relaxation in response to angiotensin (ANG), is for examining the role of the RAS in the control of vascular tone. Many avian species show elevated blood pressure (BP). ANG causes vasocontraction by releasing catecholamines. ANG II also causes endothelium-dependent relaxation of the fowl aorta inhibited by hemoglobin and hydroquinone, but independent of arachidonate metabolism. ANG II receptors exist in the aortic endothelium, and relaxation may be mediated by cyclic GMP. ANG II-induced relaxation becomes more dominant as chickens mature, but decreases after atheromatous lesions develop. Thus, the fowl vascular system provides a useful model for investigating interactions among the vascular endothelium, smooth muscle, and RAS in the control of vascular function and BP.

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36.2

COMPARATIVE STUDIES ON HORMONES, CELLULAR CALCIUM REGULATION AND CARDIOVASCULAR FUNCTION

Peter K.T. Pang
Department of Physiology, University of Alberta, Edmonton, Alberta, Canada T6G 2H7

Hormones are important in the maintenance of a stable plasma calcium level. Intestinal absorption, bone turnover and renal excretion all contribute to produce such an equilibrium. However, cells use calcium as an intracellular messenger. Plasma calcium is the source of intracellular calcium. Therefore, the use of calcium by the cells is part of the overall balance, as indicated by plasma calcium level. Hormones can affect the regulation of intracellular calcium balance. Our recent studies on the endocrine control of cellular calcium regulation in lower vertebrates reveal some interesting evolutionary findings, some of which have led to significant discoveries in mammals and humans.

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36.3

REPTILIAN MODELS FOR THE STUDY OF CARDIOVASCULAR HOMEOSTASIS. Harvey B. Lillywhite. Univ. of Florida, Gainesville, FL 32611

Reptilian cardiovascular systems exhibit wide variation in form and function attributable to phylogeny, variation in body architecture and ecological diversification. In addition, temporal instability of circulatory processes is imposed by variations of body temperature (related to ectothermy), activity and pH of body fluids. From a regulatory point of view, these unstable components, in addition to adaptive variation, provide useful experimental probes for discovering what properties of the cardiovascular system are regulated, the mechanisms involved, and how they interact with other aspects of integrated homeostasis. Comparative studies allow identification of those aspects of the circulation that are susceptible to perturbation and the range of adaptations that are employed to offset instability. Therefore, reptiles have provided useful models for understanding cardiovascular homeostasis and its attendant adaptations (e.g., 1-3). Because, in general, vertebrate cardiovascular systems have evolved in parallel with metabolic and respiratory requirements of tissues, knowledge of primary processes in reptilian systems is usually transferable to other vertebrates. For reasons related to practicality, availability and social or regulatory issues, in addition to advantages already mentioned, the value of reptilian models in cardiovascular research will likely continue to increase.

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36.4

Hereditary Nephrogenic Diabetes Insipidus in Domestic Fowl: A Model for Basic Studies. Eldon J. Braun. Dept. of Physiol., Col. of Med.,Univ. of Arizona,.Tucson AZ. 85724.

Nephrogenic diabetes insipidus is the excessive intake of water caused by a failure of the kidneys to respond to antidiuretic hormone (ADH). The physiologically appropriate response of the kidneys to ADH is to excrete solutes in excess of water. Much of what is known of HNDI has been learned from one animal model, a strain of domestic mice described by Falconer et al.('64). The present paper describes a second animal model-a strain of domestic chickens that can be exploited to study HNDI. In these birds, the males drink water at a rate of 24.0% of their body mass (BM) per day (controls 5.4%) and the females drink at the rate of 51.4% (controls 11.7%) of BM per day. The plasma osmolality of the HNDI birds tends to be higher than that of normal controls (males 319 vs. 311; females 323 vs. 310), and the urine osmolality is substantially lower than that of controls (males 90 vs. 524; females 70 vs. 245). The basal ADH levels were markedly higher in the HNDI birds than in normal controls (males 9.9 μU/ml vs. 1.73; females 2.45 vs. 7.04). Additional data will be presented to support the idea that these birds indeed can serve as a model to study HNDI.

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36.5

CONTROL OF RENAL HEMODYNAMICS: THE AVIAN RENAL PORTAL CIRCULATION AS A MODEL. R.F. Wideman, The Pennsylvania State University, University Park, PA 16802.

A simplified avian kidney model has been developed and validated (1). This model permits independent manipulation of renal arterial perfusion pressure (RAPP) and renal portal flow. Avian GFR is autoregulated between 60 and 120 mmHg RAPP. The autoregulatory profile is unaltered by large differences in dietary sodium. As RAPP is reduced below 60 mmHg, reductions in GFR are not associated with sustained glomerular intermittency. Positive correlations exist between RAPP and sodium excretion (pressure natriuresis), while RAPP and urine osmolality are negatively correlated (2,3). Effective renal plasma flow, estimated by PAH clearance, remains constant over the entire RAPP range tested (30-120 mmHg). Constant PAH clearances could reflect RAPP-induced alterations in PAH extraction efficiency, or co-autoregulation by the portal system. Renal plasma flow (RPF) was assessed at normal (100-110 mmHg) or reduced (40-50 mmHg) RAPP in birds with ambient or restricted portal flow. PAH extraction efficiency was unaffected by RAPP. RPF was perfectly autoregulated in birds with ambient portal flow, but RPF decreased along with RAPP in birds with restricted portal perfusion. The avian renal portal system contributes to overall RPF autoregulation, maintaining constancy of renal blood flow after RAPP is reduced well below the GFR autoregulatory limit. "Perfect" RPF autoregulation may subserve cell maintenance during glomerular intermittency.
KEY WORDS: Autoregulation, Pressure Natriuresis.

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36.6

FISH ADAPTATION TO CHANGES IN SALINITY: A MODEL FOR UNDERSTANDING THE PHYSIOLOGICAL ROLE OF VASOACTIVE PEPTIDES. Sara M. Galli. Deptx of Physiology, University of Florida, Gainesville, FL.

Lower vertebrates offer useful models for the study of hormonal control of body fluid and Na+ excretion. We have studied peptide hormones in Na+ balance in fish. The shark, Ginglymostoma cirratum was used after the removal of the rectal gland as a model to study the effect of Na+ load in fish. It was found that plasma angiotensin II levels rises in parallel with the increase of Na+ in the plasma. The effect of Na+ depletion, by adapting the fish to 50% SW caused a 100% increase in pAng II levels (1). Since euryhaline fish move between sea water and fresh water, they present a biological model to study hormonal interactions with Na+ changes. Atrial natriuretic peptide (ANP) was measured by RIA and HPLC in Fundulus heteroclitus Opsanus tau, Mugil cephallus and Tilapia mosambicus. Each species showed a significant decrease in plasma ANP but a pronounced increase in brain and pituitary ANP levels as they were moved from sea water to fresh water. These effects were reversible. The results demonstrated that ANP plays a physiological role in the control of Na+ excretion in fish. This ancient function may have been conserved throughout evolution as an adaptive mechanism in response to changes in Na+ intake. Further studies also point out an independent role for ANP in the brain and pituitary, where ANP may serve as a neurotransmitter controlling dopamine and other peptides involved in Na+ balance such as angiotensin and prolactin. Lower vertebrates can revel fundamental osmoregulatory functions which have been preserved. They have unique features which can be used to advantage for physiological research.

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37.1

INTRACELLULAR AND EXTRACELLULAR ACID-BASE REGULATION IN ANIMALS: AN OVERVIEW. James N. Cameron. Univ. of Texas, Marine Science Institute, Port Aransas, TX 78373

An argument can be made for pH as a master control in biological systems. A majority of metabolic reactions both influence and are affected by pH, setting the stage for a complex feedback regulation system whose objective is maintaining constant protein charge ("Z-stat model"). The principal determinants of extracellular pH are H^+ influx from metabolism and H^+ efflux either directly via ionic exchange or indirectly via changes in CO_2 excretion. This general relation is true for all animals, though the organs and pathways for both ion movement and gas exchange differ. In aquatic animals CO_2 is excreted to water via gills or skin, but since the dominant problem in water is obtaining oxygen, CO_2 excretion is not closely regulated. Ion exchanges dominate extracellular pH regulation, with gills playing a primary role and kidneys a minor one. In terrestrial vertebrates, both lungs and kidneys have major roles in extracellular pH regulation, with a complex partitioning of responses either temporally or according to the type of acid-base challenge. The primary determinants of intracellular pH are metabolic H^+ generation and the counterbalancing ion exchanges carried out by membrane proteins. Several models are currently advanced, including a Na^+/H^+ antiporter, Na-dependent Cl^-/HCO_3^- exchange, $Na+/-HCO_3^-$ cotransport, and Na^+/monocarboxylate exchange. The similarities between animals as diverse as squid and man suggest that pHi regulating mechanisms are old and strongly conserved.

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37.2

ACID-BASE REGULATION IN TERRESTRIAL MOLLUSCS. M. Christopher Barnhart. University of San Diego, San Diego, CA 92111

The control of pH via ventilatory control of PCO_2 evolved convergently in at least 3 groups of land animals: vertebrates, decapod crustaceans, and pulmonate snails. In active snails, Otala lactea, diffusion in the gas phase presents only about 25% of total resistance to O_2 uptake but accounts for nearly 97% of resistance to CO_2 release via the lung. Thus, CO_2 release is much more ventilation-sensitive than is O_2 uptake. Changes in lung and hemolymph gas tensions demonstrate control of pH via PCO_2 during temperature change and in compensation for metabolic acidosis. In contrast to active periods, periods of dormancy are accompanied by hypoventilation, acidosis and fluctuations of pH due to accumulation and episodic release of respiratory CO_2. During dormancy, lung ventilation becomes limiting for O_2 uptake and sensitive primarily to PO_2. The precise ventilatory control of PCO_2 and pH is abandoned. Measurements using DMO indicate that CO_2 affects intracellular and extracellular pH similarly in most tissues. Effects of CO_2 on oxygen consumption of intact snails are consistent with a role in metabolic regulation during dormancy. However, the mechanism of influence on cellular metabolism is unknown and may be indirect. Unlike the respiration of whole animals, that of isolated cells and tissues of Otala incubated in physiological saline is relatively insensitive to PCO_2.

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37.3

EXTRACELLULAR AND INTRACELLULAR ACID-BASE REGULATION IN CRUSTACEANS. Michele G. Wheatly. Univ. of Florida, Gainesville, FL 32611

The crustacean subphylum encompasses water and air-breathing species; differences in acid-base status and regulation are related to gas properties of the media. Body fluid compartments include intracellular (IC), extracellular (EC, possibly subcompartmented) and external (for aquatic and semi-terrestrial species). pH is determined by total buffer, PCO_2 and strong ion difference (SID). IC pH, (pHi, typically 0.5 pH units below EC), plays a pivotal role in regulating cell metabolism. Regulation of pHi (via buffering, metabolism or passive inorganic electroneutral ion exchange, 1) will be illustrated during exercise, temperature change, hyperoxia and aerial exposure (aquatic species) and hypercapnia (terrestrial). The ECF is the intermediary between cells and external exchangers. pHe homeostasis also preserves the function of EC respiratory proteins. Regulation of EC acid-base disturbances (2) generated endogenously (exercise, molting) and exogenously (changes in external gas tensions, ionic composition, temperature, pH or combinations thereof) will be discussed in terms of (a)buffering by ECF and mineralized tissues (b) regulation of SID at gills and antennal gland (predominantly water breathers) and (c) ventilatory control of PCO_2 (air breathers). Evidence will be presented for bidirectional exchange of ions with the external medium at the gill and unidirectional efflux via the kidney. Finally an integrated approach to whole animal acid-base balance (3) will be illustrated in aquatic crustaceans under the following experimental conditions: hyperoxia, external dilution, exercise and aerial exposure. (Supported by NSF 89-16412).

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37.4

RELATIONSHIPS BETWEEN ION AND ACID-BASE REGULATION IN FISH. C.M. Wood and S.F. Perry, Biology Depts., McMaster Univ., Hamilton Ont. L8S 4K1 and Univ. of Ottawa, Ottawa Ont. K1N 6N5, Canada.

Na^+/"acid" and Cl^-/"base" exchanges on the gills of freshwater fish are dynamically manipulated so as to correct internal acid-base disturbances, in accord with electroneutrality and SID relationships. In trout, both influx and efflux components of strong ion movements are adjusted. Kinetic analyses demonstrate that the affinities (Km) of the Na^+ and Cl^- influx mechanisms are normally maximal, and can only be decreased, but maximum capacities (Jmax) can be either increased or decreased for the purposes of acid-base correction. Changes in Jmax can be explained partially by changes in the internal availability of "acid" and "base" counterions, and partially by morphological adjustments of the gill epithelium. The branchial "chloride cell" appears to be an important site of Cl^-/"base" exchange. In catfish, reduced Cl^-/"base" exchange during compensation of hypercapnic acidosis is paralleled by a reduction in the surface area of filamental chloride cells. This phenomenon is apparently caused by a covering by adjacent "pavement cells". In addition, the pavement cells exhibit an increase of apical microvilli density and proliferation of mitochondria. We suggest the pavement cell response may contribute to elevated Na^+/"acid" exchange at this time. (Supported by NSERC grants to CMW and SFP).

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37.6

INTRACELLULAR pH REGULATION BY HEPATIC TISSUES. Patrick J. Walsh and Thomas P. Mommsen, Univ. of Miami, FL 33149 and Univ. of Victoria, BC

Because of its structural complexity and metabolic diversity, liver was not the tissue of choice in initial experiments on the ionic mechanisms of pHi regulation. However, as our basic understanding of pHi regulation for ostensibly simpler tissues grew, much more research focused on acid-base regulation in hepatic tissue from mammals, fish and crustaceans. This review examines three aspects of acid-base regulation in hepatic tissues from a comparative viewpoint: (1) ionic transport mechanisms (e.g., Na^+/H^+ exchange, lactate transport, bile acid transport, etc.); (2) the role of physicochemical buffering; and (3) the complex interplay between metabolism and acid-base regulation. We pay particular attention to recent studies which demonstrate marked transport and metabolic heterogeneity within and between hepatocytes, and to the potential of hepatocytes in long-term culture to serve as models for adaptations to chronic acid-base disturbances.

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37.7

REGULATION OF ACID-BASE STATUS IN HUMANS DURING EXERCISE. Norman L. Jones, McMaster University, Hamilton, Canada.

During and shortly after heavy exercise intramuscular $[H^+]$ may exceed 300 nEq/l (pH less than 6.5). The response to this acid challenge involves the movement of water, strong ions and CO_2 between a number of body fluid compartments and tissues. The main contributors to the increase in $[H^+]$ in the active muscle are reductions in [SID] of up to 35 mEq/l (net effect of a >45 mEq/l increase in $[La^-]$, >20 mEq/l reduction in $[K^+]$ and 30 mEq/l reduction in $[CrP^{---}]$), and increased PCO_2 to >100 mmHg, together with a 7% increase in muscle water. In venous blood draining the active muscle, large increases in $[La^-]$ and $[K^+]$ are found in plasma and RBC, PCO_2 increases and plasma water falls by 15%, tending to increase [Atot]. CO_2 is rapidly excreted in the lungs; thus in arterial plasma, reductions of 10 mEq/l in [SID], secondary to increases in $[La^-]$, are counteracted by reductions in PCO_2. Erythrocytes in venous and arterial blood take up La^-, but $[La^-]$ increases to only half the plasma $[La^-]$; K^+ is also taken up in RBC. Inactive tissues take up K^+ and also take up and metabolize La^-, at the expense of an increase in CO_2 production. Studies in isolated muscle and intact animals during exercise indicate important roles for osmolar factors together with active and passive membrane ion transport, in addition to local fuel utilisation, circulation and ventilation, in the overall response of the organism to an acute acid-base challenge.

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52.1

EVOLUTIONARY HISTORY OF THE BLOOD O_2 CARRIERS. Charlotte P. Mangum. College of William & Mary, Williamsburg, Va. 23185.

Based on composition of the active site there are three categories of O_2 carriers in animal bloods: heme proteins, hemerythrins and hemocyanins. High resolution crystallography has recently revealed striking structural similarities in their metal-binding helices, which has led to the hypothesis that the three had a common origin from an ancestor of the hemocyanins (Volbeda and Hol, 1989). This inference is inconsistent with both the zoological distribution and the respiratory properties of the O_2 carriers. An interpretation of function in the light of phylogenetic relationships and respiratory-circulatory design as well as quaternary molecular structure suggests a minimum of 5-6 separate origins, with a simple hemoglobin as the archetype. The integrated evidence also elucidates selection of O_2 carriers in various taxa, including elaboration within the lower vertebrates of a heterotetrameric hemoglobin capable of having distinctive intrinsic properties in different species as well as extrinsic modulation within species. I suggest that, when invoked in isolation, macromolecular evidence is no more (or less) capable of distinguishing convergence from conservatism in evolution than any other.

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THE ROLE OF CONCENTRIC GRANULES IN NITROGENOUS EXCRETION AND ION REGULATION IN BIRDS, MOLLUSCS AND INSECTS

55.1

STRUCTURE AND COMPOSITION OF UREIC ACID GRANULES FROM THE FAT BODIES OF INSECTS. J.S. Buckner. USDA, Fargo, ND.

Uric acid, a major excretory product of nitrogen metabolism in insects, is synthesized mainly in fat body cells. For lepidopteran insects during metamorphosis, the excretory system is not functional and the fat body cells serve as the major site for uric acid storage. Electron microscopic examinations of fat body cells from last-instar larvae of the tobacco hornworm, *Manduca sexta*, (L.), revealed that uric acid storage is associated with discrete membrane-bound fibrous structures, designated as uric acid storage vacuoles. The round- or elliptical-shaped vacuoles are 0.5 to 1.5 μm in diameter with electron-dense fibrous interiors. Dense uric acid granules have been purified from the fat body of larval *M. sexta*. The near spherical or biconcave shaped granules are composed of tightly coiled fibers of crystalline uric acid/urates (mainly potassium) and each fiber appears to be enveloped with proteins/glycoproteins. The current understanding of the formation, composition, dissolution and function of these granules will be presented. Comparisons will be made with other uric acid concretions in terms of structure and composition.

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55.2

URIC ACID TRANSPORT IN THE MALPIGHIAN TUBULES OF RHODNIUS PROLIXUS AND OTHER INSECTS. M.J. O'Donnell, Dept. Biology, McMaster U., Hamilton, Ontario, L8S 4K1, Canada.

Uric acid is the major nitrogenous excretory product of insects (1). Because of its high (33%) nitrogen content and low solubility under the acid conditions of the insect hindgut, its elimination leads to excretion of large amounts of nitrogen without incurring much loss of water. In the blood-feeding bug R. prolixus urate is transported against an electrochemical gradient into the lumen of the proximal Malpighian tubule. In vivo, higher urate transport rates are induced by the increase in haemolymph urate concentration that follows feeding. The induced rate of transport is sufficient to account for the quantity of urate eliminated (2). In vitro experiments using isolated Malpighian tubules (3) of the tsetse fly Glossina suggest a possible induction of transport as a direct response of the tubule cells to increased urate concentration in the bathing saline. Urate transport has been demonstrated in tubules of insects from several different orders, suggesting that the mechanism is widespread. Insect urate transport differs from that of vertebrates; it is ouabain-insensitive and results in the precipitation of free uric acid instead of urate salts.

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55.3

INTRA- AND EXTRACELLULAR CONCENTRIC GRANULES IN THE MALPIGHIAN TUBULES OF INSECTS. T.J. Bradley. Univ. of California, Irvine.

In a large number of insect species, mineralized concretions are associated with the Malpighian tubules. The most common and widespread concretions in insects are those termed "laminate spheres" or "concentric concretions". These occur either as intracellular concretions bound by a vacuolar membrane, or as extracellular concretions in the lumen of the Malpighian tubules. The intra- and extracellular concretions are similar in ultrastructure, consisting of concentric circles of alternating electron lucent and electron opaque material. The chemical composition of concretions from numerous insect tissues and species have been chemically analyzed. Although the elements present are diverse, the common theme seems to be the presence of divalent cations, particularly calcium. It is my intention to review our present understanding of the formation, composition and function of concentric concretions in insect Malphighian tubules. Recent advances including the use of selected strains lacking intracellular concretions will be discussed.

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55.4

STRUCTURE AND FUNCTION OF CONCENTRIC GRANULES IN MOLLUSCS. H. Silverman and T.H. Dietz. Louisiana St. Univ., Baton Rouge, LA 70803

Granules composed of calcium carbonate or phosphate are located in tissues of gastropods and bivalves. Most of these granules have a "concentric ring" type structure and are morphologically similar. However, the inorganic and biochemical composition, and function of the granules varies with species and even among organs in the same species. The best studied are intracellular granules found in the digestive organs of land snails and the gills of freshwater (FW) bivalves. Functions of the granules include the binding of toxic metals for detoxification and storage of calcium for reproductive purposes. The concretions found in the gills of FW mussels are characterized for their mineral phase, inorganic composition, partial biochemical characteristics, and specific function in the animal. These concretions are mobilized during reproduction and the liberated calcium is transferred to embryos which develop in the gill. Similarly, for other molluscan concretions, partial characterizations of chemical composition, morphology, and function have been documented. We will briefly review progress on FW mussel concretions and several other molluscan concretion systems. Comparison will indicate some similarity between systems, but more importantly lack of chemical and functional uniformity for these granules. They play several different key roles in molluscan physiology that have been identified, and it is likely that additional roles will be discovered.

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55.5

Structure and Composition of Spherical Concretions of Avian Urine. Eldon J. Braun. Dept. of Physiol., Coll. of Med., Univ.of Arizona, Tucson, AZ. 85724.

Birds excrete nitrogen primarily in the form of uric acid. At the pH of plasma (ca. 7.4), uric acid exists primarily as an anion forming monobasic salts. Furthermore, uric acid is secreted by the renal tubules as an anion and therefore should appear in the urine as monobasic salts of various cations (sodium, potassium, etc.). Based on these considerations, when avian urine is allowed to dry on a surface, crystals of uric acid and urate salts should be observable. However, given these conditions few if any crystal types are seen when avian urine is allowed to dry. Instead, small, spherical structures are observed that range in diameter from 0.5 to about 15 μm. Analysis of pellets of avian urine formed by centrifugation and dried to a constant mass show that these spherical structures are composed of at least 60% uric acid. The chemical form of uric acid in the spheres is not known at present. X-ray microanalysis of individual spheres shows that they contain significant quantities of calcium, potassium and other cations and anions. The nature of the material constituting the remainder of the sphere mass (the organic matrix) is unknown at this time. The evolutionary significance of excreting uric acid in this form will be discussed.

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56.1

STUDIES OF MARINE BACTERIA AND AMPHIPODS UNDER HIGH PRESSURE WHILE AT SEA. A. Aristides Yayanos. Scripps Institution of Oceanography, UCSD, La Jolla, CA 92093-0202

The pressure gradient in the oceans is one of its major environmental features. Over the past twelve years, bacteria were isolated from a variety of deep-sea samples. These were taken from the Pacific Ocean, the Celebes, Sulu, and Mediterranean Seas. The Pacific bacterial isolates came from a 2^{o}C environment. The other seas offer deep-sea temperatures as great as 13.5^{o}C. Study of the pressure dependence of the rates of reproduction of bacteria from depth-separated habitats shows that pressure itself must be one of the key determinants of zonation and evolution in the sea. If we assume that animal tolerance to environmental change will be less than that of bacteria, then the bacterial results provide values for the upper bounds of pressure tolerance for any other organism. Pressure tolerance studies of amphipods retrieved under pressure from 2,000, 5,800 and 10,500 m suggest that animals are, indeed, less tolerant of pressure change than are bacteria. Although studies with deep-sea bacteria are straightforward with small-scale pressure apparatus, future work with deep-sea animals will continue to develop slowly because of expensive shiptime and of costly and unwieldy pressure vessels.

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56.2

SOCIAL SIGNALS IN SOUTH AMERICAN GYMNOTIFORM ELECTRIC FISH. Mary Hagedorn. Inst. of Neuroscience, University of Oregon, Eugene, OR. 97403

During the breeding season, the South American gymnotiform, Hypopomus occidentalis, exhibits both a sexually dimorphic electric organ discharge (EOD) and electric organ morphology that are sensitive to social and environmental conditions (Hagedorn, 1986; Hagedorn and Carr, 1985). The biphasic EOD is symmetric in females and asymmetric in males. The second phase of the male's signal was lower in amplitude and longer in duration. When Fourier analyzed, the male's EOD had a lower peak-power frequency than the EOD of the female. Lower peak-power frequency EODs reflected higher dominance status amongst males, as was demonstrated in behavioral exclusion experiments. If males were removed from social conditions in the field, however, their EOD reverted to a female-like EOD within 24 Hrs. Electrical and morphological changes that naturally occurred in males during the breeding season could be mimicked in females by treatment with androgens. This resulted in cells in the electric organ enlarging and a reduction in the peak-power frequency of the female's EOD. Physiological recordings suggested that these changes in the EOD correlated with physiological changes that occurred at the level of single cells within the electric organ.

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56.3

DIVING PHYSIOLOGY AT SEA: SEALS, PENGUINS AND COMPUTERS. Michael Castellini. Institute of Marine Science, University of Alaska, Fairbanks.

While laboratory based studies have provided significant insights into the physiological abilities of diving vertebrates, to understand how these animals regulate diving in nature requires a different approach. Experiments must be designed that can gather remote physiological data from animals at sea. Two separate approaches have been utilized: The first uses physiological recorders that must be retrieved and the second uses satellite technology to transmit physiological data. The goal of this work is to understand the metabolic cost of diving using a comparative approach as well as to create a working model of foraging energetics. Based on this model, it appears that a significant factor in diving physiology is the need for high efficiency. If a diving vertebrate is trying to spend as much time underwater as possible, then certain physiological pathways must be chosen (for example, the need to reoxygenate as rapidly as possible at the surface). By combining physiological data from both the laboratory and the field, we can better model how diving vertebrates are able to routinely tolerate the physiological demands of repeated bouts of hypoxia.

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56.4

FIELD MEASURES OF MARINE MAMMAL BODY COMPOSITION USING BIOELECTRICAL IMPEDANCE ANALYSIS. Graham A.J. Worthy* (SPON: M.A. Castellini). Texas A&M University at Galveston, Galveston, TX 77553-1675

Critical features in the field application of any technology are its speed and simplicity. Body composition has been measured in a variety of ways, but most of these techniques require expensive, bulky equipment or lengthy equilibration periods. Bioelectrical impedance analysis (BIA) is a rapid portable method of assessing body composition that has only recently been applied to non-humans. I have validated the BIA system, against tritium dilution, with California sea lions and northern elephant seals and have derived a predictive equation incorporating length, girth, mass and resistance (R=0.92, n=40). This relationship has been used to determine body compositions of these two species plus bottlenose dolphins in order to monitor seasonal and annual changes in body condition. This technique is accurate and easy to use, allowing for the processing of large numbers of animals. The applications of BIA are twofold: 1) it facilitates the collection of condition data from wild animals to set body condition standards for captive animals, and 2) it allows for effective monitoring of wild populations to act as an index of environmental quality and food availability.

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AVIAN FASTING PHYSIOLOGY - HOW BIOCHEMISTRY INFLUENCES BEHAVIOR IN EMPEROR PENGUINS. Yvon Le Maho* and Jean-Patrice ROBIN*. LERP-CNRS, 67087 Strasbourg cedex, France.

Under natural conditions, the male emperor penguin is fasting for 3-4 months in association with courtship and incubation. He is usually relieved by the female. However, when she does not come back, he prolongs his fast and finally leaves, abandonning egg or chick to refeed at sea. We found that the lowest body masses of emperors correspond to the situation of prolonged fasting where there is a progressive increase in protein utilization. At this stage, as much as 20% of lipid reserves still remain available, which allows the birds to walk over the long distance of sea-ice (up to 200 km) between the colony and the sea. Since other investigators found that the fasting induced rise in locomotor activity in laboratory rats reflects search for food, we studied the changes in locomotor activity in emperor penguins kept into an enclosure. There was a dramatic rise in their activity when they entered into the stage of increasing protein utilization. Altogether, these data accord with the idea that there is an "internal signal" which triggers refeeding in emperor penguins. It is associated with a physiological change that anticipates a critical depletion in energy reserves. Other data for wild animals suggest that the existence of this "signal" could be generalized.

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56.6

MEASURING METABOLIC RATE IN THE FIELD - LABELED WATER USED IN CONJUNCTION WITH ACTIVITY BUDGETS Daniel P. Costa Institute of Marine Science, University of California, Santa Cruz, CA 95064

Simultaneous measurements of energy expenditure derived from doubly labeled water (DLW) and time-activity budgets can provide significant insights into an animal's physiology and ecology. With respect to diving vertebrates, such measurements provide insight into the physiological constraints associated with breath hold diving (Castellini and Kooyman 1989). For example, data on dive duration and oxygen consumption derived from time depth recorders and DLW measurements of Australian sea lions suggests that their dives routinely exceed the oxygen stored in their blood, muscle and lungs. Whereas equivalent data on California sea lions indicates that their dives do not exceed their oxygen stores. An understanding of the costs associated with different behaviors can also be acquired from such measurements (Costa 1988). For example, data on dive pattern and energy consumption provide information on the energetic cost and benefit of particular foraging patterns. Data on fur seals and penguins suggest that deep diving is only energetically beneficial while foraging on large prey. Large prey can supply a significant fraction of the energy requirement of the predator with each dive. In contrast, predation on small prey, where many individuals must be captured per dive, appear to be limited to shallow depths. Several possible explanations for these patterns rely on differences in transit time and rate of oxygen utilization during the dive (Costa 1990). The application of these techniques will be summarized along with a discussion of the ways such data can be intrepreted to increase our understanding of the physiology of freely living animals.

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57.1

PHYSIOLOGY OF ATRIAL NATRIURETIC FACTOR (ANF): OVERVIEW OF MOLECULAR PROPERTIES, SYNTHESIS, MECHANISM OF ACTION AND PHYSIOLOGICAL IMPLICATIONS. Tadashi Inagami. Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, TN.

At least four related genes for ANF exist. While major sites of synthesis are the atria of the heart, they are synthesized in the brain and many other tissues. ANF precursors undergo complex processing in different tissues. The expression of ANF action is mediated by its receptors which contain the ANF binding domain and guanylate cyclase domain. The ANF mediated receptor function is mediated by various factors such as ATP and protein kinase C. Two major groups of ANF receptors are distributed very widely in many tissues. Its natriuretic and diuretic functions and inhibition of renin release is the major physiological functions involving the kidney. In addition to hemodynamic effect, ANF has a direct action on a Na-channel in collecting duct. ANF is also inhibitory to many endocrine and neuro endocrine functions. In diseases, it is markedly elevated in congestive heart failure. While it has a potent hypotensive effect, it does not seem to be related to hypertension.

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57.2

ATRIOPEPTIN IN FISHES: PRESENCE AND POTENTIAL SITES OF ACTION. David H. Evans, University of Florida, Gainesville, FL 32611, and Mt. Desert Isl. Biol. Lab., Salsbury Cove, ME 04672.

Osmotic and ionic gradients across the permeable branchial epithelia of fishes result in chronic gains or losses of water or salts depending upon the salinity. There is an emerging literature which indicates that a cardiac, peptide hormone (atriopeptin or atrial natriuretic peptide) may play a role in fish osmoregulation. Antibodies directed toward mammalian AP detect a putative hormone in plasma, atria, ventricles, and brain of a variety of fish species. Acclimation of two euryhaline species of teleost fishes to reduced salinity, producing a volume load, reduces the AP_{ir} in the plasma. Synthetic rat AP produces concentration-dependent dilation of ventral aortic rings from a variety of species. Mammalian AP produces natriuresis in both a freshwater, glomerular and marine, aglomerular teleost, as well as stimulation of elasmobranch rectal gland secretion and teleost chloride cell salt extrusion, but inhibition of teleost intestinal salt uptake. Homologous atrial, ventricular, and brain extracts also produce vasodilation, and a vasoactive and natriuretic peptide hormone has now been isolated and sequenced from Japanese eel atria. Taken together, these data suggest strongly that a fish atriopeptin exists and may function in control of branchial hemodynamics and/or salt extrusion, rather than reduction in plasma volume, as it apparently does in mammals. (Supported by NSF DCB 8801572 and DCB 8916413)

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57.3

CARDIOVASCULAR EFFECTS OF ATRIOPEPTIN IN FISH. K. R. Olson. Indiana University School of Medicine, South Bend Center, University of Notre Dame, Notre Dame, IN 46556.

Atriopeptin-like peptides (AP) are, for the most part, ubiquitous in the hearts and plasma of fish. As is the case in mammals, AP exerts profound and stereotypical responses in vitro, whereas the physiological function of these peptides in vivo is unclear. Vascular rings or strips from fish arteries, either unstimulated or precontracted with a variety of agonists, exhibit a dose-dependent and endothelium-independent relaxation when exposed to synthetic AP or fish heart extracts. AP levels required for half-maximal inhibition are in the low to mid-nanomolar range; around 100 times higher than plasma levels. AP effects on vascular smooth muscle appear to be mediated through classical guanylate cyclase-activated mechanisms. AP decreases vascular resistance in perfused tissues including elasmobranch rectal gland and teleost gill, splanchnic and skeletal muscle-renal preparations. Injection of fish heart extracts or synthetic AP into intact fish may produce a depressor (shark, eel, toadfish) or pressor (trout) response, or have no effect (shark, toadfish). The pressor response observed in trout appears to be mediated through sympathetic nervous system activation and it is likely that many of the physiological functions of AP in vivo involve secondary reflexes. Future research using homologous peptides, at physiological doses, is clearly required to delineate the role of these peptides in the piscine vasculature. Supported by NSF Grants PCM 840497 and DCB 8616028.

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57.4

EFFECTS OF ATRIOPEPTIN ON INTESTINAL AND GILL ION TRANSPORT IN FISHES. Scott M. O'Grady, College of Veterinary Medicine, University of Minnesota, St. Paul, MN 55108.

Serosal addition of atriopeptin (ANP) to the isolated intestinal epithelium of the winter flounder resulted in inhibition of short-circuit current, transepithelial Na and Cl absorption and ^{86}Rb influx across the apical membrane (1). These effects appear to result from a direct action of ANP on the epithelium since pretreatment with tetrototoxin or indomethacin did not alter the response to ANP. The concentration-response curve for atriopeptin 3 showed half-maximal inhibition of NaCl absorption at 7 nM. ANP produced a 4 fold stimulation of cGMP content without altering the cAMP content of the tissue (2). The actions of ANP were closely mimicked by 8-Br-cGMP but not 8-Br cAMP. The effects of ANP and cGMP were reversed by the isoquinoline sulfonamide derivative H-8 which inhibits cGMP dependent protein kinase activity. These results suggest that ANP stimulates cGMP synthesis which in turn inhibits Na-K-2Cl cotransport activity in the apical membrane of the enterocyte by a phosphorylation dependent mechanism. Although ANP had no effect on electrogenic ion transport across the opercular epithelium of the winter flounder, it was found to stimulate Cl secretion across the operculum of the killifish (3). Atriopeptin stimulation of killifish operculum was present in both sea water and short-term fresh water adapted animals. The effects of atriopeptin were not mimicked by treatment with 8-Br-cGMP. The results of these studies suggest that ANP release following volume expansion inhibits additional fluid uptake by the intestine. In some species, ANP may also act to decrease extracellular fluid volume by simulating the secretion of Cl across the gill epithelium.

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57.5

THE ROLE OF ATRIAL NATRIURETIC PEPTIDE (ANP) IN ELASMOBRANCH PHYSIOLOGY. R. Solomon, P. Silva, and F.H. Epstein

ANP is produced by myocytes of both the atrium and ventricle of the heart of Squalus acanthias. It bears strong homology to mammalian forms of ANP. ANP in shark plasma increases during in vivo isotonic volume expansion and the isolated perfused heart releases ANP in vitro following atrial stretch but not an increase in the perfusate osmolality or chloride concentration. In vivo volume expansion produces an increase in atrial pressure, no change in dorsal aortic blood pressure and an increase in the transport of electrolytes and water across the rectal gland epithelium. Exogenously administered ANP increases rectal gland secretion of salt and water in vivo but does not affect renal function. In vitro, ANP dilates the aorta and branchial vessels. In the isolated perfused rectal gland, ANP stimulates chloride secretion by releasing vasoactive intestinal peptide (VIP) from neurons within the gland. The released VIP stimulates chloride secretion via activation of adenylate cyclase. The release of VIP by ANP is a calcium dependent process. These observations suggest that ANP serves a volume regulatory role in the elasmobranch. It is released during states of volume expansion and acts upon the rectal gland to facilitate the elimination of the excess volume.

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57.6

A FAMILY OF NATRIURETIC PEPTIDES ISOLATED FROM EELS. Yoshio Takei. Department of Physiology, Kitasato University School of Medicine, Kanagawa 228, Japan

Immunohistochemistry and radioimmunoassay (RIA) using antibodies raised against human atrial natriuretic peptide (ANP) indicated the presence of ANP in the eel heart and brain. However, since the ANP content measured by RIA for human ANP was much smaller than that measured by the vaso-depressor bioassay in the eel, the amino acid sequence of eel ANP may differ from that of human ANP. Thus, we isolated ANP from eel atria and sequenced it, and established a RIA for eel ANP. The ANP content in eel atria measured by the homologous RIA was 700 times greater than that measured by RIA for human ANP, but the contents in eel ventricles and brains were only 7 and 25 times greater, respectively. Thus, we expected the presence of new types of ANP in these organs. We could isolate ventricular natriuretic peptide (VNP) from eel ventricles and brain natriuretic peptide (BNP) from eel brains. The eel VNP and BNP have sequence homologies of 61% and 65% to eel ANP, respectively, and are characterized by the C-terminal elongation and deletion, respectively. Eel ANP, VNP and BNP are 100 times as potent as human ANP for the vasodepressor effect in eels, but 1/10 as potent for the vasodepressor and natriuretic effects in rats. It appears that eel VNP is secreted continuously into the circulation and its plasma level is very high. We are cloning cDNA of eel VNP to examine whether or not VNP is a novel peptide that has not been identified in mammals.

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58.1

COMPARATIVE MORPHOLOGY OF SKELETAL MUSCLE. O. Mathieu-Costello. Dept. of Med., M-023A, Univ. of California, San Diego, La Jolla, CA 92093.

This review focuses on the comparative analysis of the relationship(s) between capillary-to-fiber geometry and O_2 demand (mitochondrial amount) in skeletal muscles. The capacity of a muscle for O_2 supply during maximal exercise depends on several aspects of capillary-to-fiber geometry. At a given capillary diameter, **capillary length density** (capillary length per fiber volume) determines the amount of capillary surface available for O_2 supply per volume of muscle fiber and mitochondria. **Capillary-to-fiber perimeter ratio** in transverse sections is an index of the amount of capillary surface available for O_2 diffusion per muscle fiber surface area; one of the determinants of O_2 flux rate. Several indices of muscle capillarity (capillary density, intercapillary distances, capillary-to-fiber perimeter ratio) are affected by **fiber size**. We investigated the structural characteristics of muscle potential for high O_2 flux rate, by comparing ultimate cases of extreme O_2 demand in birds, mammals, reptiles and fishes (i.e. flight muscle of hummingbird and bat, shaker muscle of rattlesnake and red muscle of tuna). Large capillary length density, small fiber size and large capillary-to-fiber perimeter ratio are characteristic features of highly aerobic muscles. A small fiber size and a large capillary-to-fiber perimeter ratio obviously result in both a large blood-tissue interface (capillary surface/ unit area of fiber surface) and small diffusion distances (small fiber diameter). Interestingly, however, in two bat muscles of similar fiber size (quadriceps, less aerobic; flight muscle, highly aerobic), greater potential O_2 flux rate was achieved through a larger capillary-to-fiber interface, i.e. a greater circumferential distribution of capillary surface available for supply around the muscle fiber, in the flight muscle. Supported by NIH grants HL-01534 and HL-40015.

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58.2

COMPARATIVE ASPECTS OF OXYGEN TRANSPORT AND MUSCLE FUNCTION. James H. Jones. VM: Physiol. Sci., Univ. California, Davis, 95616.

Almost all vertebrates can recruit sufficient quantities of skeletal muscle during exercise to exceed the capacity of the respiratory system to supply energy aerobically to the working muscle. Activity at intensities above that required to elicit the maximum rate of oxygen consumption (V_{O_2max}) is fueled by anaerobic processes, primarily glycolysis with the accumulation of lactate as end product. Theoretically, the limitation to an animal's capacity to utilize O_2 metabolically during exercise could be set by any part of the respiratory system, from the oxidative capacity of mitochondria that set the demand for O_2 to the diffusive and/or convective steps of the O_2 transport system that deliver it to the working muscle. Most vertebrate respiratory systems are fundamentally similar in functional design, comprising alternating convective and diffusive transport steps that: 1) ventilate the external gas exchanger, 2) diffuse O_2 and CO_2 between medium and blood, 3) circulate blood to respiring tissues, 4) diffuse O_2 and CO_2 between blood and active mitochondria, and 5) carry out oxidative phosphorylation at the inner mitochondrial membrane. Although significant structural differences exist between the design of specific components of the system, e.g., the external gas exchanger, similar general relationships define the interactions of the convective and diffusive transport steps throughout the system. Analysis of the nature of these interactions suggests that V_{O_2max} in vertebrates can be limited by the single step of mitochondrial oxidative capacity in some cases. However, when mitochondrial oxidative capacity exceeds the capacity of the O_2 transport system to deliver O_2, unless extraction of O_2 ventilated from the medium is complete, no single step of the respiratory system can limit aerobic capacity. Interactions between adjacent diffusive and convective transport steps compensate for differences in capacities of adjoining steps and dictate that the maximum transport capacity that is achieved is not dependent on any single step.

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58.3

MAXIMUM EXERCISE IN FISH. A. P. Farrell. Simon Fraser University, Burnaby, B.C., Canada, V5A 1S6.

Fish exercise in a viscous environment which has a low oxygen content relative to air. Generally, maximum oxygen consumption rates are an order of magnitude lower in fishes compared with mammals. Insights into the strategies and potential limitations for maximizing oxygen transport in fishes are provided from three types of studies. First, interspecific comparisons are revealing because resting oxygen consumption varies over approximately two orders of magnitude. Gill diffusive conductance, cardiac output, blood pressures, [hemoglobin] are correspondingly higher in more active fish. Second, swimming fish increase oxygen consumption up to fifteen fold. They can increase gill diffusive conductance, cardiac output, the arteriovenous oxygen difference, [hemoglobin] and red muscle blood flow. Some fish ram ventilate the gills to save the energy. Third, studies on exercise-trained fish are informative because training improves maximum aerobic swimming performance in a variety of fishes and reveals information on intraspecific plasticity in the oxygen transport system. Supported by NSERC Canada.

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58.4

MAXIMUM EXERCISE IN AMPHIBIANS. S.S. Hillman, Dept. of Biology, Portland State Univ., Portland, OR 97207

Limits to maximal rates of oxygen consumption ($\dot{V}O_2max$) in amphibians have been evaluated using experimentally induced variation, natural variation and mathematical modelling. Variation in $\dot{V}O_2max$ induced by exercising in hypoxia, anemia, erythrocythemia[2], B-blockade and osmotic effects on isolated mitochondria support a systemic oxygen transport limit to $\dot{V}O_2max$. Natural variation assessed by interindividual variation and allometry of respiratory, mitochondrial and cardiovascular variables also supports a systemic oxygen transport limitation. Mathematical modelling supports a systemic oxygen transport limit to $\dot{V}O_2max$ while pulmonary variables limit $\dot{V}CO_2max$. This analysis provides a rationale for the apparent overdesign of pulmonary variables in oxygen influx, since CO_2 efflux must match O_2 influx and the resistances at each transport step are different for O_2 and CO_2.

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58.5

MAXIMUM EXERCISE IN BIRDS

P.J. Butler, School of Biological Sciences, University of Birmingham, Birmingham B15 2TT, U.K.

Migration, particularly long-distant, non-stop, migration, imposes large demands on the respiratory, cardiovascular and muscular systems of those birds that use predominantly flapping flight. From data of birds flying in a windtunnel, the minimum metabolic rate during flapping flight is approximately 10 times the resting level and 2.3 times the maximum rate seen in running mammals of similar body mass (1). During flapping flight, the major consumers of power are the flight muscles - pectoralis and supracoracoideus. The former may constitute up to 35% of total body mass and consists primarily of fast highly oxidative (FOG) fibres (50-100%) with fewer (0-50%) fast glycolytic (FG) fibres(2). Associated with pre-migratory fattening is an increase in the mass of the pectoralis muscle and in the activity of a number of oxidative enzymes. The relative importance of hormones and locomotor activity (training) in these changes is unknown. At ambient temperatures below approximately 20°C, ventilation volume increases by a similar proportion to oxygen uptake, but respiratory water loss exceeds its metabolic production at ambient temperatures above approximately 5°C. It has been suggested that during migrations, birds ascend to altitudes where the air is cool enough to enable heat to be dissipated by non-evaporative means, thus keeping them in water balance. In the one study on the response of the cardiovascular system to flapping flight(3), it was found that the 10-fold increase in oxygen demand in pigeons is met by a 6-fold increase in heart rate and 1.8 times increase in arterial mixed venous oxygen content, with no change in cardiac stroke volume.

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58.6

MAXIMUM EXERCISE IN HORSES AND MAN. Peter D. Wagner.
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This presentation illustrates that not only are there considerable differences in how mammals maximally transport and use O_2 compared to other vetebrates, but that within mammalian species, there are large differences. Per kg body weight, the horse greatly outperforms man in all facets of O_2 transport.

Approximate Values at $\dot{V}O_2max$ (per kg Body Weight:*)

	$\dot{V}O_2$*	$\dot{V}_A$*	$\dot{Q}_T$*	[Hb]	CaO_2	$C\bar{v}O_2$	O_2 Extr.	$P\bar{v}O_2$	$PaCO_2$	$AaDO_2$	$\overline{PAP}$
	ml/min	L/min	L/min	gm/100ml	ml/100ml	ml/100ml	%	torr	torr	torr	torr
Man	50	1.53	0.3	14.5	19.8	3.5	82	19	35	30	40
Horse	140	3.15	0.6	18.0	24.5	1.8	93	12	40	35	90

Highly trained equines reach 140-160 ml/min/kg $\dot{V}O_2max$; humans anywhere from 40-80 ml/min/kg. Maximal alveolar ventilation and cardiac output are about twice as high/kg in the horse; arteriovenous O_2 content difference is 20-50% greater, due both to a higher [Hb] and to greater tissue O_2 extraction. These adaptations cause the equine to pay a price at the lungs: 1) Pulmonary artery pressure rises to near-systemic levels and pulmonary hemorrhage is not infrequent (although a cause and effect relationship has not been established.) 2) There is evidence of considerable diffusion limitation of O_2 transport across the blood gas barrier resulting in arterial hypoxemia, and 3) Despite the high ventilation, there is often relative CO_2 retention with its well-known effect on pH.

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72.1

CARDIOVASCULAR AND RESPIRATORY FUNCTION IN LOWER VERTEBRATES.
G. Shelton. Univ. of East Anglia, Norwich, UK.

Some fish and amphibians breathe air to supplement oxygen uptake when concentrations in the environmental water are reduced, the air breathing organ (ABO) being intermittently ventilated. This leads to uneven distribution of oxygen and carbon dioxide exchange between air and water and to fluctuations of all respiratory variables in blood and tissues. Anatomy of the ABO vasculature differs significantly in different species, though connexions are less important in non steady state systems in which blood coming to the ABO between breaths is progressively depleted in oxygen. In all intermittent breathers blood flow to the ABO increases during breathing and decreases between breaths. There is a sleective advantage in undivided or partially divided hearts in these animals because they allow unlimited central shunts. In all reptiles, except crocodiles, the interventricular septum is incomplete. In turtles variable perfusion of the lung still occurs because of this central shunt. In monitor lizards, though the septum is incomplete, a muscular ridge divides the ventricle during systole so that complete separation of left and right sides occurs, the former being a high pressure and the latter a low pressure pump. The crocodile ventricle is completely divided by the septum but the left aorta emerges from the right ventricle and joins with the conventionally connected right aorta to from the dorsal aorta. There is still the possibility of a right to left shunt, therefore, but with a high systemic and a low pulmonary pressure complete division exists.

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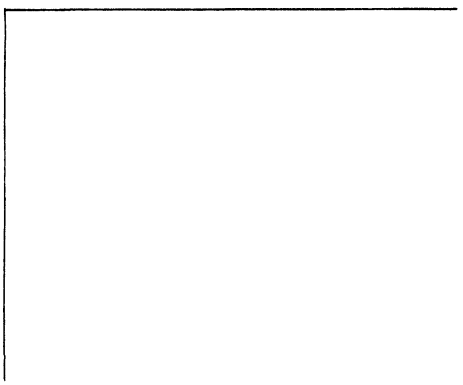
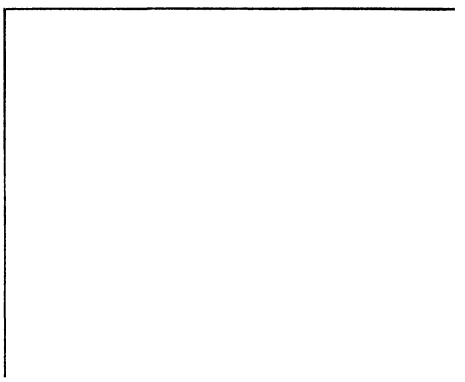
NEW INSIGHTS IN VERTEBRATE KIDNEY FUNCTION

75.1





75.2

SINGLE NEPHRON FUNCTION IN FISH
J A Brown, Dept. Biol. Sci., Univ. Exeter, Exeter EX4 4PS, UK.

High urine flow rates of freshwater-adapted, euryhaline teleosts reflect high glomerular filtration rates (GFR) and in many species are severely reduced on adaptation to seawater. Single nephron glomerular filtration rates (SNGFR) do not explain variations in GFR; mean SNGFR is elevated in seawater-adapted fish. In trout, glomeruli exist in three functional states (filtering, non-filtering but arterially perfused and non-arterially perfused) and intermittent glomerular activity is of major importance in the ultimate determination of urine output. Factors determining whether arterially-perfused glomeruli filter are still unclear but ultrastructure of the glomerular capillary epithelium suggests variations in hydraulic permeability (1), and renal blood flow is reduced in seawater-adapted trout. Identification of double afferents and efferents and distinct glomerular capillary lobules suggests a finer level of regulation of glomerular activity is feasible. Recent studies of isolated glomeruli suggest glomerular receptors for angiotensin II (2) which induces similar renal effects and ultrastructural changes to those occurring on seawater adaptation (3). An intrarenal role of the renin-angiotensin system in regulation of glomerular function is likely to be part of a complex interaction of endocrine control also involving catecholamines, arginine vasotocin, prolactin, atrial natriuretic factor and prostaglandins.
Supported by SERC, NERC and The Nuffield Foundation.

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See also J.A. Brown and C.S. Cobb, abstract at this meeting.

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75.3

MICROPUNCTURE STUDIES OF FISH RENAL FUNCTION J. Cliff Rankin. Institute of Biology, University of Odense, DK 5230, Denmark

Studies on a few of the 20,000 or so fish species provided important information in the early development of renal physiology and there may be still much we can learn from them about basic mechanisms and control processes. Structurally, vertebrate kidneys have much in common and the diversity of fish kidney form and function makes it dangerous to generalise about "advances" in the course of evolution. It is well known that only birds and mammals posess loops of Henle. However, nephrons of the two groups of fish which have been the subject of micropuncture investigations - lampreys and elasmobranchs - also posess loops, whose functions are unclear. Micropuncture investigations have concentrated on the ability of fishes to change urine volume and composition as external salinity changes and how this is regulated. Few investigations have been conducted in recent years, partly because of practical difficulties of working with fish, which have almost precluded micropuncture work on the largest group, the teleosts. This review will stress the likely benefits of renewed attempts, especially in the study of hormonal and neural control mechanisms.

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75.4

ORGANIC ACID (OR ANION) AND ORGANIC BASE (OR CATION) TRANSPORT BY REPTILIAN RENAL TUBULES. William H. Dantzler Dept. of Physiol., Col. of Med., Univ. of Arizona, Tucson, AZ 85724

Organic acids (or anions) and organic bases (or cations) are transported by proximal renal tubules of reptiles. Work with isolated perfused and nonperfused renal tubules and with renal membrane vesicles has begun to supply information on the transepithelial transport processes and the transport steps at individual cell membranes. Most organic anions (e.g., p-aminohippurate) undergo net transepithelial secretion by a common process in the distal portion of the proximal tubule. Net secretion involves secondary active transport into the cells at the basolateral membrane apparently via countertransport for dicarboxylates (which, in turn, enter the cells by a Na^+-dependent process) and movement from the cells across the luminal membrane down an electrochemical gradient apparently via carrier-mediated anion exchange. Urate undergoes net secretion throughout the proximal tubule by a separate process involving Na^+-independent secondary active transport into the cells at the basolateral membrane and possibly simple diffusion from the cells across the luminal membrane. Organic cations apparently can undergo either net transepithelial secretion or reabsorption, depending on the cation. For example, tetraethylammonium (TEA) undergoes net secretion. Apparently, this involves secondary active transport into the cells at the basolateral membrane, possibly via countertransport for another cation such as choline, and movement from the cells across the luminal membrane down an electrochemical gradient via H^+-TEA exchange. On the other hand, N^1-methyl-nicotinamide undergoes net reabsorption. Apparently, this involves entry into the cells across the luminal membrane down an electrochemical gradient via a carrier-mediated, Na^+-dependent process and transport from the cells across the basolateral membrane against an electrochemical gradient via a secondary active process, possibly utilizing countertransport for other cations.

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75.5

CONTROL OF KIDNEY FUNCTION BY PEPTIDE HORMONES

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Our purpose is to review the effects of several peptide hormones, including ADH, PTH, calcitonin and glucagon, on the transport of water and electrolytes (Na^+, Cl^-, Mg^{++} and Ca^{++}) along different segments of the nephron. Micropuncture studies on superficial nephrons demonstrate that PTH inhibits water and NaCl transport along the proximal tubule, and that glucagon and calcitonin act similarly, in spite of the absence of glucagon and calcitonin (but not PTH) - sensitive adenylate cyclase along this nephron segment. In the loop of Henle, all four hormones stimulate NaCl as well as Ca^{++} and Mg^{++} transport, in accordance with *in vitro* data obtained on cortical and medullary portions of thick ascending limbs. Along the distal tubule, all four hormones stimulate NaCl, Ca^{++} and Mg^{++} transport, to different extent however.

Since the thin descending limbs of juxtamedullary nephrons are located in the vicinity of medullary thick ascending limbs, the consequences of hormonal stimulation of medullary thick ascending limbs on juxtamedullary nephrons nephron function, determined by micropuncture carried out at the papillary surface, will be summarized.

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1.

2.

3.

75.6

The Avian Kidney: Unique Structure and Function. Eldon J. Braun. Dept.of Physiol. Coll. of Med., Univ. of Arizona, Tucson AZ. 85724.

Among the vertebrates, the kidneys of birds are rather unique in that the nephron population is composed of nephrons that have loops of Henle and nephrons that completely lack loops of Henle. This anatomy invites speculation and investigation in all areas of kidney function, in particular glomerular filtration rate (GFR) and its control, urinc concentrating ability, hormone action, and acid /base regulation. With the two very different nephron types in the avian kidney, the GFR of birds is more variable than that of mammals. This variability is caused primarily by intermittent nephron filtration. A portion of this intermittence is controlled by the antidiuretic hormone-arginine vasotocin (AVT). In comparison to mammals, the bird kidney can only weakly concentrate the urine (avg. U/Posm 2.5). However, a direct comparison of urine concentrating ability between birds and mammals is not valid on several grounds (these will be discussed). The axial pattern of hydrogen ion secretion of the avian nephron appears to be different from that observed in mammals. Data on the presence of a juxtaglomerular apparatus (JGA) in birds are conflicting, however recent work suggests the presence of a JGA in both types of nephrons. Other recent data on avian renal function will be presented and discussed.

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75.7

COUNTERCURRENT URINE CONCENTRATION IN BIRDS. Hiroko Nishimura. Univ. of Tennessee, Memphis, TN 38163

Birds and mammals have undergone a long period of parallel evolution and appear to have independently developed urine concentrating mechanisms. In bird kidneys, cortical reptilian-type nephrons and medullary mammalian-type (MT) nephrons that have a loop of Henle exist; the architectural organization of the medullary cone differs from that in mammallan kidneys, and the inner medulla is absent. The thick ascending limb (TAL) of Henle of the MT nephron from the quail, *Coturnix coturnix*, has structural and functional characteristics of the diluting segment. Epithelial cells of the thin descending limb (tDL) show morphological heterogeneity, and the upper segment of the tDL has low permeability to water and high and nearly equal permeability to Na^+ and Cl^-. The collecting duct (CD) of the cortical zone exhibits dark mitochondria-rich cells and mucus-secreting cells, whereas only mucus-secreting cells are seen in the medullary CD. The medullary CD shows low basal volume flux (J_V) and diffusional water permeability (P_{dw}). Neither arginine vasotocin nor 8-(4-chlorophenylthio) cAMP stimulated J_V or P_{dw}. Based on these findings, we propose a countercurrent multiplier model using NaCl recycling. NaCl extruded actively from the TAL enters the tDL without the accompaniment of water. This single effect may be multiplied by a counterflow and by the transport cascade of solute formed by graded hairpin turns, which help develop an osmotic gradient along the medullary cone. Urine concentration may be facilitated by a reduction of the CD flow due to the decrease in glomerular filtration rate. The mechanisms of control of CD water permeability remain to be determined.

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THE PHYSIOLOGY OF DEVELOPING MARSUPIALS

76.1

THE PHYSIOLOGY OF DEVELOPING MARSUPIALS: CHAIRMAN'S INTRODUCTION

R.A.B. Holland, School of Physiology & Pharmacology, University of New South Wales, Kensington, Sydney, NSW 2033, Australia

Marsupials, compared with the more common eutherian mammals, are born not only at a small size but at a very immature stage. Much of the development that takes place *in utero* in the eutherians, takes place after birth, in the characteristic pouch from which this group is named (Latin: *marsupium* = pouch). It should be noted that although the term "placental mammals" is often used as a contrast to "marsupials", this is not strictly correct. While all eutherians have well developed placentae, the marsupials also have placentae, commonly of the yolk-sac type, although in some, such as the bandicoot, a true chorio-allantoic placenta develops. Another feature, unique to marsupials, is the ability, of some species, to hold a partly developed embryo dormant in the uterus at the blastocyst stage until there is appropriate activation with subsequent normal development.

Special features of marsupial development include the need to adjust to air breathing at a very early stage. Surfactant is needed, and central shunts must be closed. The desirable position of the O_2-Hb equilibrium curve after birth is to the right of its desirable position *in utero*. Also, although the newborn tammar wallaby has only one layer of cells in the cereberal cortex it is able to co-ordinate its immediate post-partum climb to the pouch. Many physiological processes mature later in pouch life preparing the young for independence. The occurrence of so much development in the pouch rather than *in utero*, provides an excellent opportunity for the study of many processes. This is not only of interest in the study of marsupials, but is also of relevance in the general biomedical field.

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76.2

PREGNANCY DEFERRED IN THE TAMMAR WALLABY: ROLE OF PHOTOPERIOD, MELATONIN AND PROLACTIN

L.A. Hinds and C.H. Tyndale-Biscoe.
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The tammar wallaby is a highly seasonal short-day breeder in which melatonin (MLT) exerts its effects via prolactin rather than the GnRH pulse generator. Females give birth about 6 weeks after the summer solstice (December 22) and undergo a post-partum oestrus. The newly formed corpus luteum (CL) is inhibited by the pituitary via the sucking stimulus of the pouch young in the first half of the year, while after the winter solstice (June 22), the pituitary inhibition of the CL is maintained via MLT and the increasing photoperiod (1).

A change in daylength from 15L:9D to 12L:12D induces reactivation of the CL and births occur about 32 days later, 6 days longer than after removal of the sucking stimulus. The major events in the pineal and pituitary which lead to reactivation of the CL are as follows. The significant component of the MLT message is a minimum change in duration of elevated secretion from 9 to 10 h, for at least 3 successive nights (2). The inhibitory signal from the pituitary is a pulse of prolactin (PRL) of 2 hours duration, which occurs around the time of lights on. After a stimulatory photoperiod change the PRL peak is abolished within 3-4 days. If the peak is maintained experimentally then so is the inhibition of the CL (3).

The absence of the PRL peak for 3 days irreversibly releases the CL from quiescence and it secretes a pulse of progesterone on day 8 or 9 after the stimulatory light change. The progesterone peak, which is essential for the completion of pregnancy, is followed 21-22 days later by birth.

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76.3

THE DEVELOPMENT OF AN ADULT METABOLISM IN THE TAMMAR

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The tammar (*Macropus eugenii*), a macropodid marsupial, spends its first 200 postnatal days in a pouch, during which time much physiological maturation occurs. We have studied the development of an adult standard metabolic rate (SMR) and the ontogeny of thyroid function in this excellent model system for mammalian development.

Newborn tammars weigh about 400mg and have SMRs typical of adult reptiles of the same size. When they leave the pouch, tammar young have typically mammalian SMRs. To follow the development of an adult metabolic rate, liver, brain, kidney and heart from young throughout development were weighed and their mitochondrial membrane surface areas (MMSA) determined stereologically. Tissue MMSA in neonates was similar to that in comparably sized reptiles but had increased to mammalian levels by pouch exit. The increase was attributable both to an increased density of mitochondrial membrane and to organ growth. Heart and liver grew in a simple allometric manner while brain and kidney growth was biphasic.

Total plasma thyroxine (T4) was below 15nM early in pouch life, rose to about 80nM at Day 150 and fell to a mean of 12nM in adults. Total plasma triiodothyronine (T3) was about 0.2nM until Day 100, rose to a mean of 3nM by Day 200 and fell to 0.8nM in adults. Free T4 and free T3 followed similar patterns but peaked at 45pM and 166pM respectively. Liver and kidney 5'-deiodinase, undetectable before Day 80, reached adult levels by Day 220. These changes indicate a correlation between maturation of thyroid function and attainment of a mammalian level of metabolism in the developing tammar, although no causal relationship has yet been demonstrated.

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76.4

Development of cardiovascular and respiratory systems in the marsupial.

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It is the purpose of this review to point out areas where significant differences occur in cardiorespiratory function and anatomy between marsupials and the general eutherian pattern. Marsupials have analagous central vascular shunts to those in eutherians, but differ in the structure and timing of closure of these shunts. The two atria communicate by a number of wall fenestrae without valves, as they do in birds, and closure is delayed up to 4 days after birth. In mice there are no functional shunts 24 hours after birth. In the newborn marsupial, the lung parenchyma is still at the terminal air sac stage and alveoli formation is not completed until around day 75. This pattern of development is slower than that seen in even altricial eutherians. Pulmonary surfactant is present from birth and comparisons between the tammar wallaby and the rat have shown the same fatty acid profile but higher levels of free cholesterol in the former. Cardiorespiratory structures appear to have a delayed development but are functional in the marsupial neonate and cutaneous gas exchange is unimportant.

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76.5

THE RESPIRATORY FUNCTION OF MARSUPIAL BLOOD AT ABOUT THE TIME OF BIRTH

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The Tammar Wallaby (*Macropus eugenii*) is born at a weight of about 350 mgm compared with an adult weight of 5-10 kg. At birth, it has immature lungs and the red cells are all large and nucleated. Special features of blood O_2 carriage in the first 2-3 days after birth are (i) decreased oxygen affinity -- the P50 in the first few days at 35.5°C and PCO_2 = 34 Torr being between 40 and 50 Torr (adult P50 is approx 25 Torr); (ii) A Bohr effect half or less than half that in adults; (iii) A steeply climbing OEC above about 50% saturation with Hill n (nH) in the upper part being up to 5.6. At this stage four different Hb types are present, each different from the one major and one minor type found in adults; and the carbonic anhydrase level is about 30% of the adult levels. Blood 1-2 days before birth was due showed similar features, with the same four Hb types being present. In several cases at this prenatal stage, the Bohr effect was reversed in the lower part of the OEC. The chemical basis for the nH values greater than 4 is not known but it is presumably aggregation of Hb tetramers. The right shifting of the prenatal OEC should be an advantage in tissue delivery of O_2 but it decreases the ability of the embryo to take up oxygen from the mother *in utero*. Uptake of O_2 in the immature lung after birth, and in the yolk-sac placenta before birth, is assisted by the steep climb of the OEC above 50% satn. The carbonic anhydrase level, the P50, the Bohr effect, and the shape of the OEC are all similar to the adult by 10 days after birth. P50 continues to fall over the remaining 250 days of pouch life. Adult Hb begins to appear at about 3 days but embryonic Hb types are still detectable until about 14 days. This is the only recorded instance of a species where the prenatal OEC is significantly to the right of the maternal OEC.

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76.6

DEVELOPMENT OF MICROVASCULAR GEOMETRY IN THE MARSUPIAL CENTRAL NERVOUS SYSTEM. Gregory K. Snyder
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The microvasculature in the central nervous system (CNS) of eutherian mammals forms anastamotic meshworks, similar to the capillary arrangements found in other tissues. The microvasculature in CNS of marsupials is unique, with individual capillaries forming hairpin-like loops without anastamotic connections. The development of capillary loops follows from the development of the overlying CNS vasculature. Feeding arterioles and collecting venules arise from overlying pia in pairs and all branches from these vessels produce subsequent vessel pairs. Afferent ends of capillaries arise at fairly regular intervals along arteriolar segments and efferent limbs terminate at points contiguous with their origins on the adjacent venous vessel. Thus, each network of capillary loops is a terminal vascular unit, separate from all other such units, and all arteries are end arteries. Capillary loops may play an important role in oxygen exchange during early development and they may be important in buffering CNS tissue from systemic changes in carbon dioxide later in life. This work was supported by NSF DCB8818647 and NIH HL32894.

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76.7

DIFFERENTIATION AND DEVELOPMENT OF THE MARSUPIAL BRAIN.
N.R. Saunders. Department of Physiology and Pharmacology, University of Southampton, Southampton, England, SO9 3TU

Marsupials are born at an extremely early stage of brain development although a few restricted regions appear to be functionally in advance of the rest of the CNS eg those parts of the brain stem and upper spinal cord that are involved in respiration, suckling and forelimb movements. These functions are being studied using electrophysiological techniques in isolated CNS preparations from neonates that can be maintained in vitro for several days (2). The rest of the brain especially the forebrain and caudal spinal cord are at an "embryonic" stage of development at the time of birth (1,3). Thus the neocortex of all newborn marsupials so far studied consists of only two layers: ventricular zone and primordial plexiform layer. These are the distinctive zones that characterize the fetal neocortex in eutherian development. Therefore the whole of the development of the neocortex and of many other CNS regions can be studied in the much more accessible postnatal marsupial.

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77.1

MORPHO-PHYSIOLOGICAL ASPECTS OF THE NEURAL CONTROL OF BREATHING IN FISHES. S. Dunel-Erb. CNRS, Strasbourg, France.

The distribution of the branchial nerves has been studied in teleosts (perch and trout) using several techniques including TEM, immunohistochemistry, surgical and chemical denervation.

The validity of the current concept according to what pretrematic branches of cranial nerves IX and X are sensory and posttrematic branches are sensory and motor has been re-examined. From this study it appears to be partly wrong.

An important innervation controls the gill vasculature:

i-Cholinergic, parasympathetic fibers innervate the spincter located at the base of each efferent filament artery (1)

ii-Serotonergic fibers originating from large population of intrabranchial neurons innervate these spincters, but also the whole efferent side of the lamellar and filament vasculature (2)

iii-Catecholaminergic, sympathetic components parallel these innervations counteracting the vasoconstrictor effects of cholinergic and serotonergic components (1 & 2)

A less important innervation controls the musculature (3).

In addition, neuroepithelial cells, containing serotonergic granules, are present within gill epithelium, Strucutre, location and anoxic degranulation suggest an O_2 sensor function. These cells are in close association with serotonergic and sympathetic fibers.

All these nervous components must play an important role in breathing control in fish.

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77.2

THE ROLE OF CHEMORECEPTORS IN THE CONTROL OF BREATHING IN FISHES. W.K. Milsom and M.L. Burleson. Department of Zoology, University of British Columbia, Vancouver, B.C., V6T 2A9, Canada.

The brisk ventilatory response of teleost fishes to hypoxia suggests that this reflex is mediated primarily by arterial chemoreceptors, possibly located within the central nervous system. The precise location of these receptors was unknown and it was believed that ventilatory responses to CO_2 were due to Bohr and Root effects on arterial O_2 saturation and content (1). More recent studies indicate that complete branchial denervation can abolish chemoreflex responses to hypoxia and NaCN in some species (2). This is in stark contrast to several earlier studies. Differences may be due to difficulties denervating the pseudobranch in species which possess them (2). Heymans type chemoreceptors have been demonstrated recently in teleost gills with response characteristics similar to those of carotid bodies (3). These receptors respond strongly to acetylcholine but weakly to catecholamines. Their response to hypoxia can be inhibited by both atropine and propranolol, yet effects of these agents on the whole animal response to hypoxia are equivocal. This recent evidence suggests that the hypoxic ventilatory response may be mediated primarily by branchial O_2 chemoreceptors with a small contribution from extrabranchial adrenergic receptors.

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77.3

CONTROL OF BREATHING IN AIR-BREATHING FISHES. Neal J. Smatresk. University of Texas at Arlington, Arlington, TX 76019.

A variety of afferent sources modulate the activities of the central branchial and air-breathing pattern generators in bimodally breathing fishes. Of these, oxygen sensitive chemoreceptors appear to exert dominant control over the balance between air and water breathing. For gar, aquatic hypoxia stimulates air breathing and inhibits gill ventilation, but hypoxemia stimulates both gill ventilation and air breathing. These and cyanide localization studies suggest at least two loci for these receptors in or near the gills; one set facing the environment, responding to changes in water P_{O2}; and an internally oriented group responding to changes in mixed venous P_{O2}. Sectioning the branchial branches of the vagus and glossopharyngeal nerves abolish the responses to hypoxia and hypoxemia, supporting the contention that both sets of these receptors are located primarily in the gills. These results also suggest that a critical level of chemoafferent input is necessary to initiate air breathing, but that chemoafferent input is not needed to maintain branchial rhythmicity. There is currently no compelling evidence for intracranial chemosensitivity in air-breathing fishes, but vigorous responses to hypercapnia and changes in breathing following exercise suggest the potential for central or peripheral CO_2/pH chemosensitivity in some bimodally breathing fishes. Supported by NSF Grant DCB-8801846.

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77.4

THE ROLE OF CIRCULATING CATECHOLAMINES VERSUS BLOOD/WATER RESPIRATORY STATUS IN THE CONTROL OF BREATHING IN TELEOSTS. Steve F. Perry and Richard Kinkead. University of Ottawa, Ottawa, Ontario, CANADA.

The catecholamines, noradrenaline and/or adrenaline, are frequently released into the circulation of fishes during periods of hyperventilation. These periods of hyperventilation, in turn, are associated with changes in the water and/or blood respiratory status. There is evidence that both catecholamines of humoral origin and changes in water/blood respiratory status can affect gill ventilation (see review by Shelton *et al.* 1986; Peyreaud-Waitzenegger, 1979). For this reason, we have assessed the relative importance of elevated circulating catecholamines versus altered blood/water respiratory status in the control of ventilation in the freshwater rainbow trout (*Salmo gairdneri*) and seawater Atlantic cod (*Gadus morhua*). During mild hypoxia in rainbow trout (PwO_2 = 72 torr), there is a pronounced hyperventilation despite little if any change in plasma catecholamine levels suggesting that changes in oxygen status are solely responsible. During severe hypoxia in Atlantic cod (PwO_2 = 40 torr), catecholamines are released into the circulation but appear to play no role in the hyperventilatory response since pre-treatment with adrenoceptor antagonists did not significantly alter the hyperventilation. Similar experiments utilizing hypercapnia as a tool to simultaneously modify plasma catecholamine levels and blood/water respiratory status also do not support a significant role for circulating catecholamines in promoting hyperventilation. On the other hand, the results do demonstrate that respiratory acidosis, alone, is a potent ventilatory stimulant of ventilation during hypercapnia.

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77.5

EVIDENCE OF A ROLE FOR CATECHOLAMINES IN THE CONTROL OF BREATHING IN FISHES. E.W. Taylor and D.J. Randall.
Univ. of Birmingham, U.K. and Univ. of British Columbia, Canada.

Ventilation volume in the trout varies with the oxygen content of the arterialised blood whether the changes are induced by hypoxia, anaemia or hypercapnia.[1] The same variables cause an increase in circulating catecholamines.[2] Intra-arterial injection of catecholamines causes ventilation rate to increase in teleosts and in elasmobranchs.[2] Acid injection in the trout causes an increase in the circulating levels of catecholamines and in gill ventilation. During hyperoxia neither response was obtained. The ß-adrenergic antagonist, propranolol, inhibited the ventilatory response but not the increase in catecholamines.[3]

Branchial denervation abolished the ventilatory response to hypoxia in *Amia* but the fish continued to show a blunted response to injection of catecholamines, which was abolished by propranolol injection, suggesting central mediation of the ventilatory response to catecholamines by stimulation of ß-receptors.

Catecholamines cross the blood brain barrier in fishes. Direct recordings of central respiratory drive and single unit recordings from respiratory motoneurones in elasmobranchs reveal that generation of respiratory motor activity in the CNS is stimulated either by i.v. injection or by microinjection into the CNS of catecholamines.[2] These data infer that catecholamines stimulate ventilation by direct effects on either the central pattern generator or on respiratory motor neurones.

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77.6

EXERCISE, CARBON DIOXIDE, AND THE CONTROL OF BREATHING IN FISHES. C.M. Wood. Dept. of Biology, McMaster Univ., Hamilton Ont., Canada L8S 4K1.

Several recent studies indicate that in addition to the primary O_2 drive on ventilation in fish, internal acid-base status may also play an important role. In trout, greatly increased ventilation occurs after strenuous exercise, a time when arterial blood O_2 is close to normal, but Pa_{CO2} is elevated, pHa depressed, and plasma catecholamine levels markedly increased. The extent of hyperventilation is well correlated with the extent of pHa depression. In trout blood *in vitro*, catecholamines cause a transient inhibition of net CO_2 excretion from the plasma through the RBC's. The phenomenon is associated with ß-adrenergic activation of RBC Na^+/H^+ exchange and pHi regulation, the same mechanism involved in maintaining arterial blood O_2 content in the face of post-exercise acidosis. *In vivo*, pre-treatment with exogenous carbonic anhydrase does not affect exercise performance, but reduces the post-exercise Pa_{CO2} build-up and the associated depression of pHa. The elevation of ventilation is similarly reduced. It is suggested that the normal post-exercise "CO_2 retention" is an adaptive response which reflects a catecholamine-induced inhibition of net CO2 flux through the RBC's. The associated respiratory acidosis helps to drive the needed increase in ventilation at a time when O_2 and proprioceptive feedback are not appropriate signals. (Supported by NSERC).

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78.1

REGULATION OF AMINO ACID METABOLISM IN FISH. C.B. COWEY. Dept. of Nutritional Sciences, University of Guelph, Guelph, Ontario, Canada, N1G 2W1.

The metabolic fate of amino acids, post-assimilation, is governed partly by the activity of amino acid degrading enzymes, especially those in the liver, and partly by plasma or tissue concentrations of amino acids. A gross change in dietary protein level has little effect on the activity of enzymes which initiate amino acid catabolism. Even when an effect has been observed the change has usually been small (less than twofold). This contrasts with omnivorous mammals where similar changes in dietary protein level cause changes of tenfold or so in the activities of amino acid catabolizing enzymes. Variation in diet levels of individual amino acids such as Trp, Lys, Arg and Met had no significant effect on the activities of tryptophan pyrrolase, lysine-ketoglutarate reductase, arginase and methionine adenosyl transferase in rainbow trout liver. Such variation in intake does, however, affect the rate at which the amino acids are oxidized, i.e. tissue concentration is important in regulating oxidation of indispensible amino acids. Metabolism of individual amino acids will be discussed with reference to Met, where control appears to be vested at the level of homocysteine but may also affect polyamine synthesis, and branched chain amino acids where, even at high levels of Leu intake there is little evidence in rainbow trout of branched chain amino acid antagonism.

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78.2

FISH *METABOLIC STRATEGIES* AS INFLUENCED BY LIFE STAGE AND LIFE HISTORY. T.W. Moon* and G.D. Foster. Dept. of Biology, University of Ottawa, Ottawa, Ont. CANADA. K1N 6N5.

The fish life cycle can be divided into three stages - a egg-larval stage; a growth stage; and, a reproductive stage. In some species, especially those species which migrate, these are distinct and sequential, but in many species the latter two stages occur on a cyclic bases. The metabolic strategies employed during these latter two stages in particular may depend in a complex way upon the life history of the species. It is clear that the majority of research has been done on a relatively limited number of fish species, most of which are carnivores. Yet, metabolic comparisons are often made between species (within and outside taxonomic classes) without consideration of how nutrient type (carnivory vs herbivory) and capacities (fat vs lean), thermal classification (ecto- vs endothermy), muscle growth patterns, migratory capacities, or fasting abilities might affect such comparisons. Recent studies on fish hormones have identified a number of interesting interspecific structural differences which may reflect distinct functional differences. In addition, certain differences in the control of metabolic pathways have been identified. It is quite likely that such differences in hormones and metabolism are shaped by life stage and life history of the species. These possibilities will be discussed together with appropriate experiments and systems to address the metabolism - life history question.

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78.3

REGULATION OF LIPID METABOLISM IN HETEROTHERMIC VERTEBRATES. Mark A. Sheridan. North Dakota State University, Fargo, ND 58105.

Regulation of lipid deposition and lipid mobilization is critical for striking a balance between adaptive advantages and disadvantages of lipid storage. Patterns of lipid storage and utilization reflect the special life histories of the animal group. Heterothermic vertebrates (fish, amphibians, reptiles) have evolved a number of life history patterns (smoltification, metamorphosis, hibernation) which provide problems for lipid storage regulation. A general theme among these animal groups is to store lipids among several sites (mesenteric fat, liver, muscle) as opposed to a single depot type (adipose tissue). Lipids are stored primarily as triacylglycerols, but various other lipid classes are also stored and constituent fatty acids tend to be more complex (longer chain, polyunsaturated).

Lipid storage is influenced by de novo synthesis and deposition from various plasma lipoproteins. Lipid mobilization is controlled by an intracellular lipase enzyme. Lipid accumulation generally occurs in most heterotherms during periods of feeding when plasma insulin levels are elevated. Lipid depletion occurs during in transitional and nonfeeding periods and is especially apparent during salmonid smoltification and amphibian metamorphosis. Information concerning hormonal modulation of lipid deposition and mobilization is generally lacking in heterothermic groups. In salmonid fish, lipid mobilization from liver seems to be influenced by a number of hormones, especially pancreatic peptides (insulin, glucagon, somatostatin). Supported by NSF DCB 8901380.

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78.4

ENERGY SOURCES AND THEIR REGULATION IN CARNIVOROUS ECTOTHERMIC VERTEBRATES. R. deRoos. Univ of Washington, Seattle, WA.

Endothermic vertebrates generally use glucose as the preferred fuel and glucose is a required fuel for some tissues, notably the central nervous system. The ketones,B-hydroxybutyrate and acetoacetate, are the only additional fuels used by the CNS to an appreciable extent. Carnivores that rely heavily on proteins and ruminants that rely on short-chain fatty acids are exceptions. The dominant role of glucose in herbivorous and omniverous endothermic vertebrates commonly is extrapolated to include ectothermic vertebrates, although the majority of ectothermic vertebrates are carnivores that consume abundant and reliable amounts of protein and lipids and relatively little carbohydrate. The only documented requirement for glucose is to maintain locomotory skeletal muscle glycogen stores that are mobilized for glycolysis during even short bursts of activity. Recent evidence suggests that many tissues of carnivorous ectothermic vertebrates rely upon protein and lipid metabolites. However, there is virtually no information concerning the neuro-endocrine controls of protein and lipid energy sources in carnivorous ectothermic vertebrates as a consequence of the emphasis on the regulation of circulating glucose and tissue glycogen levels. Future studies on the uses and controls of energy sources in ectothermic vertebrates will provide better understanding if the hypotheses place more emphasis on the phylogenetic position and the natural history of the species chosen for investigation.

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78.5

REGULATION OF GLUCONEOGENESIS FROM PROTEINS IN BIRDS
Malcolm Watford, Dept. of Nutr. Sciences, Rutgers University, New Brunswick, NJ 08903, and Bao-Ji Chen, Duck Research Center, Taiwan Livestock Research Institute, Taiwan, R.O.C.

In mammals the liver is the major site of gluconeogenesis from lactate, glycerol, and amino acids. The kidney is not believed to make a significant contribution, except under severe conditions. However, in chicken liver the exclusive mitochondrial location of phosphoenolpyruvate carboxykinase (PEPCK)

Activity limits the use of gluconeogenic substrates to lactate (1). Chicken kidney possesses cytosolic PEPCK activity and has been shown to be gluconeogenic in vivo and in vitro. It has been estimated that the kidney may account for approximately 30% of total gluconeogenesis in the chicken (2). Similarly, in Peking and Muscovy ducks we found cytosolic PEPCK only in the kidney, and high rates of gluconeogenesis from amino acids were observed in kidney tubules, but not in isolated hepatocytes. Using a cDNA to chicken cytosolic PEPCK we have shown that the abundance of the mRNA in chicken kidney is increased during starvation, metabolic acidosis, and rapidly decreases after glucose feeding (3). These findings suggest that renal gluconeogenesis is regulated by the carbohydrate level of the diet and support the hypothesis that the kidney is the major organ for gluconeogenesis from substrates other than lactate in granivorous birds.

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78.6

METABOLIC CONSIDERATIONS IN BIRD MIGRATIONS. M. Ramenofsky. University of Washington, Seattle, Washington 98195.

Migration is one of the most energetically demanding processes in the biological world. In birds, fat stores are the major energy source during flight. However, various migration "strategies" have evolved to solve problems presented by geographic obstacles (e.g. mountain ranges, oceans, deserts) enroute. For example, the Garden Warbler (Sylvia borin) Blackcap Warbler (Sylvia atricapilla), and Golden Plover (Pluvialis fulva) migrate over barren deserts or open oceans and thus must fly nonstop over great distances (prolonged flyers). These species deposit all the fuel for the journey at its outset and may arrive at the destination in a depleted state. Other species such as White-crowned Sparrow (Zonotrichia l. gambelii), Dark-eyed Junco (Junco Hyemalis) and Western Sandpiper (Calidris mauri) migrate overland with opportunities to stop and refuel (short-distance flyers). These species experience short cycles of fuel deposition and utilization and deposit less fat in proportion to body mass than do prolonged flyers even though they cover similar distances during the migratory period as a whole. It is suggested that the diverse patterns of migration that evolved in response to availability of feeding areas en route are reflected in mechanisms of lipid and protein metabolism. Comparisons of the enzymes and hormones that regulate lipid and protein metabolism in species displaying these prominent patterns of migration may offer new insight into the regulation of energy metabolism during migration.

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78.7

DOWN-SHIFTING METABOLISM: BIOCHEMICAL REGULATION OF METABOLIC RATE DEPRESSION. Kenneth B. Storey. Carleton Univ., Ottawa, Ont., Canada K1S 5B6

Anaerobiosis, hibernation, and estivation all have one feature in common - facultative metabolic rate depression. By strongly reducing metabolic rate animals greatly extend the survival time under environmental stress. The biochemical regulation of metabolic depression is proving to have common molecular principles that extend across phylogenetic lines and are conserved in different types of arrested states. Our studies of anoxia tolerance in marine molluscs have identified three mechanisms of glycolytic rate depression: post-translational modivication of regulatory enzymes, reversible enzyme binding to the particulate fraction of the cell, and fructose-2,6-biphosphate regulation of the anabolic use of carbohydrate reserves. In marine molluscs phosphorylation of PFK-1, PFK-2, and pyruvate kinase is coordinated during the aerobic to anoxic transition to produce much less active enzyme forms. The process is mediated by the action of cGMP-dependent protein kinase and is independent of changes in cellular pH that accompany anaerobiosis. Equivalent mechanisms of metabolic arrest are used by estivating snails and by hibernating small mammals to depress aerobic carbohydrate catabolism. Among hibernators control appears to be focused on the arrest of mitochondrial metabolism including phosphorylation inactivation of pyruvate dehydrogenase.

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78.8

ENDOGENOUS AND EXOGENOUS REGULATION OF XENOBIOTIC METABOLISM John.J. Stegeman, W.H.O.I., Woods Hole, MA 02543

Cytochrome P450 enzymes are products of a supergene family, catalyzing oxidative transformation of xenobiotics (drugs, pollutants, carcinogens), and the synthesis and degradation of endogenous substrates (e.g., steroids,) (1). Some P450 enzymes that metabolize xenobiotics can be induced by substrates, constituting a mechanism of adaptation to the chemical environment (2). Studies in whole animals, primary cell cultures and established cell lines indicate that induction of P450IA subfamily proteins by hydrocarbons involves a common receptor mechanism in vertebrates from fish to mammals. This exogenous regulation can be modified by endogenous factors, including the hormonal environment and cell specific factors. Patterns of hormone effect on induction differ in different vertebrate groups. However, induction in some cell types, notably endothelium, is being recognized increasingly as common to virtually all organs of diverse vertebrates. Regulation of P450IA proteins can determine effects of many chemicals in various organs and cell types, with important physiological and toxicological consequences. The regulation and role of P450 proteins in other subfamilies are less well known in non-mammalian than in mammalian species. Further comparative studies may reveal the basic physiological significance and the evolution of additional P450 forms and their regulatory systems. (Supported by PHS grant ES-04220.)

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3.

10.1

DIEL AND SEASONAL CHANGES IN RESTING LEVELS OF VARIOUS BLOOD PARAMETERS IN FRESHWATER ADAPTED BROOK CHARR (*SALVELINUS FONTINALIS*). C. Audet and G. Claireaux. INRS-Océanologie, Rimouski (Québec) CANADA, G5L 3A1.

In fish, daily variations or rhythmicity in a variety of blood parameters are relatively well documented. These rhythms are linked to factors such as photoperiod, temperature changes, time of feeding, etc... The purpose of our study was to verify 1) if freshwater adapted brook charr, submitted to natural environmental conditions (temperature and photoperiod) also displayed diurnal changes in resting levels of some hormonal (plasma T_3, T_4, cortisol), ionic (plasma chloride osmolality), metabolic (plasma glucose), and blood (Ht, Hb and MCHC) parameters; 2) if the amplitude and/or frequency of these dial changes were modified along a 12 months period. One of the major goal underlying this study was to find some insights on how manipulate the seawater acclimation potential of brook charr for aquaculture purposes. A parallel was then drawn between these dial cycles and the osmotic and endocrine response of brook charr directly transferred to seawater, such transfer being done every month over a year period.

10.2

POSSIBLE NEUROENDOCRINE CONTROL OVER CALCIFICATION IN THE OCTOCORAL LEPTOGORGIA VIRGULATA. Roni J. Kingsley, Kristina L. Krider*, Michael L. Corcoran* and Lisa C. Broaddus*. Univ. of Richmond, VA 23173

Calcification is a widespread phenomenon among the invertebrate phyla. The gorgonian or whip coral Leptogorgia virgulata is extensively impregnated with intricately structured microscopic calcium carbonate (calcitic) spicules. The potential roles of neuroendocrine activity in the regulation of spicule formation in gorgonians have been investigated. Histological stains specific for neurosecretory substances reacted strongly not only in the polyp region but in the scleroblasts (spicule-forming cells) as well. The role of thyroxine in the gorgonian calcification process was examined. The rationale for specifically studying this hormone include its role in the decalcification of human bone and jellyfish statoliths and the striking presence of its precursors in gorgonians. Localization of thyroxine was achieved at both the light and electron microscope levels via immunocytochemical techniques. There was very strong localization of the hormone in specific areas of the gastrodermal tissue, the mesoglea, and the cytoplasm of the scleroblasts, suggesting a possible mechanism of action.

10.3

ULTRASTRUCTURAL AND IMMUNOHISTOCHEMICAL OBSERVATIONS ON THE DEVELOPING OPOSSUM ADENOHYPOPHYSIS. **William J. Krause* and Dedora M. Sherman* (Spon. R.H. Freeman). Department of Anatomy, School of Medicine, University of Missouri, Columbia, MO 65212; Department of Botany and Plant Pathology, Purdue University, West Lafayette, IN 47907.**

To determine the time and sequence of appearance of cells comprising the adenohypophysis, 45 opossums Didelphis virginana of various ages were examined using electron microscopy and immunohistochemical probes. The animals studied were divided into the following groups: prenatal animals (10 1/2, 11 1/2, and 12 day embryos), newborns (12 1/2 days postconception) and animals 4.5,7.0,14,28,35,47, and 105 days old. Each stage consisted of at least 3 animals. Pituitaries of 6 adults (3 males and 3 females) also were examined. The dorsal region of a multichambered vesicle, that forms from Rathke's pouch, comes to lie adjacent to the presumptive infundibulum by the 10 1/2 day of gestation. The dorsal wall of the upper chamber of this vesicle forms the pars intermedia; the ventral wall gives rise to cells of the pars distalis. Corticotropes, lactotropes and somatotropes can be identified in the presumptive adenohypophysis of the 11 1/2 day embryo with corticotropes being the most numerous. Thyrotropes and gonadotropes appear about one day later, shortly after birth. The adult distribution of the five cell types appears to be established within the pars distalis by the end of the second postnatal week.

10.4

EFFECTS OF HEAT STRESS ON SERUM PROLACTIN AND INSULIN CONCENTRATIONS IN LACTATING DAIRY COWS. Alan M. Lefcourt* and Anthony Capuco* (SPON: M. Paape). USDA-Agricultural Research Service, Beltsville, Md. 20705

Six heat-adapted cows were housed in environmental chambers (lights on 600-2200h, 50% RH, food and water ad lib). Integrated 15-min blood samples for insulin (Ins) and Prl along with cortisol, T_3, T_4, GH, IGF_1, urea-nitrogen, ammonia-nitrogen and glucose were taken from two cows at 20°C (normal) and for all cows at 33°C (stress). Sampling lasted for 48h and, for heat stress, started on day 5. Body temperatures were monitored continuously using radiotelemetry. Mean Prl values (ng/ml) were under normal conditions 14.3 ± .3 and during heat stress 26.6 ± .3 (22.7 ± .4 for the 2 cows also examined under normal conditions). Mean Ins values (ng/ml) were under normal conditions 1.89 ± .02 and during heat stress 1.50 ± .01 (1.52 ± .01 for the 2 repeat cows). Spectral analyses confirmed the visual observation that the dynamic range (i.e. the high frequency content) of both Prl and Ins was diminished during heat stress. Under normal conditions Ins had a circadian rhythm and an approx. 80 min rhythm; neither rhythm was apparent during heat stress. There were no consistent rhythms for Prl although there were numerous distinct peaks distributed throughout the day. In conclusion, the decrease in Ins during heat stress is consistent with a reduction in metabolism. Increased Prl during heat stress has been reported for bovines. The loss in dynamic range during heat stress for both Ins and Prl is consistent with responses of other measured variables. Apparently, regulation of metabolic variables is tighter during heat stress; perhaps due to a decrease in tolerances.

10.5

FUNCTIONAL ASSOCIATIONS BETWEEN THE OOCYTE, FOLLICLE CELLS, AND BASAL LAMINA IN THE COCKROACH *BLATTELLA GERMANICA*. M. Anderson, E. Bowdan, J.G. Kunkel and E.K. Tapman*. Smith College, Northampton, MA 01063 and University of Massachusetts, Amherst, MA 01003-0027

The panoistic oocytes of the cockroach *Blattella germanica* are surrounded by a single layer of follicle cells, and the outer (basal) surfaces of the follicle cells are enclosed in a thin basal lamina. Using mid-vitellogenic oocytes, we have employed several techniques to investigate the association between oocyte, follicle cells and basal lamina. 1. Scanning electron microscopy reveals filopodia that extend from the follicle cells toward the oocyte plasma membrane. Lucifer Yellow injection of the oocyte results in fluorescence of the follicle cell cytoplasm. These data suggest that the filopodia from the follicle cells are connected to the oocyte by gap junctions. 2. It is possible to remove the follicle cell layer by dissection. Using both intracellular and vibrating probe recording, we have shown that defolliculated oocytes remain viable. We assume that, during defolliculation by dissection, the connections from the follicle cells break and seal over. 3. Treatment of the intact ovariole with 0.05% elastase disrupts the basal lamina, leaving the follicle cell epithelium intact, and causes the terminal oocyte to change from a "banana" shape to spheroidal. However, after removal of the basal lamina and follicle cell layer by dissection, the defolliculated oocyte does not become spheroidal, but retains its normal shape for hours. 4. Elastase treatment of defolliculated oocytes facilitates impalement by intracellular microelectrodes. Results 3 and 4 suggest that extracellular material sensitive to elastase lies between the follicle cells and the oocyte. This extracellular material appears to help maintain the oocyte's normal shape. Supported by NSF Grant DCB 8905552.

11.1

ADAPTATION OF INTEGUMENTAL TRANSPORT IN *MYTILUS* TO REDUCTIONS IN EXTERNAL SALINITY. A.L. Silva* and S.H. Wright. Department of Physiology, University of Arizona College of Medicine, Tucson, AZ 85724.

Taurine, the principal osmolyte in molluscan integument, is actively transported by *Mytilus* gill. This process, which can occur against gradients in excess of 10^7 to 1, is dependent on external Na^+. We previously showed that taurine transport is sensitive to changes in external salinity, and presumed this reflected, at least in part, the requirement for Na^+. In this study we examined short-term adaptation of transport in *Mytilus* gill to reduction in external salinity. Acute exposure of isolated gills from *M. californianus* to 60% artificial seawater (ASW), which corresponds to a reduction in external Na^+ from 425 mM to 255 mM, resulted in >90% inhibition of taurine uptake. The tissue initially increased in wet weight following exposure to 60% ASW, but within 30 minutes returned to near control weight. Similarly, taurine transport in the gill, following step-wise acclimation (20 minutes per 10% step reduction) of tissue to 60% ASW, approached that of control gills held in normal ASW. Acute exposure of isolated gills to 60% ASW made isosmotic to normal ASW with mannitol resulted in <20% inhibition of taurine transport. Replacement of Na^+ with Li^+ to 60% of normal ASW reduced transport by >50%. These results suggest that *Mytilus* gill responds to reduced external salinity by adaptive changes in integumental transport that run contrary to the predicted effect of the concomitant reduction in external Na^+. This adaptation may involve both a volume regulatory response and a synergistic action of Na^+ and other ions on active taurine accumulation. Supported by NSF Award DCB88-19367.

11.2

BOTH NA^+ AND CL^- GRADIENTS ARE DRIVING FORCES FOR NACL-L-GLUTAMATE COTRANSPORT IN LOBSTER HEPATOPANCREATIC BRUSH BORDER MEMBRANE VESICLES. L.M. Balon* and G.A. Ahearn. Univ. of Hawaii, Honolulu, HI 96822.

Our previous work indicated that 3H-L-glutamate transport by lobster (Homarus americanus) brush border membrane vesicles (BBMV) was stimulated by the presence of both Na and Cl ions in the external medium, but the catalytic or energetic nature of this action was undefined (J. Exp. Biol. 130: 175-191). In the present study, a zero-trans time course experiment using inwardly-directed transmembrane Na or Cl gradients led to similar transient accumulations of 3H-L-glutamate above equilibrium values in the presence of equilibrated concentrations of the respective counterions. The uptake overshoots observed in the presence of single ion gradients were doubled when gradients of both Na and Cl were used simultaneously. In equilibrium shift experiments where vesicles were pre-equilibrated with 3H-L-glutamate and either of the monovalent ions, an inwardly-directed gradient of each counterion led to the transient accumulation of additional labelled amino acid above its equilibrium concentration, indicating that either ion gradient was capable of energizing the net flow of L-glutamate. A cotransport stoichiometry of 1 Na/1 Cl/1 glutamate was confirmed using the Static Head analysis where a balance of ion and amino acid driving forces were attained with a 10:1 Na or Cl gradient against a 10:1 L-glutamate gradient. Supported by NSF grants DCB88-09930 and DCB89-03615.

11.3

DIFFERENTIAL SCALING OF MASS-SPECIFIC METABOLISM AND NUTRIENT TRANSPORT DURING LARVAL DEVELOPMENT OF AN ANTARCTIC AND A TEMPERATE ECHINODERM. Fraser M. Shilling and Donal T. Manahan Dept. of Biol. Sciences, Univ. So. Calif. Los Angeles CA 90089

We examined the oxygen consumption rates and maximum rates (J_{max}) of alanine transport across the integument in similar-sized (mass) bipinnaria-stages of the antarctic asteroid Odontaster validus and the temperate asteroid Asterina miniata. The purpose of this study was to determine the relative scaling (to mass) of energy needs and nutrient inputs for similar larvae developing in environments with different temperatures (Antarctica: -1.0°C; California: 15.0°C). The mass-specific metabolic rate of bipinnaria of A. miniata was 25-times greater than that of O. validus; in contrast, the mass-specific J_{max} for alanine was only 3-times greater. When metabolic demand was expressed as alanine-equivalents (3 mol O_2 = 1 mol alanine), it was found that for the temperate form, the J_{max} for alanine (31.7 pmol alanine/larva-h) could account for metabolic demand. However, for the polar form, the J_{max} for alanine could supply 8-times the metabolic demand. These results suggest that invertebrate larval forms living in environments with low nutrients and temperatures have lower mass-specific metabolic rates while maintaining relatively higher mass-specific rates of nutrient transport. This suggestion is supported by our observations that during the early development of O. validus there was a doubling in dry organic weight from the egg (625 ± 18 ng) to the gastrula-stage (1355 ± 71 ng). Thus, growth occurred for those stages lacking a digestive system.

11.4

EFFECTS OF DIETARY COMPOSITION ON INTESTINAL NUTRIENT TRANSPORT IN A EURYHALINE TELEOST. E. Titus*, W.H. Karasov and G.A. Ahearn. University of Hawaii, Honolulu, HI 96822.

Dietary modulation of intestinal nutrient uptake as a function of varying carbohydrate and protein composition was investigated in the tilapia Oreochromis mossambicus. D-glucose, L-proline and acetate transport were measured utilizing isotopic uptake into brush border membrane vesicles. Adult fish were raised for approximately four weeks on either a high protein/low carbohydrate (HP) diet (65% protein) or a low protein/high carbohydrate (LP) diet (4% protein). The rate of D-glucose transport was enhanced in fish raised on the LP ration over those raised on the HP ration (Vmax: 84.2 ± 18.2 pmol/mg protein/sec vs. 37.4 ± 10.9 pmol/mg protein/sec., respectively, $p < 0.05$). This change in transport rate was specific in that there was no significant effect on Vmax for either L-proline or acetate as a result of dietary ration. There was no significant effect of dietary ration on the apparent Km for D-glucose (LP: 0.34 ± 0.17 mM vs. HP: 0.12 ± 0.03 mM, $p > 0.2$). Additionally, there was no significant dietary effect on apparent Km for either L-proline or acetate. These results indicate that D-glucose transport across the intestinal brush border membrane adapts to the dietary levels of carbohydrate. This adaptation is apparently an effect of increased transport rate or number of glucose carriers rather than enhanced carrier affinity, as indicated by the relative difference in Vmax and relative similarity in Km for the two diet groups. Supported by NSF grant DCB87-15278.

11.5

DIURNAL AND POSITIONAL DIFFERENCES IN ACETATE UPTAKE IN THE HINDGUT OF PRAIRIE VOLES. I. D. Hume and W. H. Karasov (SPON: H.V. Carey). Dept. Wildlife Ecology, Univ. of Wisconsin, Madison, WI 53706

As part of a research program on acetate uptake in hindgut fermenters of different size and dietary habit, we studied acetate uptake in the cecum, proximal colon and distal colon of 16 prairie voles (Microtus ochrogaster, body mass 32-68g) fed a mixture of high-alfalfa rabbit pellets and laboratory chow. Lengths (cm) and nominal surface areas (cm^2) of the hindgut of these herbivores were, respectively, 7.6 and 9.6 (cecum); 9.3 and 6.8 (proximal colon); and 11.1 and 7.0 (distal colon). We measured uni-directional uptake of ^{14}C-acetate (not transmural flux) by intact tissue in vitro over a concentration range 0.05 - 100mM. We found evidence of mediated uptake (apparent $K_m \leq 1mM$), but uptake was primarily passive over the concentration range 10-50mM, the likely concentration of acetate in the lumen. At 50mM, uptake (nmol/min·cm^2) was higher ($P<0.001$) in the distal colon (193 ± 12) than in the proximal colon (89 ± 11) and cecum (83 ± 4) ($\bar{x}$ ± SE, n = 8). This pattern of higher uptake in the distal than in the proximal colon is notably different from that seen in other species. A further consistent finding was a 30% higher uptake at night than during the day; at other concentrations this diurnal difference was as great as 90%. Supported by NSF BSR8452089.

11.6

INTESTINAL NUTRIENT TRANSPORT (INT) IN MAN M.E. Gumpper* (Spon: R.F.Tislow) Univ. of PA. Med. Sch. and Marriott Lifecare Community, Haverford, PA 19041

INT is essential in man who are unable to swallow food. Jejunostomy is used if gastric input is not possible. Prolonged nasal feeding can lead to complications. It is important that the nutrient preparation should be neither constipating (threat of impaction) nor producing diarrhea. The intestinal food response of stroke-aphasic patients should be obtained from families or referring physicians. Otherwise a trial and error method will be needed as described in the following case: 85 y. FEM. with L.CVA, aphasic and dysphagic developed after six months on Jevity (R, Ross) a life threatening fecal impaction in the sigmoid, found by competent nursing care. Skillful intervention by the intestinal surgeon with removal of the impacted masses, restored intestinal motility. By resuming jejunal feeding with decreasing amount of Jevity (R.) and increasing amounts of Osmolite (R., Ross) and 25% springwater no further problems were encountered. In todays society with increasing demand for health care, it is imperative to have a good nutritional state to maintain body weight and healing power. This procedure lends itself to further research in man and animals.

12.1

VENTILATORY RESPONSES TO INSPIRED GAS VARIATION IN LARVAL BULLFROGS. Robert L. Infantino, Jr. Dept. of Zoology, Univ. of Mass., Amherst, MA 01002.

Previous studies of the ontogeny of ventilatory regulation in bullfrogs (*Rana catesbeiana*) suggest that pulmonary ventilation is not important during early larval development, and that adjustments in gill ventilation constitute the major functional response to aquatic hypoxia. To test this suggestion, the effects of changes in gas phase PO_2 and PCO_2 on gill and lung ventilation were measured in larvae (Taylor-Kollros Stages III-X) at 25 ^{o}C. Lung ventilation frequency (f_L) was determined using impedance techniques. Gill ventilation frequency (f_G) was counted by visual inspection. Since these larvae rarely ventilate their lungs under normoxic/normocapnic conditions, larvae were first exposed to aquatic hypoxia (PO_2 = 30 mm Hg). This resulted in a near two-fold increase in f_G and a 14-fold increase in lung ventilation (f_L = 0.3/minute). While maintaining aquatic hypoxia, animals were exposed to hypoxic (PO_2 = 50 mm Hg), hyperoxic (PO_2 > 500 mm Hg) or hypercapnic (PCO_2 = 21 mm Hg) gas. Hypoxic gas exposure resulted in an increase in f_L to more than double that in aquatic hypoxia alone. In hyperoxic gas exposure, f_L returned to pre-treatment levels. During both hyperoxic and hypoxic gas exposure, f_G was reduced relative to that during hypoxic water exposure alone. Hypercapnic gas had no effect on f_G or f_L. Collectively, these data show that the PO_2 of inspired gas has a potent influence on both gill and lung ventilation early in larval development. Carbon dioxide does not affect f_G or f_L though it is known to be important in respiratory regulation in adult frogs. Depression of f_G after hyperoxic or hypoxic gas exposure suggests an ability to adjust f_G to reduce oxygen loss across the gills. *Supported by a Sigma Xi Grant-in-Aid of Research and NSF grant DCB-8916938 to Warren Burggren.*

12.2

THE SIGNIFICANCE OF THE BOUNDARY LAYER IN CUTANEOUS BREATHING, AQUATIC LUNGLESS SALAMANDERS David T. Booth*. (SPON: M.E. Feder) The University of Chicago, Il 60637.

Theory predicts that in aquatic amphibians a layer of oxygen-depleted water will form adjacent to the skin because of the relatively high kinematic viscosity of water and relatively low diffusivity of oxygen in water. This boundary layer may contribute considerably to the resistance to cutaneous oxygen exchange. Here I report experimental data from submerged lungless salamanders that clearly show the boundary layer to be a major resistance to cutaneous oxygen exchange. The development of reliable oxygen microelectrodes has enabled the mapping of PO_2 gradients adjacent to the skin in submerged salamanders. In still water the PO_2 at the skin-water interface of salamanders is consistently less than 20 Torr, compared to 150 Torr in the free stream. At 15 ^{o}C the critical PO_2 for adult *Desmognathus quadramaculatus* is approximately 60 Torr. Two surprising conclusions result from this data. Firstly, approximately 90% of resistance to cutaneous oxygen uptake resides in the boundary layer in still water. Secondly, whenever these animals are in still water they must experience severe hypoxia. Flowing water decreases the magnitude of the boundary layer resistance considerably. However, even in rapidly flowing water (14.5 cm/s), the PO_2 at the skin-water interface does not exceed 80 Torr, indicating that at least 50 % of resistance to oxygen uptake still resides in the boundary layer. Obviously the boundary layer is a major factor that must be considered when modeling regulation of cutaneous oxygen uptake in aquatic amphibians. In this respect the behavior of the animals can play a major role in regulation. By seeking microenvironments with increased flow or by skin ventilation an amphibian can decrease the boundary layer resistance considerably and thus increase cutaneous oxygen uptake. Funded by NSF grant DCB 8718264.

12.3

EFFECT OF GABA ON GILL AND LUNG VENTILATION IN AN IN VITRO ISOLATED BRAINSTEM PREPARATION IN THE TADPOLE. R. Walker, R.J. Galante, A.P. Fishman and A.I. Pack. University of Pennsylvania, Philadelphia, PA 19104

A preparation has been developed of an isolated brainstem of the tadpole (R. catesbeiana). The brainstem is superfused with oxygenated physiological solution and neural activity is recorded extracellularly from the facial motor nucleus using tungsten electrodes. The pattern of recorded activity is similar to the buccal pressure changes measured in freely swimming tadpoles (West NH and Burggren WW, Respir Physiol 47: 165-176, 1982). Moreover, in in vivo studies we have confirmed the relationship between our neural recordings and buccal and intra-pulmonary pressure changes associated with gill and lung ventilation. In our in vitro studies we have shown no effect of alterations in pH over a wide range (pH 7.2 to 7.8), produced by changes in CO_2 concentration in the physiological solution, on the frequency of gill and lung ventilation. Thus, there is no evidence of a central chemoreceptor in this preparation. At a fixed pH (7.4), however, superfusion of GABA produced changes in lung and gill ventilation. The dose response of this effect was studied over the range 1-20 mM. At lower concentrations (of the order of 5 mM) there was reduction in gill frequency and amplitude of neural activity without observable effects on lung ventilation. At higher concentrations (10 mM and above) both gill and lung ventilations were essentially abolished. These differential effects are compatible with there being separate, although interacting, pattern generators for gill and lung ventilation. In conclusion, we describe a preparation that should be of value in developing a comparative approach to elucidating mechanisms of respiratory rhythmogenesis. (Supported in part by HL-39775.)

12.4

PREY CAPTURE AND PROCESSING IN SAURIAN REPTILES. Deborah J. Hautau* and C.J. Swanson. Wayne State University, Detroit, MI. 48202.

In saurian reptiles, approach patterns, mode of capture, and processing of prey is quite varied. Mechanisms range from protractile tongue projection to inertial feeding. Amongst the various saurian forms, initial visual and odor cues, fast motor performance, and effective prey processing are essential prerequisites for successful foraging. Few studies have attempted to quantify the biomechanics and subsequent physiological changes during the feeding maneuver in lizards. Utilizing a 2-channel A/D recording system, acclimated individuals of *Anolis carolinensis* were instrumented with trans-thoracic and trans-caudal external impedance electrodes to register the pneumogram and heart rate, respectively, under controlled conditions. A 2-plane videographic system simultaneously recorded motor performance onto tape whereupon freeze-frame allowed for quantification of acceleration, velocity, and details of food capture and processing. These were compared to videotaped sequences of other saurian species which were analized in the same fashion. Four general approach patterns were noted for all species examined (n=7). Of all the species examined, the greatest average maximum velocity of 37.53 cm/sec and average maximum acceleration of 45.41 cm/sec/sec(n=10) was seen in *Basiliscus plumifrons*. In *A. carolinensis* ventilation was variable but showed increases with exertion prior to procurement of prey followed by varying periods of apnea.

12.5

CONFLICT BETWEEN LOCOMOTOR AND VENTILATORY FUNCTION OF THE HYPAXIAL MUSCLES OF LIZARDS. David Carrier* (SPON: R. J. Full). Univ. of California, Berkeley, CA 94720

Consideration of the anatomy and mode of locomotion of lizards leads to the suggestion that they may not be able to run and breathe at the same time. The actions of the hypaxial muscles that appear to be necessary for lung ventilation are incompatible with the expected actions of the same muscles during locomotion. To test this, the patterns of hypaxial muscle activity during lung ventilation and walking were measured in green iguanas (*Iguana iguana*). Electromyography shows that only four hypaxial muscles are involved in breathing. Expiration is produced by the transversalis and retrahentes costarum muscles. Inspiration is produced by the external and internal intercostal muscles. In contrast, all of the hypaxial muscles are active during walking. During walking, the rectus abdominis, superficial and deep layers of the external oblique, external intercostal and ventral portion of the internal intercostal on one side of the trunk act synergistically with the lateral portion of the internal intercostal and internal oblique on the other side. During the course of a single locomotor cycle each muscle contracts first on one side of the trunk and then on the other. Thus, a single hypaxial muscle on one side of the body acts antagonistically to its counterpart on the other side to effect locomotion, but acts synergistically with its counterpart to produce ventilation. Consequently, the locomotor activity of the hypaxial muscles of iguanas does conflict with and limit breathing. These results, also, suggest that the basic organization of the hypaxial muscles of tetrapods is due to the demands of locomotion, and that lung ventilation is a function that has secondarily been imposed on the hypaxial musculo-skeletal system. Supported by NIH F32 AR08073-01.

12.6

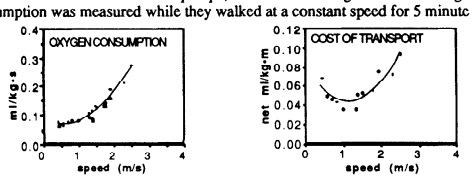
THE FIRST BREATH:LOCOMOTION AND RESPIRATORY DEVELOPMENT IN LARVAL COD (GADUS MORHUA). I. Hunt von Herbing* and R.G. Boutilier, Biology Department, Dalhousie University,Halifax, N.S., Canada B3H 4J1.

Locomotion, respiratory pump activity and gill development were studied in larval cod (G. morhua) from yolk-sac to preflexion stages. Yolk-sac larvae tend to be stationary with intermittent periods of burst swimming. Buccal pump activity is visible but infrequent at 4 days post-hatch, although cartilaginous elements are present for buccal pump functioning prior to hatching. No filaments are present on ventral branchial arches until 2 weeks post-hatch when larvae are $\geq$ 5mm. Thereafter, buccal cavity movements are continuous and locomotion is characterized by beat-and-coast swimming. Development of the gill structures proceeds rapidly, numerous filaments appearing by 4 weeks post-hatch, with secondary lamellae developing at 5 weeks post-hatch. At this time, caudal fin rays are developing, adding both to stability, and to larval swimming speed. Subsequently, opercular bones develop, allowing for co-ordinated functioning of the buccal and opercular pumps as respiration changes from cutaneous to branchial. The co-ordinated nature of respiratory pump and gill development indicates that respiratory surface area changes may be related to maximum aerobic scope.

13.1

AFRICAN ELEPHANTS: ENERGETICS OF WALKING IN A LARGE MAMMAL. V. A. Langman, T. J. Roberts*, J. Black*, G. M. O. Maloiy*, N. C. Heglund, J.-M. Weber, R. Kram*, and C. R. Taylor. Museum of Comp. Zoology, CFS, Harvard University, Old Causeway Rd., Bedford, MA 01730.

Elephants walk, but don't run. The muscles and bones of such large animals operate at stresses close to mechanical failure at top walking speeds, and switching to a run could have disastrous consequences. Their long limbs should let them walk rapidly at a low energetic cost, perhaps compensating for the single gait, and the purpose of this study was to to find out how fast they walk and how much it costs. Three female African elephants (ave wt. 1,540 kg) were trained to wear a gas mask and follow a motorized cart which carried air pumps, flow meters and gas collection bags. Oxygen consumption was measured while they walked at a constant speed for 5 minute intervals.



The net amount of oxygen used to transport each kg a meter (walking rate-standing rate divided by speed) reached a minimal value of 0.4 ml O_2/kg·m at a speed of about 1 m/sec and doubled at both slower and faster walking speeds. Minimal cost of transport for the elephant was predicted remarkably well by allometric equations, and was 1/2 that of a pony and 1/4 that of a dog. Although minimal cost of transport differs by four-fold over this size range of dog to elephant, the speed where minimal cost was reached was nearly identical: a finding which we had not expected and brings into question the "pendulum paradigm" for explaining the link between energetics and mechanics of walking. This work was supported by NIH grant 5 RO1 AR18140-14.

13.2

THE IMPORTANCE OF REST PAUSES DURING INTERMITTENT EXERCISE IN THE GHOST CRAB, *OCYPODE QUADRATA*. R.B. Weinstein* and R.J. Full. U.C. Berkeley, Berkeley, CA 94720

Previous laboratory studies of animal locomotion have focused on the physiological responses to continuous treadmill exercise, yet most animals move intermittently. We have examined the importance of rest pauses by exercising medium sized ghost crabs (mean weight = 28.0 g) intermittently on a treadmill. Crabs exercised intermittently at 0.30 m/sec, a supramaximal speed twice the speed that elicits 75% maximal rate of oxygen consumption. When both the exercise and pause period durations were 120 sec, crabs exhibited a 6-fold increase in endurance compared to crabs exercised continuously at 0.30 m/sec and a 2-fold increase in endurance compared to crabs exercised continuously at 0.15 m/sec (a submaximal speed). In these crabs, lactate was cleared from the legs during the pause periods. When both the exercise and pause period durations were 30 sec, crabs exercised intermittently at 0.30 m/sec exhibited greater endurance than crabs exercised continuously at 0.30 m/sec, but not at 0.15 m/sec. In these crabs, lactate was not cleared from the leg during the pause periods and arginine phosphate levels remained low, but the 30 sec pause was sufficient to maintain constant ATP levels. Our results suggest that pause periods, if long enough, play an important role in clearing lactate and maintaining ATP levels in the leg muscles of intermittently exercised crabs. Supported by NSF Grant DCB89-04586 and an NSF Graduate Fellowship.

13.3

ENERGETICS OF UNDULATIONS IN CENTIPEDES. B.D. Anderson, R.J. Full, and C.F. Herreid. Univ. of Calif., Berkeley, CA 94720 and SUNY Buffalo, NY 14260

Lateral undulations have been hypothesized to significantly increase the cost of locomotion in animals using metachronal gaits. To test this hypothesis we exercised large twenty-two legged centipedes from Arizona (*Scolopendra heros*; 5.32 g ± 0.10 S.E.) on a treadmill enclosed in an airtight lucite respirometer. Oxygen consumption (V_{O2}) was determined by open-flow respirometry. Flow rate was 240 ml/min. Speeds ranged from 0.16 to 0.74 km/h. Resting V_{O2} was 0.22 ml O_2/g/h ± 0.004 S.E. O_2 consumption (ml O_2/g/h) increased linearly with speed (v, km/h); V_{O2} =1.81 (±0.40 S.E.) v + 0.30 (r^2=0.67). Stride frequency and wave frequency (f, Hz) also increased linearly with speed (v, cm/sec; f = 0.13 v + 2.3, r^2=0.59). Based on the minimum cost of locomotion (1.8 ml O_2/g/km), cost per stride (1.8 J/stride) and ground contact cost (i.e. cost relative to the time a leg is on the ground generating force, 1.1 J/kg), we can reject the hypothesis that lateral undulation necessarily results in a considerable amount of "wasted energy" (Manton, 1953). In fact, when compared to all other pedestrian locomotors centipedes fall below the predicted costs for their body mass. Supported by NSF Grant DCP 89-04586.

13.4

DESIGN OF MUSCULAR SYSTEMS. Lawrence C. Rome and Andrzej A. Sosnicki*. Biology Dept, Univ of Penn, Philadelphia, PA 19104

The basic components of muscle contraction are understood and the ones that are varied (e.g., actin filament length, maximum velocity of shortening [V_{max}], and fiber orientation) can be considered design parameters. Are there rules (design constraints) that govern how these design parameters vary? Over the past 2 years we have identified two such constraints from studies on carp. A first constraint is the extent of myofilament overlap. Due to their helical orientation, the white muscle fibers have a 4-fold higher gear ratio than red ones. Hence, the white fibers can power the extreme "escape response" and the red ones power slow swimming, while each works at maximum overlap and force generation. A second important design constraint is V/V_{max} (where V is the shortening velocity of fibers). We know from isolated muscle experiments that maximum power generation and maximum efficiency are achieved over a narrow range of V/V_{max} values (.2 to .4). Carp power their slow swimming with red muscle (low V_{max}) and their fast movements with white muscle (high V_{max}) while each works within the optimal range of V/V_{max}. Further, if temperature is dropped by 10°C, the 1.6-fold drop in V_{max} of red muscle is matched by a 1.6-fold drop in maximum V (and swim speed), so that the muscle operates over the same V/V_{max} at each temperature. Finally, in mammals, the scaling of stride frequency and V with body size is matched by a similar scaling exponent for V_{max}. Hence mammalian muscles operate at the same V/V_{max} values. Supported by NIH AR38404.

13.5

OXYGEN CONSUMPTION CORRELATES WITH TRUNK MUSCLE METABOLIC ENZYME ACTIVITIES IN LARVAL AND EARLY JUVENILE CALIFORNIA HALIBUT, PARALICHTHYS CALIFORNICUS. Sandor E. Kaupp. Scripps Institution of Oceanography, Univ. of California, San Diego, La Jolla, Ca. 92093

The activity of the mitochondrial enzyme citrate synthase and the glycolytic enzyme lactate dehydrogenase of the 'white' (fast-twitch, glycolytic) trunk muscles of halibut correlated with resting (i.e. maintenance, post-absorptive) and routine (maximum specific dynamic action, post-prandial) rates of oxygen consumption, respectively. The difference between these rates of oxygen consumption represent a kind of scope for metabolism. The relative concentration of the two enzymes represent an index of the metabolic 'poise' of the muscle, that is, its aerobic and anaerobic metabolic capacity. This can be thought of as a tissue level index of metabolic scope. The 'white' trunk musculature is the largest organ system of most fish (>50% of body mass), known to be used for high speed swimming and used as an energy depot. It is speculated that the fish's growth metabolism has produced similar trends in both whole-fish and white trunk muscle measurements of metabolic scope.

13.6

SKELETAL MUSCLE GLUCONEOGENESIS: GLYCOGEN SYNTHESIS FROM LACTATE IS STIMULATED BY EPINEPHRINE. Todd T. Gleeson and Alan S. Kolok. Univ. of Colorado, Boulder, CO 80309-0334

Reptilian skeletal muscle is known to possess a considerable gluconeogenic capacity in vitro. It is known that this mechanism is responsible for at least 2/3 the glycogen replenishment following exhaustive exercise in vivo, a period when plasma catecholamines are elevated. Experiments were conducted to determine what influence post exercise epinephrine (E) levels have on muscle glycogenesis, since E is understood to depress hepatic glycogen synthesis in other vertebrates. Red and white fiber bundles from the iliofibularis (rIF, wIF) muscle of the lizard *Dipsosaurus dorsalis* were incubated 2 hr at 40°C, pH = 7.2 in the presence or absence of 15 ng/ml E and 15 mM lactate, 8.5 mM glucose, or lactate plus glucose; conditions similar to those post-exercise. Labelled CO_2 evolution was used as evidence of substrate oxidation, while label incorporation into glycogen was used as evidence of glycogenesis. Lactate and glucose metabolism in rIF was always approximately 3X that in wIF. Approximately 4-5 times as much lactate carbon as glucose was oxidized or converted to glycogen in both rIF and wIF, independent of E. Epinephrine stimulated lactate metabolism, but had no effect on glucose metabolism. Epinephrine increased lactate incorporation into glycogen 2-3X, but stimulated lactate oxidation in wIF only. Total lactate metabolism (oxidation + glycogenesis) was stimulated by E in both rIF and wIF, in both the presence and absence of glucose. We conclude that the catecholamine changes associated with exercise in lizards facilitate muscle glycogen resynthesis and lactate removal by stimulating muscle gluconeogenesis. Supported by NSF DCB 8615603.

14.1

ALTERATION OF URINE SODIUM/POTASSIUM RATIOS AND SECRETION RATE IN THE CRICKET, *ACHETA*, BY HPLC-PURIFIED NEUROPEPTIDES. J.H. Spring and I.S. Kim*. University of Southwestern Louisiana, Lafayette, LA 70504.

Fluid secretion by the Malpighian tubules of *Acheta* is controlled by the actions of three neuropeptides found in the corpus cardiacum. These can be isolated and partially-purified using high performance liquid chromatography (HPLC). When assayed on Malpighian tubule preparations *in vitro*, two o the peptides act as diuretic hormones (DHs), stimulating secretion, whereas the third is an antidiuretic hormone (ADH), reducing tubule secretion by roughly 80%. Further experiments using single Malpighian tubule preparations clearly demonstrate that all three peptides act on the secretory region of the tubule, i.e. on a single cell type. In our current model, DH_1 is assumed to increase the permeability of the basolateral membrane to sodium via the action of cAMP, while DH_2 and ADH act respectively to decrease and increase intracellular calcium concentrations. Potassium egress through the basolateral membrane is presumed to be altered by a calcium-dependent mechanism. All three hormones ultimately act by affecting the concentration and species of cation available to the common cation pump on the apical membrane. Support for this model comes from data indicating that exogenous cAMP (1 $mmol.l^{-1}$) increases fluid secretion by increasing sodium, but not potassium, transport. Elevating the intracellular calcium levels with the divalent cation ionophore, A23187 (5 $\mu mol.l^{-1}$), decreases fluid secretion by slowing potassium transport, although sodium is unaffected. Supported by NIH grant AI28399 to JHS.

14.2

POSTMOLT CALCIFICATION IN CRAYFISH AS A FUNCTION OF AMBIENT pH IN NORMAL AND DECARBONATED FRESH WATER (FW). Flavia P. Zanotto* and Michele G. Wheatly. Univ. of Florida, Gainesville, FL 32611

In postmolt, crayfish exhibit net influx of Ca and basic equivalents (+2500; +3500 $\mu mol\ Kg^{-1}\ h^{-1}$), associated with $CaCO_3$ deposition. A net uptake of Na and Cl (+750; +1250 $\mu mol\ Kg^{-1}\ h^{-1}$) offsets the hemodilution resulting from FW uptake at ecdysis. Two experimental series were run on Procambarus clarkii. In Series 1, the pH of artificial tap water was altered directly to either pH 5.2 (H_2SO_4) or pH 9.2 (KOH), and fluxes compared with control (pH 7.2). In pH 5.2 Ca and base uptake were both reduced by 65%; Na uptake was initially reduced, but Cl uptake and ammonia output were unaffected. In pH 9.2 calcification was similarly impaired but only by 50%. In Series 2, water was decarbonated prior to use (acidified to pH 3.5 then back titrated) in order to avoid complicating effects of varying PCO_2 amongst treatments. In decarbonated water postmolt fluxes were the same in all treatments. However, Ca and base uptake in neutral decarbonated water were 70% reduced compared to Series 1 controls. Ammonia efflux and Cl uptake were 50% reduced, but Na uptake was unaffected. These data suggest that calcification is strongly dependent on ambient HCO_3. In decarbonated pH 5.2 and 9.2 (Series 2), calcification is impaired by reduced HCO_3, not pH per se. However, the effect in pH 9.2 in Series 1 must be attributed to some other mechanism. (Support by NSF 89-16412 (MGW), & CNPq, Brazil (FPZ)).

14.3

LOCALIZATION AND PURIFICATION OF BETAINE ALDEHYDE DEHYDROGENASE IN MITOCHONDRIA ISOLATED FROM HORSESHOE CRAB HEART TISSUE. Julia Dragolovich and Sidney K. Pierce. Univ. of Maryland, College Park, MD 20742.

Glycine betaine is an important intracellular osmolyte utilized by a variety of organisms. Its accumulation in response to hyperosmotic stress has been found in plants, bacteria, mammalian kidney cells, and marine invertebrates. Glycine betaine is the end-product of choline oxidation (choline $\xrightarrow{1}$ betaine aldehyde $\xrightarrow{2}$ glycine betaine). Step 1 is catalyzed by choline oxidase and step 2 by betaine aldehyde dehydrogenase (BADH). Previously, we have shown that in the presence of the precursor choline, mitochondria isolated from heart tissue of horseshoe crabs (*Limulus polyphemus*) are able to synthesize glycine betaine. Therefore, we have developed a purification scheme for BADH which includes ammonium sulfate fractionation and ion-exchange and hydroxyapatite column chromatography. The presence of BADH is detected spectrophotometrically. We have found that approximately 80% of the activity is associated with the mitochondrial matrix fraction, while the remaining activity is retained by the inner mitochondrial membrane fraction. The enzyme reaction is substrate specific, requires the co-factor NAD^+, and is regulated by end-product (glycine betaine) inhibition.
(Supported by NSF Grant # DCB-87-10067 and Sigma Xi)

14.4

SALINITY TOLERANCE DIFFERENCES BETWEEN CHESAPEAKE BAY AND ATLANTIC OYSTERS: DIFFERENCES IN AMINO ACID AND GLYCINE BETAINE METABOLISM. Sidney K. Pierce, Laura R. Faux and Shelia M. O'Brien. Univ. of Maryland, College Park, MD 20742

We obtained *Crassostrea virginica* from 11 Atlantic coast sites ranging from Florida to Cape Cod and from 8 sites on both the western and eastern shores of the Chesapeake Bay. Initially, all oysters were exposed to full strength sea water (920 msom) and 300 mosm. Incredibly, none of the Bay oysters survived exposure to sea water. However, Bay oysters acclimated to 700 mosm for a month would then tolerate the higher salinity. Following a 30 day acclimation to low salinity, the amino acid pool of adductor muscle from Atlantic oysters averaged 500 µM, predominantly taurine. In Bay oysters adapted to the same salinity the content was 360 µM, largely aspartate and glycine. In gill tissue, low salinity adapted Atlantic oysters had about 500 µM, predominantly taurine, while Bay oyster gill had about 400 µM. Glycine betaine in low salinity adapted Atlantic oysters averaged about 350 µmoles in adductor muscle and 300 µM in gill. In Bay oysters, glycine betaine averaged about 25 µM in both tissues. Following high salinity adaptation, the amino acid pool in Atlantic oyster adductor muscle increased to about 800 µM and gill to about 700 µM. Bay animals had values of 670 µM for muscle and 750 µM for gill. In addition, glycine betaine increased up to 500 µM in the gill of high salinity adapted Atlantic oysters. It did not change from the the low salinity levels (25 µM) in high salinity adapted Bay animals. Thus, the Bay oysters have smaller amino acid pools and the intracellular glycine betaine pool is 10 fold smaller (25 fold in high salinity) and does not change with salinity adaptation. These biochemical results suggest that the Bay animals should not be as salinity tolerant as the oceanic oysters and, indeed, they are not. (Sup. by UMAES)

14.5

OSMOTIC AND VOLUME REGULATION OF PLASMA ARGININE VASOPRESSIN IN FERAL HOUSE MICE. H. Haines, T.M. McKenna and D.L. Secor.* Univ. of Oklahoma, Norman, Ok 73019

Plasma concentrations of immunoreactive arginine vasopressin (pAVP, µU/ml) were measured in feral Mus musculus under differing states of plasma osmolality (pOsm, mOsm/kg) and blood volume (Δ%, [1 - [control/expt'l. hematocrit]] 100). pAVP was measured with radioimmunoassay: Calbiochem antiserum (#969115), final dilution $1:10^5$; <1% crossreactivity with AVT, LVP and OT; 0.51 µU minimum sensitivity; WHO lst Int'l. Stand. Blood samples were collected from decapitated mice after ketamine anesthesia. Plasma was extracted with acetone and petroleum ether with 76.5% recovery of internal standards. pOsm was manipulated with 2% body weight IP injections of NaCl ranging from 200 to 3000 mOsm/kg. pOsm rose with increasing NaCl concentration and pAVP varied directly with pOsm; pAVP = 1.8(pOsm - 306); n = 71, P<.001). Δ% was manipulated with 2% body weight IP injections of polyethylene glycol (PE) solutions ranging from 50 to 300mg/ml. Ninety minutes was allowed for fluid equilibration. Hematocrit increased with PE concentration, reflecting a short term decline in blood volume. pAVP rose with increasing Δ%; pAVP = 11.5 + 4.3(Δ%); n = 37, P<.001). Comparison with other species shows the mouse to have high control levels of pAVP (13.5 + 5.7, mean ± sem, n = 10) and an unusually sensitive pAVP vs pOsm response. Supported by USPHS Grant 5 R01 AM 25189.

14.6

LIQUID WATER EXCHANGE OF REPTILIAN EGGS. A. Ar, H. Koltai, A. Belinsky, R. Dmi'el, Tel Aviv Univ., Tel Aviv, 69978, Israel, and R.A. Ackerman, Iowa State Univ., Ames, IA 50011

Do soft shelled reptilian eggs exchange liquid or vapor water with their substrate? We followed mass change of developing hardun (*Agama stellio*) and tessellated water snake (*Natrix tessellata*) eggs (incubated in soil of a water potential, Ψ, <100kPa) in distilled water and in -2000kPa solution aerated with O_2 for 2h. Most eggs tolerated the treatment and hatched. An initial mass increase was observed, followed by either a linear gain or loss, respectively. Using mass change values per unit surface area (A) and time, the overall Ψ of the eggs and their hydraulic mass transfer coefficients (Kh) were obtained. The Kh of isolated eggshells was obtained from flux measurements under 10kPa hydrostatic pressure. Results (± coeff. of var. or range) were:

	Egg Mass (g)	A (cm^2)	Egg Ψ (kPa)	Egg Kh $\mu g/(kPa.cm^2.h)$	Shell Kh	n
Agama	5.33(±26%)	14.2(±15%)	579(±18%)	2.2(±82%)	960-218000	10-27
Natrix	9.28(±14%)	19.1(±10%)	928(±26%)	2.3(±44%)	910-112000	8-27

Hence, only the egg/shell interphase offers a significant resistance to liquid water diffusion. Soils of Ψ > -600-900 kPa permit water gain. Since exchange rate of liquid is comparable to vapor, eggs may use both, but initial mass gain of dipped eggs indicates a gas filled eggshell matrix in soil of low -Ψ. Liquid water exchange of reptilian eggs appears to be limited to water saturated soils only.

14.7

ION-SELECTIVE MICROELECTRODE STUDIES OF IONOREGULATION DURING LOCUST EMBRYOGENESIS. Erika Hawkins and M. J. O'Donnell. McMaster University, Hamilton, Ont. L8S 4L8

Although the cleidoic egg is one of the pre-eminent adaptations of insects to the terrestrial environment, little is known about pH- and iono-regulation in chorionated eggs after ovoposition. In many insect eggs the chorion forms a tough shell. However, measurement of transmembrane potentials (V_m), input resistance (R_{in}) and ion activities (H^+, K^+, Na^+, Cl^-) in locust eggs is feasible because the relatively soft egg membranes are readily impaled by double-barrelled theta-glass microelectrodes for the first 5 days (d) of the 10 d embryo development at 37°C. By day 5, the embryo occupies 75% of the egg volume. V_m declines from -55 mV preovoposition to -25 mV on d 1-2, then increases to -75 mV during d 3-5. Increases in V_m are not correlated with changes in R_{in}. Two results suggest a metabolic pump contributes to membrane electrogenesis: 1) V_m is 15-30 mV below the equilibrium potentials of H^+, K^+, Na^+, and Cl^- on d 3-5, and 2) anoxia causes a rapid, reversible depolarization. Data also shows pH is actively regulated at 7.2 throughout development. aNa^+, aCl^-, and aK^+ are regulated independently during embryogenesis and water uptake (d2 to d5) from the moist sand around the eggs. Data suggest release of K^+ from cellular stores on d1-d2, while aCl^- remains relatively constant. Also, ion activities were constant or decreased less than predicted from the increase (>50%) of water content during d3 and d4.

14.8

HANDLING STRESS INDUCED CUTANEOUS OSMOTIC WATER FLOW (J_V). Robert H. Parsons, Fardad Mobin*, HySoo Ka*. Dept. of Biology and Biophysics Center. Rensselaer Polytechnic Institute, Troy, N.Y. 12180.

Handling stressed (*Rana pipiens*, were turned on their backs and forced to right themselves for 1.5 min) frogs had a J_V of 28.12 ± 2.88 x10^{-7} cm^3/cm^2 sec. (SEM, 14 frogs) during the first hour after being stressed. After two hours of equilibration this value dropped to 18.01 ± 4.4 x10^{-7} (14). Tritiated water (THO) diffusion was also significantly increased by handling stress. THO diffusion in stressed frogs was 7.7 x10^{-5} cm/sec (SEM, 7 frogs) and dropped by 43% to 4.39 x10^{-5} (7) after two hours. Previous experiments have shown that an antidiuretic hormone induced increase in J_V is not associated with an increase in THO diffusion; while a circulation induced increase in J_V is associated with an increase in THO diffusion (Parsons et al., Physiol Zool., in press, 1990). These results suggest handling stress increases J_V by a circulation associated mechanism.

14.9

INHIBITION OF SORBITOL SYNTHESIS CAUSES CELLULAR DAMAGE IN PRIMARY CULTURES OF RAT RENAL MEDULLARY EPITHELIUM EXPOSED TO HYPEROSMOTIC MEDIUM. M.G. Beyer*, S. Githens*, and C.K. Bartell. University of New Orleans, New Orleans, LA 70148

Cell volume regulation in the hyperosmotic environment of the renal medulla is achieved through the regulation of intracellular organic osmolyte concentration. Sorbitol, whose synthesis from glucose is catalyzed by aldose reductase (AR), is one of these osmolytes. Sorbitol is also synthesized and accumulated by non-renal tissues in diabetics and is presumed responsible for much of the tissue damage associated with diabetes. The AR inhibitor, Sorbinil (Pfizer, Inc.), is one of several agents being tested as a means of reducing tissue damage in diabetics. Primary cultures of medullary epithelium were used to study the effect of hyperosmotic medium and AR inhibition on intracellular sorbitol and on epithelial growth and survival. Intracellular sorbitol levels correlated positively with the osmolality of the medium made hyperosmotic with NaCl and urea (1:1 ratio). Sorbinil blocked the elevation of intracellular sorbitol levels at 1200 mOsm and also caused degeneration and detachment of established epithelia, as well as leakage of lactate dehydrogenese into the medium. At 900 mOsm, Sorbinil slowed epithelial growth. In contrast, Sorbinil had no effect on growth, epithelial viability, or LDH release at 300 mOsm. Sorbinil, therefore, is deleterious to renal medullary epithelium in hyperosmotic culture medium because it interferes with osmotic regulation by inhibiting sorbitol synthesis.

14.10

METABOLIC COST OF IONIC REGULATION IN RAINBOW AND STEELHEAD TROUT. George K. Iwama and John Morgan *. Dept. of Animal Science, University of British Columbia, Vancouver, B.C. Canada

In freshwater fish, passive efflux of ions are compensated by the active uptake of ions to maintain ionic homeostasis. While reported estimates of the energetic cost of that active component vary and are as high as 27 % of resting metabolic rate, calculations based on theoretical considerations yield estimates that are an order of magnitude less. We tested the hypothesis that the energetic cost of ionic regulation would be minimal at the isotonic water salinity. Rainbow and steelhead trouts were acclimated and grown, up to 15 weeks, in a range of hypotonic to hypertonic salinities, including one that was near isotonic. Metabolic rate was measured by indirect calorimetry for eggs, newly hatched alevins, and fry at each salinity. Growth rates, haematocrits, and plasma ion concentrations were also measured in fry at all salinities. Mortality rates and hatching success were also determined where appropriate. Metabolic rate was at minimum at the near isotonic salinity for newly hatched steelhead alevins. While growth and survival were optimal from the lowest to isotonic salinities, there were high mortalities and poor growth in alevins at the hypertonic salinity. Metabolic rate was constant for eggs acclimated at all salinities. Metabolic rates in fry increased with water salinity. The lowest rates of oxygen consumption were in fresh water. The metabolic costs associated with ionic regulation were about 20% and 1% for the rainbow and steelhead trouts, respectively. Growth rates declined in all fish with increased water salinity and were strongly correlated to metabolic rate. Anadromous steelhead trout may be better adapted for ionic regulation than the rainbow trout. Ionic regulation at hypertonic salinities is not developed in alevins.

14.11

ATRIAL NATRIURETIC PEPTIDE AND SALT ADAPTION IN THE SEA LAMPREY *PETROMYZON MARINUS*. J.D. Freeman* and R. A. Bernard. Michigan State Univ., East Lansing, MI 48824

The possible role of atrial natriuretic peptide (ANP) as a mediator of Agnathan anadromic euryhalinity was investigated in the recently established Great Lakes population of Petromyzon marinus in a repeated measures design. All lamprey were in the sexually immature feeding phase. Blood plasma was collected by intracardiac puncture in an unanesthetized state over a series of three four-day acclimatization periods in which the fish were exposed to stepwise increases in tank water osmolality (118, 315, 611, and 927 mosmol/kg). Plasma osmolality (303 ± 5 mosmol/kg) remained unchanged over the acclimatization period ($p<0.05$), indicating the fish were osmoregulating. However, plasma levels of immunoreactive (ir) ANP, measured by direct radioimmunoassay using rat atriopeptin III (rAPIII) and antiserum directed to rAPIII, significantly increased ($p<0.05$) from the freshwater condition (384 ± 2 pg/ml) to the marine condition (1016 ± 201 pg/ml). Moreover, a second group of fish acclimatized and held in the marine condition for approximately three months had irANP plasma levels of 1580 ± 39 pg/ml. This correlates well with similar studies completed on teleosts, elasmobranchs, holocephalians, and the hagfish Myxine glutinosa. (Supported in part by NIH grant DC 00340.)

14.12

EFFECTS OF SALINITY AND VOLUME EXPANSION ON TROUT PLASMA ANF. D. W. Duff and K. R. Olson. Biol. Dept., Ind. U., South Bend, South Bend, IN 46634 and Ind. U. Sch. Med., South Bend Ctr., U. Notre Dame, Notre Dame, IN 46556.

Atrial natriuretic factor (ANF) has been proposed to play a role in fish osmoregulation (Am. J. Physiol. 26:R945, 1989). Plasma immunoreactive ANF (ir-ANF) was measured using established methods (Am. J. Physiol. 26:R945, 1989) in fresh water (FW) trout (*Salmo gairdneri*) or trout adapted to sea water (SW; 9 or 30 days) and 0.5, 4, 8, and 12 h after transfer from FW to SW. Trout were volume expanded with plasma (10 or 20% of estimated blood volume) for 1 h. Ir-ANF levels in 9 (n=10) or 30 (n=9) day SW adapted trout (110.2±6.8 and 98.7±6.4 pg/ml, respectively) were no different than levels in FW (n=23) adapted trout (98.2±10.6 pg/ml). Plasma ir-ANF did not change significantly after transfer from FW to SW (130.5±30.1, 109±16.3, 153.7±13.7, 150.8±8.2, and 129.2±10.7 at 0, 0.5,4,8, and 12h respectively, n=7). Volume expansion did not affect plasma ir-ANF (99.3±7.9 to 120±15.5 pg/ml after 10% volume expansion (n=9) and 81.9±8.9 to 83.4±10.9 pg/ml after 20% volume expansion. n=8). These results suggest that, in trout, ANF is not involved with either osmoregulatory responses accompaning salinity transfer or volume expansion. **(Supported by NIH grant R15 37237 and NSF grant No. DCB 8616028).**

15.1

Na^+-K^+ PUMP FUNCTION AND INTRACELLULAR CALCIUM DURING HYPOXIA IN CANINE MYOCARDIAL TISSUE. Mohit L. Bhattacharyya and Shukla Sarker, Meharry Medical College, Nashville, TN 37208.

We reported earlier the beneficial effects of dextrose and magnesium in canine myocardial tissue during hypoxia, hyperkalemia and acidosis (HHA, produced by changing KCl, $NaHCO_3$, NaCl to (mM) 4.6, 5.5, 150 respectively in Tyrode, gassed with 95% N_2 and 5% CO_2). Membrane potential and contractile force were recorded. A subdued Na^+-K^+ pump and elevated $(Ca)_i$ were implicated during HHA. Here, the Na^+-K^+ pump and $(Ca)_i$ were assessed by testing the OVERDRIVE INDUCED HYPERPOLARIZATION (OIH) and POST DRIVE (PD) alterations in the membrane potential. Purkinje fibers are normally driven at 1Hz. During the overdrive the driving rate was increased to 3Hz for 1-1.5 min. In Tyrode OIH was 8.0 ± 1.2 mV (6 expt.). During HHA, the OIH is lost. High Mg(5 mM) or high dextrose(50mM) during HHA, restored the OIH. High Mg or high dextrose in Tyrode increased the OIH a little, compared to that in Tyrode alone. High calcium (5.4mM) Tyrode did not change the OIH but produced small fluctuations in the membrane potential during the PD period. Reoxygenation after HHA, did not alter OIH but fluctuations in the membrane potential were seen during the PD period. We conclude that the Na^+-K^+ pump activity is partly lost during HHA and high Mg or high dextrose restore it. The fluctuations in the membrane potential during the PD period may be due to increased $(Ca)_i$.

15.2

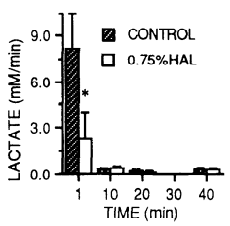
CARDIAC ELECTROPHYSIOLOGICAL AND MECHANICAL EFFECTS OF COCAINE. Hassan T. Sherief*, Bernell R. Coleman, Dali J. Patel and Robert G. Carpentier. Department of Physiology and Biophysics, Howard University College of Medicine, Washington, D.C. 20059.

The effect of cocaine (COC) on membrane potentials and contractile function were studied in isolated atrial (AM) and papillary muscle (PM) of the rat. In AM, COC 20mg/L produced a decrease in resting potential (RP), amplitude of the action potential (AAP), overshoot (OS) and Vmax O. The effect of COC on the action potential duration (APD) was biphasic; an initial transient shortening was blocked by atropine, while a subsequent prolongation was blocked by phentolamine. In PM, the depressant effect on RP, AAP, OS and Vmax O was similar to that in AM. However, the initial shortening of APD was not observed. Prolongation of APD was the only effect on this parameter produced by COC. COC had a negative inotropic effect on both AM and PM; the peak tension developed (PTD) and maximum velocity of tension development (Vmax T) were depressed, while resting tension was unchanged. In conclusion: the depressant actions of COC on the magnitude of myocardial membrane potentials are associated with alpha adrenergic and cholinergic mediated biphasic actions on the APD in AM, but only with an alpha adrenergic mediated action on the APD in PM. COC also depressed myocardial contractility. Supported in part by Howard University Faculty Research Support Grant.

15.3

ANTIDYSRHYTHMIC EFFECTS OF HALOTHANE (HAL) DURING ISCHEMIA: CORRELATION WITH CHANGES IN ANAEROBIC GLYCOLYSIS. Nediljka Buljubasic*, Jure Marijic*, David F. Stowe, John P. Kampine and Zeljko J. Bosnjak. Departments of Anesthesiology and Physiology, Medical College of Wisconsin, Milwaukee, WI 53226

During myocardial ischemia, when oxygen delivery to the myocardium becomes limited, the myocardium increasingly depends on anaerobic glycolysis of muscle glycogen and supplied glucose as a source of energy. We examined the temporal effects of 0.75% HAL (0.24 mM) 10 min prior to, during and 10 min following a 30 min period of global ischemia (0% of normal perfusion pressure, 55 mmHg) on development of dysrhythmias and production of lactate (LAC) in isolated guinea pig hearts (N=16). We correlated the duration of the ventricular fibrillation (VF) with LAC production during a 40 min of reperfusion. Perfusate contained 12 mM glucose and 2 mM pyruvate. LAC release (mM/min) was measured photometrically with the use of a Lactate Assay (Kit 826-B Sigma Chem.). HAL decreased the production of LAC (Figure), and significantly ($p<0.05$) decreased the duration of VF from 8.1±3.25 min to 1.5±0.78 min during early reperfusion. These results suggest that by decreasing LAC production and anaerobic glycolysis with early reperfusion, HAL decreases the duration of VF. (Supported in part by NIH grant HL 34708)



* $p \leq 0.05$ vs. CONTROL

15.4

PROTONS AND SINGLE JUNCTIONAL CHANNEL EVENTS IN HEART CELL PAIRS. Walmor C. De Mello, Department of Pharmacology, Medical Sciences Campus, UPR, GPO Box 5067, San Juan, PR 00936.

The possibility that H ions reduce the junctional conductance (gj) by decreasing the unitary channel conductance (Yj) or by altering the open-closed time Kinetics was investigated in heart cell pairs isolated from adult rat ventricle. Only pairs showing low gj (2-3 nS) were used. Each cell was connected to a separated voltage-clamp circuit and whole cell clamp was then achieved. With a transjunctional voltage of - 50 mV single junctional channel events were easily recognized by their equal and opposite character in the two current traces (I1 and I2). The single channel conductance was found to be 94.7 pS (+ 30) (6.000 events). No change in single conductance was found when pHi was reduced from 7.4 to 5.7 (92.3 pS (+ 29) (P 0.10) despite the appreciable decrease (80%) of gj. As the effect of pHi 5.7 on gj is quickly reversed the number of channel is probably not changed. A decrease in open probability (Po) elicited by low pHi might explain the decrease in gj caused by acid solution. Supported by Grant GRS 2 S06 RR 08224-5.

ARTRIAL NATRIURETIC FACTORS

16.1

ATRIAL NATRIURETIC FACTOR IN GYNECOLOGIC MALIGNANCY. **Papineni S. Rao, James V. Fiorica*, and Denis Cavanagh.* Department of Obstetrics and Gynecology, University of South Florida, Tampa, Florida 33612.**

Atrial natriuretic factor (ANF) is a peptide secreted by cardiac atria and is thought to be important in volume homeostasis. Circulating levels of ANF have been studied in a variety of clinical situations but none has been reported in patients with gynecologic cancer. These patients are at risk for significant variation in intravascular volume, myocardial performance and renal function as a result of their disease and/or treatment. To evaluate this we studied 26 patients with gynecologic malignancies with Stage III or IV disease or recurrent cancer. All of the patients received at least one month of platinum based chemotherapy with some receiving multiagent therapy prior to obtaining ANF levels. Quantitative determination of plasma ANF was done using a specific radioimmunoassay following sample purification and elution. As a measure of renal function, urine output, creatinine clearance and fractional sodium excretion was evaluated. To obtain normal levels of ANF, 25 women free of malignancy served as controls. All the values are presented as mean ± SEM. The mean value of ANF in the control group was 7.3±0.3 fmol/ml of plasma, whereas in the cancer patients the value of 12.5± 1.3 was significantly higher ($p<0.01$). Eight of the control group are pre-ovulatory, 7 are post-ovulatory, and 6 are post-menopausal as determined by menstrual history. Their ANF levels are 7.6±0.7, 7.7±0.7 and 7.2±0.2 fmol/ml respectively. In the chemotherapy group serum levels of BUN, sodium, potassium and creatinine respectively are 20.0± 2.5 mg/dl, 139± 0.6 mEq/L, 4.4± 0.13 mEq/L and 1.55± 0.4 mg/dl. Urine volume was within normal limits (0.95± 0.19 ml/min) with endogenous creatinine clearance being 45.3±5.6 ml/min. Fractional sodium excretion in this group of patients was 1.67± 0.005%. The results of this pilot study suggests that plasma ANF levels in the gynecologic cancer patients are significantly higher than that of normal nonpregnant women. Whether this is due to chemotherapy or not needs further elucidation.

16.2

EFFECT OF INTRAVENTRICULAR ATRIAL NATRIURETIC FACTOR ON INTRACRANIAL PRESSURE IN THE AWAKE RAT. Marc L. Leavitt, Daniel V. Loesch*, and Joseph C. Maroon*. Allegheny-Singer Research Institute, Pittsburgh, PA 15212

Recent studies have suggested that atrial natriuretic factor (ANF) may be involved in cerebrospinal fluid (CSF) formation and the control of intracranial pressure (ICP). To test the latter possibility we measured ICP (CSF pressure) in awake adult male Wistar rats via a guide cannula implanted into the lateral cerebral ventricle. On test days, an internal cannula was used to infuse at 2µl/min either artificial CSF (art CSF) or art CSF with rat atrial natriuretic peptide (rat ANP, 2pmol /min) for 5 hrs. Although baseline ICP for control rats (10.9 ±1.7 cm H_2O) was not different from that of ANP rats (12.9± 0.3), by 230 min. the ICP of ANP rats (38.2±0.8) was significantly ($P<.05$) greater than that of the controls (29.7±4.1). The ICPs for the ANP group were significantly elevated compared to the controls for the last 70 min. of the infusions. All the ANP-infused rats had similar ICPs for the first 160 min. of the infusion after which time the pressures become greatly elevated in half the rats and eventually reached a mean level of 76.8±2.2 cmH_2O. These animals died within one day.

CSF Pressure in cmH_2O

	10min	130min	190min	250min	280min	300min
art CSF	10.8±1.7	18.6±3.3	24.5±3.8	34.4±4.6	33.9±5.3	34.6±4.2
ANP	12.9±0.3	11.9±0.3	22.1±0.5	44.3±0.9	49.0±1.0	54.0±1.0

These results suggest a role for ANF in the control of intracranial pressure.

16.3

Atrial Natriuretic Factor (ANF) and Pro-ANF During Acute and Chronic Sodium Loading in the RAT. John R. Dietz, Stanley J. Nazian*, and David L. Vesely*. Departments of Physiology and Biophysics and Medicine, University of South Florida, College of Medicine, Tampa, FL 33612.

The purpose of this study was to examine the effects of blood volume expansion and changes in sodium intake on ANF and ANF pro-hormones 1-98 and 31-67. In anesthetized rats, a 20% blood volume expansion resulted in an increase in urine flow from 2.4 ± 0.6 to 10.9 ± 2.3 µl/100g B.Wt/minute ($p<0.001$) and sodium excretion increased from 0.30 ± 0.16 to 1.67 ± 0.60 µM/100g B.Wt./min ($p<0.01$). Plasma ANF increased from 70 ± 17 pg/ml to 233 ± 62 pg/ml ($p<0.01$) while pro-ANF 1-98 increased from 611 ± 44 to 768 ± 44 ($p<0.05$). In a chronic study rats on a regular salt intake of approximately 1.5 mM per day for one week had plasma ANF levels of 253 ± 114 pg/ml which tended to be higher than ANF in rats on a low salt intake of <0.2 mM per day; 64 ± 26 pg/ml ($p>0.05$). Pro-ANF 1-98 averaged 635 ± 47 pg/ml in rats on the regular salt intake and was significantly reduced in rats on the low salt intake; 353 ± 33 pg/ml ($p<0.001$). Pro-ANF 31-67 was also significantly higher in rats on a regular salt intake compared to low salt intake; 123 ± 21 vs 59 ± 13 pg/ml ($p<0.05$). These results suggest that ANF and Pro-ANF fragments may play a role in the physiological adjustment to acute and chronic sodium loading. (Supported by AHA, Florida Affiliate and NIH grant HL37235).

THE UNDERGRADUATE LABORATORY: TEACHING BASIC LABORATORY SKILLS AND PHYSIOLOGICAL PRINCIPLES

17.1

USING A TEMPERATURE GRADIENT TO ILLUSTRATE PRINCIPLES OF ANIMAL BEHAVIOR AND PHYSIOLOGY. C.S. O'Connor* and L.I. Crawshaw. Portland State University, Portland, OR 97207

All motile organisms are able to respond to adverse temperatures in the environment. Responses range from simple avoidance of extreme temperature to sophisticated feedback systems which allow accurate regulation of body temperature within narrow limits. Many animals, including crayfish, goldfish, and mice, will exhibit reliable thermoregulatory behavior in a classroom situation. Other behaviors, such as orienting response, may also be observed in a temperature gradient, and illustrate the effect of competing drives. Physiological effects, such as the consequence of prior exposure to various acclimation temperatures, can also be demonstrated. Drugs can be used to alter thermoregulatory set point. Thermoregulatory behavior can be manipulated in a variety of simple or sophisticated ways and is easy to observe in apparatuses that are straightforward to construct and operate, making it an excellent system to use for illustrating behavioral and physiological principles in the teaching laboratory.

17.2

THE ISOLATED ALLANTOIC MEMBRANE OF THE EMBRYONIC CHICKEN AS A MODEL FOR EPITHELIAL ION TRANSPORT STUDIES. John G. Blackburn, John H.Todd and Paul F. Horton. Dept. of Physiology. Medical University of S.C., Charleston, SC 29425

The frog skin has been used as a model for studying epithelial ion transport since the introduction of the Ussing chamber-voltage clamp technique in the early 1950s. While still an excellent model, the frog skin displays seasonal changes in ion transport. Furthermore, this experimental animal can be expensive and difficult to obtain under some circumstances. The allantoic membrane of the embryonic chicken has recently been shown to be an excellent model for epithelial ion transport studies. The preparation is simple, inexpensive, and well-suited for both teaching and research experiments. Ionic transport changes during egg incubation, thus providing an excellent model for demonstrating developmental changes in ion transport. All of the usual Ussing chamber-voltage clamp procedures for demonstrating passive and active ion transport (ion channel blockers, ion substitutions, enzyme inhibitors, etc.) may be employed with this preparation. Exciting, informative experiments are easily performed by undergraduate students using inexpensive, commercially obtainable equipment and a biological membrane that is an excellent alternative for the frog skin.

17.3

EFFECTS OF THYROXINE ON GLYCEROL 3-PHOSPHATE DEHYDROGENASE ACTIVITY IN RAT LIVER: A STUDENT LABORATORY EXERCISE. Richard L. Walker Dept. of Biological Sciences, Univ. of Calgary, Calgary, Alberta, Canada, T2N 1N4

Mitochondrial glycerol 3-phosphate dehydrogenase (G3PD) activity in rat liver homogenates was determined spectrophotometrically using DCIP (dichlorophenol indophenol) as an indicator. Rats were divided into four treatment groups; control (sham-operated), thyroidectomized, thyroxine-injected (40 ug L-thyroxine/100g/day i.m.), and cold-exposed (5C). After two weeks, whole body oxygen consumption was measured, the rats were then sacrificed and 1 g of liver was removed for determination of G3PD activity. The assay is simple, requiring only crude homogenates of the liver and a spectrophotometer capable of reading at 600 nm. While differences in whole body oxygen consumption were subtle, class results show clear differences in the liver G3PD activity among the four groups. The activity in the thyroxine-injected and cold exposed rats was 2 to 3 times that of the control group, while the thyroidectomized rats showed less than half of the activity of the controls.

17.4

INTRACELLULAR RECORDING FROM BRAIN CELLS IN THE LAND SNAIL: A STUDENT LABORATORY EXERCISE FOR EXAMINING NEURONAL EXCITABILITY. B.R. Johnson, M.L. May and P.D. Brodfuehrer*. Neurobiology and Behavior, Cornell University, Ithaca, N.Y. 14853.

We use a circumesophageal ganglia preparation from the land snail, *Helix aspera*, for an undergraduate laboratory teaching exercise to study neuronal excitability. These animals are inexpensive, easy to maintain, students can learn the dissection relatively quickly, and the ganglia remain viable for at least several hours in chilled saline. The neurons in the parietal and abdominal ganglia are large (up to 200 µM in diameter) and readily accessible for standard intracellular recording techniques. The students first characterize identified cells by mapping their location in the ganglia and describing the following physiological properties: resting potential (RP), spontaneous activity, including action potential (AP) firing frequency, and synaptic potentials, the AP amplitude and duration, responses to depolarizing and hyperpolarizing current injections, input resistance and time constant. Second, the students examine AP generation in different cells by determining the threshold value for eliciting an AP, the ionic basis of an AP through ion substitution experiments (either sodium or calcium in different cells), and the potassium contribution by adding tetraethylammonium. Other successful student exercises with this preparation include demonstrating the electrogenic activity of the Na^+-K^+ pump by monitoring the RP changes following perfusion with warm saline alone and with ouabain added, further pharmacological studies of the AP, and ion substitution studies to determine ionic basis of the RP.

17.5

A RESEARCH-LIKE EXPERIENCE FOR FRESHMEN: BIOLOGY OF ALKALINE PHOSPHATASE. David W. Towle and M. Sandra Gay*. Lake Forest College, IL 60045

To gain extended experience in an open-ended research-like environment, students in the freshman core course, Biology of Cells, investigate the distribution and properties of alkaline phosphatase in an organism in which little is known about the enzyme. Over a five-week period, students learn to make buffers, construct a standard curve using a spectrophotometer, homogenize and fractionate tissue by differential centrifugation, and assay tissue fractions for alkaline phosphatase. Using their buffers and tissue fractions, students determine the effects of pH and substrate concentration, plotting their data using computer graphics. A brief independent project and a major report done in scientific format complete the experience. Because each student pair works with a different tissue, perhaps taken from organisms acclimated to different environments, a wide variety of experimental combinations is possible. Emphasis is placed on building student independence through the development and repetition of fundamental laboratory skills, at the same time providing an environment in which new scientific data can be produced. The students find the experience "electrifying".

17.6

SURVEY OF CANADIAN UNIVERSITIES REGARDING UNDERGRADUATE PHYSIOLOGY TEACHING LAB EXERCISES. Don Stevens. Zoology, University of Guelph, Guelph, Canada N1G 2W1

(support by NSERC)

I recently surveyed some teachers of comparative physiology at Canadian Universities. The goals of my survey were: 1. Discover the extent to which lab practicals are used; 2. Discover what topics are used; 3. Discover what animals are used; 4. Discover the extent to which computer simulations are used. The focus was on comparative physiology; it was not on endocrinology or cell physiology. About 100 surveys were sent to members of Can. Soc. Zool. (CBP section); 44 replied. All respondents indicated a firm conviction in the importance of lab practicals; some were vehement on this point. Although almost all courses are titled comparative physiology, most lab practicals are general physiology. There is a wide range of labs done and species used. Of 44 respondents, 10 used computer simulations. These are especially useful as replacements in the human urine flow and human respiration labs because they solve the problem of transmission of infections between students. Some voiced strong opinions against the use of computer simulations.

TEACHING OF PHYSIOLOGY: ENHANCEMENT OF THE PEDAGOGICAL PROCESS

18.1

Undergraduate Course Improvement: Neuroscience Courseware for Engineering Students. Y. Laouris* and D.G. Stuart. Department of Physiology, College of Medicine, University of Arizona, Tucson, AZ, 85724.

Undergraduate instruction in interdisciplinary neuroscience for students in a wide variety of life- and physical-science disciplines is an emerging venture at American universities. At our university, we also have a large number of undergraduates undertaking self-instruction in neuroscience to augment their student-employment and subsequent career possibilities. To meet their needs, we are currently in the process of developing computer-based courseware for courses (including independent studies) that include a substantial component of neuroscience. The main goal of this project is to provide physical-science students with an increased awareness and understanding of neuroscience. The material is presented to the student with numerous animations and computer simulations of physiological systems. Such courseware conveys knowledge in a quick and effective way with the key advantage that students can direct their *own* learning according to their individual *needs*, *time*, *skills*, and *preferences*. In order to facilitate use of the same material by students with different educational backgrounds and interests, the design of the software accommodates: 1) different layers (depth) of information; and 2) different interests with issues taken from both applied neuroscience (engineering-related issues) and clinical neurology. Planned features include videodisc (simultaneous display of still images on a TV screen) and sound support. Students currently involved in the development of the courseware include: E. Chernov, N. Stylianou and X. Xenophontos.

Supported by USPHS grants NS 07309, HL 07249, NS 25077, RR 05675 and a University of Arizona Provost's Teaching Improvement Award to YL & DGS.

18.2

CARDIOVASCULAR PHYSIOLOGY LABS TAUGHT BY INTERACTIVE VIDEODISC INSTRUCTION. J.L. Poland, C.D. Ford, T.M. Harris, J.K. Terpstra, and E.E. Turf. Med. College of Va./Va. Commonwealth Univ., Richmond, VA. 23298

Interactive Videodisc Instruction (IVI) is being used to help students learn physiological principles, typically taught via student laboratory experiments. Classic cardiovascular experiments, using dogs, were videotaped and transferred to laserdisc. There are 37 different experiments including occlusion of the carotid arteries, injection of acetylcholine or norepinephrine, and stimulation of the peripheral end of a cut vagus nerve. Comparisons are made between normal, propranolol treated, atropine treated and vagotomized dogs to demonstrate drug actions and reflexes. Each lesson allows the student to view the animal's recorded blood pressure and heart rate response to the perturbation, study a detailed computer simulation of the polygraph recording, and call up a flow diagram leading to explanations of the reflexes and drug actions underlying the changes. User input guides the visual display, providing a highly interactive, individualized form of instruction. Each student can study or review specified content and proceed at their own pace. Eight medical schools, all members of the Medical Interactive Video Consortium, are participating in developing the software associated with the videodisc. This IVI package provides an alternative method for teaching physiological principles when actual laboratory instruction is not possible.

18.3

PEER TUTORING IMPROVES PERFORMANCE OF STUDENTS IN AN ADVANCED LEVEL PHYSIOLOGY COURSE. D.A. Lake, Dept Physical Therapy, Northeastern Univ, Boston, MA 02115.

Peer tutoring has been shown to be effective in studies of primary and secondary level sciences courses. However, its effectiveness in the basic science courses of medical and allied health schools has not been demonstrated. This study was designed to assess the value of peer tutoring in an advanced Physiology course in the Physical Therapy Curriculum at Northeastern University.

The same advanced Physiology course is taught twice a year. Peer tutoring was done during thesecond presentation of the course. Five students who had previously taken the course tutored in small group sessions once a week for 2-3 hours. Attendance was recorded at each session. Grades from this course and previous physiology courses were obtained from departmental records. Student perceptions were measured by survey.

Sixty-four percent of the students taking the advanced Physiology course took advantage of tutoring. Participating students attended an average of 3.25 sessions. Sessions were valued by the students (6.4 on a scale of 10), and students were interested in having tutoring continued (6.9 on a scale of 10). Tutored students performed better in the advanced Physiology course than untutored students, and there was a good correlation between attendance at tutoring sessions and performance in the course (r^2=0.43).

18.4

KNOWLEDGE AND ATTITUDES OF CARDIOVASCULAR DISEASE PREVENTION AMONG GRADUATE NURSING STUDENTS. Marguerite M. Engler, Mary B. Engler, Dennis M. Davidson*, Robert E. Slaughter*. Univ. of California, San Francisco, CA 94143

To determine the knowledge and attitudes of cardiovascular disease (CVD) prevention, we surveyed 50 graduate nursing students, ages 20-49 (89% women, 11% men), before and after a 15-week physiology course. Approximately 1/4 had total blood cholesterol (TBC) levels >200 mg/dl. A majority ate red meat and cheese weekly, but also included fish in their diet. Parental history included myocardial infarction in 32%, hypertension in 46%, and 50% with high TBC. During the course, 66% decreased the amount of meat, eggs, and whole milk while 50% decreased salt intake. At course end, approximately 64% engaged in regular physical activity, a 37% increase. Initially, less than 1/3 correctly answered questions regarding the CVD risk of smoking in women, influence of body weight on lipids and blood pressure, the age-associated rise of TBC, and recommended percentages of calories from dietary fat; significant improvement was noted after the course. Overall, respondents had positive attitudes regarding the importance of CVD prevention and the partnership between patients and clinicians necessary to manage CVD risk. These attitudes did not change significantly following the course. These results indicate that graduate education which emphasizes CVD prevention increases knowledge and encourages individual choices toward healthy behavior.

19.1

SUBSTANCE P IS RELEASED DURING ANTIGEN INDUCED CONSTRICTION OF TRACHEAL SMOOTH MUSCLE FROM SENSITIZED GUINEA PIGS. Neven Tudoric*, Robert L. Coon and Zeljko J. Bosnjak. Department of Anesthesiology, Medical College of Wisconsin and VA Medical Center, Milwaukee, WI 53226

Capsaicin induced substance P (SP) depletion was reported to reduce antigen induced bronchoconstriction in sensitized animals. Therefore, the purpose of this study was to determine whether SP is released during antigen induced bronchoconstriction and whether it influences the magnitude of constriction. Twelve guinea pigs were sensitized by injection of 1.0 ml of 1% ovalbumine (OA), and 0.1 ml of DTP vaccine, and resensitized after 14 and 21 days with 0.25 ml of 0.1% OA. Excised tracheal rings were suspended and prestretched (3.0 g) in temperature controlled jacketed baths containing modified Krebs solution, bubbled with 95% O_2 and 5% CO_2 to maintain pH at 7.38 - 7.42 and PCO_2 at 35-40 mmHg. Constriction was induced with 0.1 µg/ml OA. After the constriction curve reached plateau an enkephalinase inhibitor phosphoramidon (PR) was added (10 µM). In another series of experiments the OA induced constriction was observed after tracheal rings were incubated with SP antagonist - [D-Arg^1, D-Trp^{7,9}, Leu^{11}]-SP (5 µM). All the results were expressed in percentage of acetylcholine induced maximal constriction (1 mM). PR prevented gradual relaxation following maximal constriction seen in the control OA constriction curve, increasing maximal constriction by 23% after 15 min, and by 28%, 30 min after the application. SP antagonist pretreatment increased spontaneous relaxation by 34% after 30 min, and by 28% after 45 min. We conclude that SP is released during antigen induced constriction of guinea pig tracheal smooth muscle and is responsible for the greater bronchoconstriction.

19.2

A PEPTIDERGIC COMPONENT TO TRACHEAL VASODILATION IN THE TRACHEA OF THE DOG AFTER VAGAL STIMULATION. T. Ito,* T. Takubo* and J.G. Martin. Meakins-Christie Laboratories, McGill University, Montreal, Quebec, Canada.

The purpose of the study was to determine whether neuropeptides contribute to vagally induced vasodilation in the trachea. Dogs were anesthetized with pentobarbital (25 mg/Kg), paralysed with pancuronium and ventilated through a low cervical tracheostomy. The tracheal branch of the cranial thyroid artery was cannulated and perfused at a constant flow. We estimated tracheal vascular resistance (TVR) from perfusion pressure and tracheal muscle tone was assessed using an intratracheal balloon. After pre-treatment with propranolol (2 mg/Kg) and phentolamine (1.5 mg/Kg) bilateral stimulation (NS) of the superior laryngeal nerves (15Hz, 7V, 2msec, 30sec) caused a decrease in TVR of 11.5±1.2% and a tracheal contraction of 7.3±2.2 cm H_2O. After atropine (1.5 mg/Kg) NS caused a smaller decrease in TVR 4.6±1.1% ($P<0.001$) but tracheal contraction was abolished. Thiorphan (0.1 mg/ml) augmented the decrease in TVR (9.1±0.8%; $P<0.05$) to NS. After hexamethonium (0.5 mg/Kg) NS still caused a small decrease in TVR (3.2±0%; $P<0.05$). Acetylcholine (ACh) caused a dose-dependent decrease in TVR which was abolished by atropine and unaffected by thiorphan and hexamethonium. We conclude that there is non-cholinergic non-adrenergic vagally induced tracheal vasodilation which is peptidergic. (Supported by the EL/JTC Memorial Research Fund and MRC of Canada).

19.3

PULMONARY EFFECTS OF A 5-HYDROXYTRYPTAMINE (5-HT) CHALLENGE AFTER 5-HT2 RECEPTOR BLOCKADE IN HEALTHY CALVES. A. Linden*, D. Desmecht*, F. Rollin*, H. Amory*, T. Art*, P. Lekeux. University of Liège, B-4000 Belgium

The purpose of the present investigation was to study if the 5-HT2 receptor blockade with a new antagonist, R 50970, could prevent the pulmonary dysfunctions induced by a 5-HT challenge, i.e., hyperventilation, diffuse bronchoconstriction and pulmonary artery hypertension. Five healthy, unsedated calves of the Friesian (n = 3) and the Belgian White and Blue (n = 2) breeds (age: 8 months ; body weight: 177.6 ± 21.5 kg) were investigated. Intrapleural pressure (Ppl) was measured with an esophageal balloon-catheter and transpulmonary pressure (PL) was obtained by subtracting the mouth pressure from Ppl. Respiratory airflow ($\dot{V}$) was measured using a Fleisch pneumotachograph n°3 connected to a face mask. PL and $\dot{V}$ were analysed by an Heres computer (ACEC, Belgium) which continuously calculated respiratory rate (RR), tidal volume (Vt), volume minute ($\dot{V}E$), total pulmonary resistance (RL) and dynamic lung compliance (Cdyn). Mean arterial pulmonary pressure (PAP) was obtained using a fluid filled catheter connected to an extravascular pressure transducer (Statham P 23D, Gould). Data were recorded a/ at rest, b/ 30 min after intramuscular injection of R 50970 (0.100 mg.kg^{-1}), c/ during the 5 min 5-HT intrajugular perfusion (0.050 mg.kg^{-1}.min^{-1}) administered 35 min post R 50970 and, d/ after 20 min recovery. Mean resting values of RR, Vt, $\dot{V}E$, Cdyn, RL and PAP were 17.6 ± 1.6 min^{-1}; 1.63 ± 0.21 L; 29.3 ± 2.73 L min^{-1}; 0.39 ± 0.02 L.cmH2O^{-1}, 2.35 ± 0.20 cmH2O.sec.L^{-1} and 29.2 ± 3.8 torr respectively. These parameters were not significantly altered by R 50970 administration. The 5-HT challenge post-R 50970 induced a significant increase in RR, $\dot{V}E$ and Cdyn while RL and PAP did not change significantly. All these changed data returned to their basal values after 20 min recovery. It was concluded that, in the bovine species, the 5-HT - induced broncho- and vaso- constriction but not the breathing pattern changes are prevented by 5-HT2 receptor blockade with R 50970.

19.4

SODIUM THIOPENTAL INHIBITS METACHOLINE INDUCED BRONCHOSPASM IN AN IN VITRO GUINEA PIG LUNG PREPARATION.

S.A. Vitkun*, W.M. Foster, E.H. Bergofsky, P.J. Poppers. Depts. of Anesthesiology and Medicine, SUNY at Stony Brook, Stony Brook, N.Y. 11794.

We previously developed an airway perfused guinea pig bronchial tree preparation for evaluation of mediators of asthma (Lung, 165: 101, (1987)) and studied the effects of ketamine, an intravenous anesthetic, on pharmacologically induced bronchospasm. We have undertaken a similar evaluation of thiopental (Thp), an anesthetic induction agent. Guinea pig lungs were excised and the bronchus of the lung lobes was cannulated at the center of several lobules. The lobes were perfused with Krebs-Ringers solution at a constant flow and perfusion pressure was measured as a gauge of airway resistance. Scarifications were made on the pleural surface to allow perfusate to exit, the main pathway for perfusate flow being through several small bronchi. Methacholine (Mch), causes a concentration-dependent bronchoconstriction. During perfusion of Thp (0.6 mg/ml), complete blockade of Mch-induced bronchoconstriction was observed (n=4, $p \leq 0.0001$). During a 0.06 mg/ml Thp perfusion (n=4), the maximum Mch bronchoconstriction was 56.8% ± 7.1 (SEM) of control (without Thp) ($p \leq 0.008$). In summary, Mch induced bronchoconstriction in the guinea pig airways is inhibited by Thp. Inhibition of histamine-induced bronchoconstriction is under study. This effect does not appear to be related to pH changes, and is contrary to previous reports on tracheal muscle constriction. (Supported by NHLBI HL-31429-06 and SUNY).

19.5

RESPIRATORY SYNCYTIAL VIRUS (RSV) VIROSOMES AS A TARGETED, INTRACELLULAR, DRUG DELIVERY SYSTEM. Arlene A Stecenko, Ken McNicol*, and Hans Schreier*. Dept of Pediatrics and Dept of Pharmaceutics, U of Florida, Gainesville, Florida 32601.

The purpose of this project was to determine if virosomes, constructed using RSV attachment (G) and the purported fusion (F) glycoprotein, targeted and then enhanced intracellular delivery of carboxyfluorescein (CF) in non-phagocytic cells. RSV F and G glycoprotein were purified using monoclonal antibodies to the Long strain of RSV and a modified affinity chromatography technique. Liposomes were prepared using a reverse-phase evaporation method with 3 mg phosphatidylethanolamine, 3 mg sphingomyelin, 1 mg phosphatidylserine, and 1.6 mg cholesterol. 160 mM CF were encapsulated within the liposome. CF encapsulated liposomes were made with F, G, or both glycoproteins on the surface of the liposome. The concentration of F used was 0.3 mol% and the ratio of F to G was 1:2. HEp 2 cells, which are known to support RSV growth, were grown on sterile coverslip flasks and 0.5 mls of a test solution added. The 5 test solutions were: 1. 1:20,000 dilution of CF; 2. CF encapsulated liposome (lip+CF); 3. lip+CF with G glycoprotein on the surface (lip+CF+G); 4. lip+CF with F glycoprotein on the surface (lip+CF+F); and 5. lip+CF with both F and G on the surface (lip+CF+F+G). After 1 and 4 hours, coverslips were removed, fixed with formaldehyde, mounted with 50% glycerol, and examined with a Zeiss Axiophot fluorescence microscope. The 1:20,000 solution of plain CF was not toxic to the HEp-2 cells and the cells did not fluoresce at 1 or 4 hours. Lip+CF did not enter the cell at 1 hour. On occasion, faint fluorescence was seen in some cells at 4 hours. Lip+CF+G showed no fluorescence at 1 hour. At 4 hours, liposomes were seen attached to the surface of some cells and there was homogeneous intracellular fluorescence of many cells. For lip+CF+F, at the 1 hour point there was questionable fluorescence at the cell surface for 2 of the 3 times this solution was tested and definite intracellular fluorescence 1 of the 3 times. At 4 hours there was clear cut homogeneous, intracellular fluorescence of many cells. Lip+CF+F+G was associated with the greatest degree of intracellular fluorescence compared to the other 4 solutions. Faint fluorescence was seen in almost all cells by 1 hour. At 4 hours, virtually all cells showed significant homogeneous, intracellular fluorescence. In summary, evidence is presented suggesting that RSV F glycoprotein is involved in viral-cell fusion. Also, virosomes using RSV F and G glycoprotein enhance intracellular delivery of CF, indicating a potential therapeutic role for such constructs. Supported by NIH grant number HL01919

20.1

ASSESSMENT OF DIAPHRAGMATIC STRENGTH BY PHRENIC NERVE STIMULATION IN AWAKE CALVES. D. Desmecht*, F. Rollin*, A. Linden*, P. Lekeux. University of Liège, B-4000 Belgium.

The purpose of this study was to assess diaphragmatic function in a standardised and reproducible way in awake and standing calves. Four calves, 262±2 (mean±SE) days of age and weighing 216±8 kg were used. Pleural and transdiaphragmatic pressure (Ppl and Pdi respectively) were measured using 2 balloon-catheters positioned in the lower third of the esophagus and in the rumen. The constancy of end expiratory Ppl for 3-4 regular breathing cycles was assumed to reflect quiet expirations to functional residual capacity (FRC). The right phrenic nerve was then stimulated with 2-sec trains of 0.2 ms pulses at 100Hz from 10 to 50V. The lowest voltage required to produce maximal pressure was considered "supramaximal voltage" (30-45V) and was used for all further stimulations. Afterwards, stimulations at 10, 20, 30, 40, 70 and 100Hz were carried out. Each stimulation was started at FRC during momentary occlusion of the inspiratory inlet of the Hans-Rudolph valve. Sets of stimulations were performed at 60 and 120-s intervals with or without a rigid cast around the abdomen and the lower third of the chest . From these data, pressure-frequency curves for the right hemidiaphragm contraction were constructed. The protocol was repeated at 2 days interval in each animal. Individual group mean values were compared by analysis of variance for repeated measurements. Absolute pressure values at 100, 70, 30 and 10Hz averaged -61,9±1,4; -53,6±1,1; -45,3±0,8 and -31,2±0,9 cmH2O for Ppl and 78,4±2,7; 67,1±2,2; 57,8±1,8 and 40,8±2,5 cmH2O for Pdi. Within-day and between-day Ppl and Pdi responses to all frequencies were not found statistically different. Neither the effect of different intervals between stimulation nor the use of a rigid cast were significant. This study establish the feasibility and reliability of right phrenic nerve stimulation in performing reproducible pressure-frequency characteristics in awake calves. This experimental model would be of considerable interest in further studies regarding diaphragmatic strength and endurance in the bovine species.

20.2

DIAPHRAGM MATURES EARLIER IN BABOONS THAN RABBITS. Francisco H. Andrade*, Leo C. Maxwell and Gregg C. Lund*. University of Texas Health Science Center at San Antonio, TX 78284.

Diaphragm (DPH) muscles in adults of several species have fiber type compositions which are within a relatively narrow range, in spite of wide variations in body size and respiratory rate. Ranges in our data for DPH of adult cats, rabbits and baboons are: Type I, 32-44%; Type IIc, 0-1%; Type IIo, 18-21%; and, Type IIg, 37-45%. Literature data for adults of several other species are generally similar. Data we have obtained for DPH of newborn rabbits and baboons after full term delivery show large differences in percentage of fiber types: Type I, 9-43%; Type IIc, 85-5%; Type IIo, 6-44%; Type IIg, 0-8%, respectively. Literature data for these and other species show great variability amongst newborns. The similarity in DPH of adults, but variability in newborns strongly suggests a different rate of development amongst species. To permit comparison, we have scaled gestational age as a percentage of full term for fetal rabbits and for fetal baboons. At 67% of gestation, percentages of fiber types in baboon DPH are: Type I, 5%; Type IIc, 77%; Type IIo, 18%; and, Type IIg, 0%. These values change toward newborn values during gestation. At both 90% of gestation and within one week of full term, rabbit DPH has a lower percentage of Type I and Type IIo fibers, and a greater percentage of Type IIc fibers than baboon DPH. Rabbits have a lower percentage of Type IIg fibers at term than baboons, but neither have Type IIg fibers preterm. These data indicate that DPH muscle fibers in baboons mature more rapidly than in rabbits, and that DPH muscles of these species ultimately achieve similar values for percentages of fiber types in adults.

Supported by NIH HL 38427.

20.3

INSPIRATORY MUSCLE ENDURANCE IN NORMAL SUBJECTS. JD Pharaoh*, MD Hammond, RD Rocha*, and JT Sharp. James A. Haley VA Hospital and U. of South Florida, Tampa, FL 33612

The goal of this study was to explore the mechanism causing inability of a subject to continue inspiratory resistance breathing (IRB). Eight normal males breathed through inspiratory threshold resistances at nonfatiguing and fatiguing levels of time tension index (TTI). Surface EMG from diaphragm, intercostal, scalenus and sternomastoid muscles were analyzed for center frequency (F_C) and moving average (Ema). Subjects breathing at 20 BPM were studied while tidal P_I value was 40% to 50% of P_{Imax} (nonfatiguing) for 30 minutes and at 70% to 80% of P_{Imax} (fatiguing) until they could no longer continue. All subjects reported sensation of dyspnea or suffocation as reasons for stopping. Subjects were studied at least twice. End tidal P_{CO2}'s rose during fatiguing runs, in one instance to as high as 57 Torr. Mean TTI values for nonfatiguing and fatiguing runs were 0.141 ± 0.071 and 0.251 ± 0.036 respectively. In no subject was there a consistent decrease in Fc during either run. Ema/P_I values generally remained stable, only occasionally showing significant increases. P_{Imax} values 1 minute after termination of the fatiguing run were within 5% of the pre-run P_{Imax} values. These data suggest that inspiratory muscle fatigue was not a major factor in causing subjects to discontinue IRB. We postulate a neural protective mechanism, which prevents primary respiratory muscle fiber (end organ) failure.

Support by VA Research Service.

20.4

M_2 INHIBITORY RECEPTORS LIMIT INTRATHORACIC AIRWAY CONSTRICTION BUT NOT CERVICAL TRACHEAL CONSTRICTION DURING VAGAL STIMULATION IN THE CAT. C.R. Killingsworth*, N.E. Robinson, T. Adams*. Pulmonary Laboratory, Michigan State University, East Lansing, MI 48824-1314

We have previously described a group of cats with tracheal hyperresponsiveness to bilateral vagal stimulation (24 V, 0.5 ms, 4 Hz). Cats are considered hyperresponsive if their tracheal constriction is greater than 2 SE above the mean for a group of healthy, respiratory virus-free, control cats. The purpose of this study was to determine if muscarinic inhibitory (M_2) receptors could be demonstrated in the cat cervical trachea and in the intrathoracic airways during increasing frequencies of vagal stimulation. We also looked for a possible role of M_2 receptors in limiting tracheal constriction in control cats compared to cats with exaggerated tracheal responses to nerve stimulation. Changes in intrathoracic airway caliber (pulmonary resistance [R_L] and dynamic compliance [C_{dyn}]) and decreases in the external diameter of tracheal ring 4 following bilateral vagal stimulation and intra-arterial acetylcholine (ACh) injection were quantitated before and after injection of the M_2 receptor antagonist gallamine. The responses of tracheal ring 4, R_L, or C_{dyn} to exogenous ACh were not altered by gallamine. Vagal stimulation caused tracheal ring 4 narrowing in a frequency-dependent manner, but constriction was unchanged by gallamine administration either in cats with control responses or those with tracheal hyperresponsiveness to nerve stimulation. The changes in R_L and C_{dyn} during vagal stimulation were significantly enhanced by iv gallamine. This suggests that M_2 receptors may play an important role in limiting intrathoracic airway constriction, but a similar modulatory role of M_2 receptors in the cervical trachea could not be demonstrated at any frequency of stimulation. (NIH Grant HL01900)

20.5

A NEONATAL MANUAL VENTILATION TRAINING DEVICE. Frank W. Bowen III, Emidio Sivieri, Vinod K. Bhutani*, Soraya Abbasi. Dept. of Peds, Univ. of PA School of Med., Newborn Pediatrics, Pennsylvania Hosp., Phila., PA 19107

Manual ventilation (handbagging), a resuscitative procedure performed on neonates is also an alternate method of oxygenation and ventilation during the course of respiratory therapy. Inexperience with the technique may cause a clinician to overdistend the baby's lungs which may result in air leaks (such as pneumothoraces) or inappropriate ventilation. To help prevent these injuries a hands-on device has been developed for teaching clinicians the most effective method of manual ventilation. This device consists of a computer integrated, mechanical infant lung simulator which contains a piston-spring-lever assembly to approximate neonatal pulmonary mechanics (i.e. a sigmoidal pressure-volume response with hysteresis). The mechanical dynamics of the assembly were adjusted to mimic the pulmonary mechanics of a typical infant "handbag" candidate: dynamic compliance = 0.75 (cm H_2O/ml), airway resistance = 50 (cm H_2O/l/s), and tidal volume = 12 (ml). A CPR doll encapsulates this assembly and helps to provide a life-like appearance while teaching the student proper handbag placement via facemask or endotracheal tube. Airflow is measured by a Fleisch pneumotach located in the simulator's trachea. Airway pressure is measured between the pneumotach and the pulmonary assembly by a pressure transducer. These two signals are interfaced to a computer based pulmonary function analysis system. As the student "handbags" the doll using a continuous airflow method, pressure-volume (P-V) loops are graphically displayed in real time by computer, and stored for later review. An onscreen template of an ideal P-V loop guides the student in refining his technique. This graphical to hands-on association allows the student to understand the interaction among tidal volume, peak inspiratory pressure, positive end expiratory pressure (PEEP), inspiratory-expiratory times, and ventilation frequencies. This teaching simulator provides direct visual feedback and essential experience in manual ventilatory techniques previously learned on a trial and error basis. It may help to reduce the inadvertent barotrauma caused by inexperienced clinicians on the neonatal respiratory system.

20.6

REGIONAL VARIATION IN CANINE DIAPHRAGM THICKNESS. S. Margulies and M. Schroeder*. Mayo Foundation, Rochester, MN 55905

Regional variations in diaphragm thickness (DT) influence the stress-bearing characteristics of the diaphragm (DPM) structure. Whereas average DPM thickness (ADT), DPM weight (DW), and surface area (SA) correlate with the body weight (BW) of animals ranging from mouse to horse, regional differences in DPM thickness have not been reported. We measured DT in 5 regions of the costal DPM and 3 regions of the crural DPM in 40 dogs (8-40 kg). The DPM was excised in toto and laid flat. With one end of a thin, sharp stainless steel tube (ID=7 mm) on the DPM muscle surface, the other end was struck with a mallet to excise a cylinder of tissue. Three tissue samples were removed from each of the 8 regions and weighed. Regional DT was determined from the equation $DT=M/(3\rho\pi R^2)$ where M = total mass of 3 samples, ρ = tissue density, and R = punch radius. SA, DW, and BW were also determined. SA and DW varied linearly with body weight, but there was no significant correlation between ADT and BW. DT varied significantly between regions (see Table) and 4 regions had systematic left-to-right differences as well. Because DPM geometry influences the DPM's function as a pressure generator, these regional differences in thickness may alter the interrelationship between the force developed by activation of a particular region of the DPM and its action on the respiratory system. (HL07222)

DPM Region	Left DT	Right DT
Costal 1 (Sternal)	.254±.034*	.287±.041
Costal 2	.263±.048*	.242±.040
Costal 3	.279±.051	.280±.042
Costal 4	.236±.048	.244±.033
Costal 5 (Dorsal)	.180±.031*	.204±.039
Crural 1 (Lateral)	.260±.042	.265±.049
Crural 2	.282±.033*	.312±.050
Crural 3 (Medial)	.317±.059	.305±.067

Mean ± SD in cm. *right≠left ($p \leq 0.05$)

20.7

SLEEP-DISORDERED BREATHING (SDB) EVENTS ARE RELATED TO PHASIC REM CHANGES IN RESPIRATORY MUSCLE ACTIVITY IN ENGLISH BULLDOGS. J.C.Hendricks, R.J.Kovalski, and L.R. Kline. Univ. of Pennsylvania, Philadelphia, PA 19104.

English bulldogs have SDB, as measured by decreased ribcage (RC) and/or abdominal (ABD) movements and $\geq$ 4% drops in oxygen saturation (SaO2). Since SDB is worst during REM sleep, we hypothesized that the changes in respiratory muscle control found during phasic REM might contribute to SDB. These include intermittent decrements in drive, pauses in inspiratory activity lasting 20 to 150 ms ("fractionations"), and asynchrony. These changes are seen in normal cats, people, and dogs. We instrumented 5 English bulldogs to record EEG, RC and ABD, airflow, SaO2, and EMG of the diaphragm and sternohyoid (SH, a sample upper airway dilator). The mean rate of SDB was 61/REM hr. In all 5 dogs, SDB events were associated with an initial decrease in drive to both muscles ($p<0.01$, paired t-test). The decrease was greater in the SH than in the diaphragm ($p<0.01$, multivariate t-test). Other changes in EMG pattern, including fractionations and asynchrony, were also significantly associated with SDB ($p<0.01$, paired t-test). We conclude from these data that REM-related changes in respiratory muscle activity compromise ventilation and, in the presence of an anatomically narrowed upper airway, cause decrements in saturation. This mechanism contrasts with the cyclic changes in automatic control of breathing thought to lead to SDB in non-REM sleep.

PULMONARY REFLEXES

21.1

MECHANISM OF BRADYPNEA INDUCED BY INHALATION OF GAS PHASE CIGARETTE SMOKE IN ANESTHETIZED RATS. I.-Y. Lee, R.F. Morton* and A.L. Wang* Univ. of Kentucky, Lexington, KY 40536

A possible involvement of oxygen radicals in evoking the acute effects of inhalation of gas phase (GP) cigarette smoke on breathing was examined in young Sprague-Dawley rats anesthetized with chloralose-urethane. Spontaneous inhalation of GP smoke (6 ml, 50% concentration) elicited a transient inhibitory effect on breathing, prolonging Te to a peak of 159±6% of the average base-line Te; this response was only slightly lower than that triggered by inhaling the unfiltered cigarette smoke (peak Te = 177±12%; p=0.04, n=20). The bradypnea started within 1-4 breaths after the onset of GP smoke inhalation, lasted for 3-5 breaths and was completely abolished by bilateral vagotomy. This inhibitory effect of GP smoke on breathing was not affected ($p>0.1$, n=11) by a pretreatment with superoxide dismutase (30,000 units/kg, i.v.) plus catalase (480,000 units/kg, i.v.), enzymes metabolizing superoxide radical and hydrogen peroxide. However, the bradypnea was largely prevented (peak Te = 109±2%, n=12) by a pretreatment with a hydroxyl radical scavenger, dimethylthiourea (500 mg/kg, i.v.). These results suggest that the gas phase is primarily responsible for eliciting the reflexogenic inhibitory effect of cigarette smoke on breathing in anesthetized rats and that hydroxyl radicals released endogenously in the lung may be involved.
(Supported by grants NIH HL-40369 and UK/THRI 41066)

21.2

CHEMICAL DESTRUCTION OF CELLS IN THE CAUDAL VENTROLATERAL MEDULLA (CVL) ATTENUATES BRONCHODILATOR REFLEXES, AS WELL AS BRONCHODILATION EVOKED FROM THE POSTERIOR MEDIAL HYPOTHALAMUS (PMH) IN DOGS. P.A. Padrid, J.R. Haselton*, M.P. Kaufman. Div. of Cardiovascular Medicine, University of California, Davis, CA 95616

The CVL in the area around the lateral reticular nucleus (LRN) is believed to be involved in integration of afferent impulses resulting in the exercise pressor reflex. This may be due in part to tonic inhibition of areas within the rostral ventrolateral medulla (RVL) which exerts a sympathetic excitatory influence on the cardiovascular response to exercise. The role of the CVL in integration of afferent impulses resulting in exercise induced reflex bronchodilation, as well as the bronchodilator responses to electrical stimulation of the PMH and sciatic nerve (SN), has not been addressed. Bronchomotor responses to the above stimuli, as measured by changes in total lung resistance (TLR), were recorded before and one hour after bilateral injection of ibotenic acid (IA) (to destroy cell bodies) into the CVL in the area around the LRN. Before placement of IA, static contraction of both hindlimbs (SC) decreased TLR ($\bar{x}$±SE) from 8.1±0.6 to 7.2±0.6 ($P<0.05$; n=8), electrical stimulation of SN decreased TLR from 9.2±0.8 to 7.8±0.7 ($P<0.05$; n=8) and electrical stimulation of the PMH decreased TLR from 9.5±0.7 to 8.0±0.7 cm $H_2O/L/s$ ($P<0.05$; n=8). One hour after injection of IA, SC resulted in an increase in TLR from 8.5±0.7 to 9.2±1.0, stimulation of SN increased TLR from 9.2±0.8 to 9.4±1.1, and stimulation of the PMH increased TLR from 9.0±0.9 to 9.1±1.5 cm $H_2O/L/s$. In 3 dogs, bilateral injection of IA dorsomedial to the LRN had no effect on the bronchomotor response to SC, SN or PMH stimulation. In one dog, bilateral injection of cobalt chloride into the CVL reversibly attenuated the above responses. We conclude that the CVL may be a site of integration of afferent impulses arising from stimulation of the PMH and SN afferents, as well as the exercise induced bronchodilator reflex.

21.3

COUGH AND THE NASAL AIRWAY IN ANAETHETIZED DOGS. James C.C. Wang* and Mary A. Lung. Department of Physiology, University of Hong Kong, Hong Kong.

The study was undertaken to investigate the action of coughing on the airflow resistance in the nasal airway. In pentobarbitone anaesthetized dogs with controlled vascular perfusion of the nasal mucosa, nasal arterial inflow, venous outflows, vascular resistance and nasal airflow resistance were monitored as described (J. Physiol. 391, 57-70, 1987). Pleural pressure was assessed by a catheter-tip pressure transducer which was inserted into the thoracic cavity via an oesophageal incision. Mechanical stimulation of the lower airways with a soft polyethylene thread induced coughing, an increase in nasal vascular resistance and venous outflows, and a decrease in nasal airflow resistance. Hence, stimulation of cough receptors causes constriction of both resistance and venous vessels resulting in a decrease in nasal airflow resistance.
(supported by HKU Research Funds 337/034/0011 & 337/034/0014, and Wing Lung Bank Research Fund 361/030/3072).

21.4

EFFECT OF INHALATION OF THE ERUCTED GASES ON THE BREATHING PATTERN IN CATTLE.
F. Rollin*, D. Desmecht*, B. Genicot*, A. Linden* and P. Lekeux. University of Liège, B-4000 Belgium

It is well known that most of the eructed gases (40-60% CO2) are inhaled in ruminants. The aim of this study was to evaluate the effect of inhaled eructed gases on the breathing pattern in cattle.
The physiological phenomenon of belching was simulated and its effect on the peripheral chemoreceptors was evaluated in 4 Friesian and 2 Belgian White and Blue calves (age : 220 ± 25 days; weight : 179,2 ± 22,0 kg) using a single tidal-breath of approximately 50% CO_2 in equal parts of O_2 and N_2. The experimental apparatus consisted of a tight-fitting mask, a Fleisch pneumotachograph Nr 3, a giant Hans-Rudolph valve, a manual bidirectional valve and a bag which contained the test gas. Respiratory gases were continuously analysed on a breath-by-breath basis, by a mass spectrometer. After a period of breathing in normal conditions, the calves were exposed to the test gas by turning the bidirectional valve during the expiratory phase of the previous respiratory cycle. On the other hand, the effects of physiological eructations were also studied.
Minute volume ($\dot{V}e$) and mean inspiratory flow ($\dot{V}_I = V_I/T_I$) were significantly increased from the second or third breath after the simulated eructation. The peak increase was 80% and 62% in $\dot{V}e$ and V_I/T_I respectively. The rise in $\dot{V}e$ was exclusively due to an increase in V_T (Tidal volume) while the respiratory rate remained constant. The same phenomena were observed after physiological eructations.
These data show that eructation significantly influences the pattern of breathing in cattle and that the ventilation in basal condition in this species is characterized by a cyclic variability coupled to belching.

21.5

DIVISION OF PERIPHERAL ERYTHROCYTES IN GOLDFISH, *Carassius auratus* L. Arthur H. Houston, A. Murad and S. Everill. Brock Univ., St.Catharines, Canada, L2S 3A1.

Respiratory stresses including phenylhydrazine-induced anemia, transient hypoxia or heat shock and chronic exposure to heavy metal pollutants lead to a common pattern of hematological response. This is characterized by increased numbers of juvenile cells, accelerated maturation, karyorrhexis and increased incidence of erythrocytes separating by an atypical form of cell division. Although mitotic figures were not observed during separation, immunoflourescent assessment of changes in tubulin and actin distributions and radioautographic determinion of ^{3}H-thymidine and ^{55}Fe uptake and nuclear and/or cytoplasmic distribution indicated that the separation process is accompanied by significant alterations in the marginal microtubular band and cytoskeletal system, is confined to immature cells, may be preceded by DNA replication and involves cytoplasmic iron uptake; events not observed in mature cells. Although erythropoietic activity increases in both pronephros and spleen following stress, these observations suggest that the separation process may provide an additional mechanism for alteration of the erythron. Supported by Natural Sciences and Engineering Research Council of Canada Operating Grant A6972 to A.H.Houston.

21.6

PAPAVERINE REDUCES VENULAR PRESSURES IN LUNGS OF NEWBORN PIGS BUT NOT IN LUNGS OF NEWBORN RABBITS. CD Fike, & MR Kaplowitz. Dept. of Peds., Baylor College of Med., Houston, TX 77030

To determine the effect of inhibiting vasomotor tone on venular pressures in lungs of newborns of different species, we isolated and perfused the lungs of 10 newborn rabbits (1-3 days old) and 5 newborn pigs (3-7 days old). We continuously measured pulmonary arterial (Ppa) and left atrial (Pla) pressures. Using the direct micropuncture technique we measured 10-50 um diameter venular pressures (Pven) before and then after the addition of papaverine to the perfusate. During micropuncture we kept Pla at 7-10 cm H_2O, airway pressure at 5 cm H_2O (zone 3) and blood flow at 50 ml·kg·min^{-1}.

Table : pressures (cm H_2O), mean ± SD.

Species	Papaverine	Ppa	Pven	Pla
Rabbit	-	16.6±3.5	10.4±0.9	9.5±0.6
	+	14.3±2.1	10.4±1.0	9.5±0.6
Pig	-	19.8±4.6	14.3±2.9	8.0±1.3
	+	13.0±1.1	9.1±1.1	8.0±1.2

We found that in lungs of both species the addition of papaverine reduced Ppa and the total pressure drop across the pulmonary circulation = Ppa-Pla. However, only in lungs of newborn pigs did inhibition of vasomotor tone reduce Pven and the pressure drop across veins = Pven-Pla. These findings suggest that the presence of active vasomotor tone in veins > 80 um is a major source of vascular resistance in isolated lungs from newborn pigs but not in lungs from newborn rabbits. (Supported by HL42883-01 and March of Dimes)

21.7

UNDERWATER SLEEP IN SEALS: DREAMING ABOUT DIVING? M. Castellini, W. Milsom, D. Jones, D. Costa, J. Castellini and S. Bahrma. University of Alaska, Fairbanks, University of British Columbia, Vancouver and University of California, Santa Cruz, California 95060

In this project, we recorded cardiorespiratory patterns and sleep state in elephant seal pups while the pups slept both on land and in shallow tanks. Sleep in elephant seal pups is associated with long duration apnea (up to 13 min) and we tested how this sleep apnea would be altered by having the seals sleep in water. The hypothesis was that a seal sleeping on land would have the luxury of ending the apnea without having to awaken to breathe, but a seal in the water would have to wake up to come to the surface. We found however, that there were no differences in any of the measured variables regardless of whether the seal was wet or dry. We found that the seals would sleep through 2-4 bouts of long apneas and usually remain in sleep throughout the period. They did not have to wake up to breathe. In water, the seals would simply float to the surface, ventilate and then sink back below the water while remaining in sleep the whole time. We conclude that the control of ventilation and the control of sleep are independent in these animals and that the ability to sleep underwater and come to the surface while still sleeping may alter our perceptions of diving behavior in nature.

21.8

VENTILATORY ACTIVITY DURING DIAPAUSE AND DEVELOPMENT IN CERCROPIA PUPAE. Geoffrey F. Birchard, George Mason Univ., Fairfax, VA 22030.

Mass loss rates were used to monitor ventilatory activity during diapause and development in the pupae of the saturnid moth Hyalophora cecropia. During diapause a two phase cycle, burst-interburst was observed. The interburst duration (T_{ib}) averaged 9.15 ± 2.68 h. During interbursts mass loss (M_{ib}) averaged 0.3999 ± .2293 mg·h^{-1}. Bursts had a duration (T_b) and a maximum mass loss rate (M_b) of 0.15 ± .04 h and 9.8362 ± .7009 mg·h^{-1}, respectively. Immediately following the termination of diapause T_{ib} was found to be significantly shorter (3.35 ± 2.09 h) and M_{ib} less than during diapause. Further, T_b and M_b were slightly reduced. With continued development T_{ib} progressively decreased and in some animals this period was not distinguishable near emergence. Measurements following diapause suggest an increasing respiratory conductance with development, approaching that seen during diapause bursts.

Supported by the T.F. and K.M. Jeffress Memorial Trust.

21.9

DYNAMIC WORK OF BREATHING IN THE HORSE AT REST AND DURING EXERCISE. C.L.Lafortuna* and F.Saibene* (SPON: G.Sant'Ambrogio). Reparto di Fisiologia del Lavoro Muscolare, I.T.B.A., C.N.R., I-20133 Milano, Italy

We measured on 5 horses (body mass 520 kg ± 41.8 SD) at rest and exercising on a treadmill (speed: 0.9-3.0 m·s^{-1}; slope 7%), the esophageal pressure, the airflow and the stride frequency (SF). The pulmonary ventilation ($\dot{V}E$), the pulmonary resistance (R_L) at isovolume and the dynamic work rate of breathing (Wresp) were determined at different work loads. We found that: 1) $\dot{V}E$ and SF increased linearly with treadmill speed, the increase in $\dot{V}E$ (up to ~12 times the resting value) being sustained more by increases in respiratory rate (RR) then in tidal volume (V_T); 2) R_L, which at any level was independent from the lung volume within V_T range, decreased up to 30% of the average resting value at the maximal $\dot{V}E$ attained, but, 3) within each work load R_L increased with $\dot{V}E$; 4) Wresp (in kgm·min^{-1}) was a positive function of $\dot{V}E$ (in l·min^{-1}) and can be described by: Wresp = $3.22 \cdot 10^{-3} \cdot \dot{V}E^{1.59}$; 5) in all animals but one SF/RR ratio was either 1:1 or 2:1 at all speed, the rear hoof striking the ground at the beginning of the inspiration.

The decrease in R_L observed during exercise implies that some mechanism(s) does counteract both the increase of airflow (and turbulence) and the airway tendency to collapse in front of relevant transmural forces as during hyperventilation. Although a direct action of catecholamines released during exercise cannot be excluded, laryngeal muscles activation may possibly play a role.

If the relationship Wresp vs. $\dot{V}E$ is normalized for the resting value, it appears that for a given increase in $\dot{V}E$, Wresp increases much less in horses than in other species: a 10-fold increase in $\dot{V}E$ corresponds to an increase in Wresp of 50-fold for horse, 150-fold for man and 225 or 75-fold for dog, during normal breathing or panting.

Moreover the locomotor-respiratory coupling implies a horizontal movement of visceral mass, loosely connected with the skeletal structure, acting synergistically with the diaphragm with a mechanical advantage for the respiratory muscles.

21.10

A PRELIMINARY ALLOMETRIC ANALYSIS OF THE RELATIONSHIPS BETWEEN VO2max AND THE MORPHOMETRIC CHARACTERISTICS OF BAT LUNGS. J. N. Maina*, S. P. Thomas, and D. M. Hyde*, Dept. Vet. Anat., Univ. of Nairobi, Kenya, Dept. Biol. Sci., Duquesne Univ., Pittsburgh, PA 15282, and Dept. Anat., School of Vet. Med., Univ. of Calif., Davis, CA 95616.

We have morphometrically analyzed the lungs of three larger-size species of bats (mean body masses = 456, 667, & 929g). These data expand by five-fold the range of body masses for which bat lung data are available, and enabled us to formulate more representative allometric equations, some of whose scaling factors (exponents) are presented below along with the corresponding VO2max value for flying bats. While the scaling factor (b) for lung volume (b=0.82) exceeds that for VO2max (b=0.70), those for lung tissue barrier surface area (b=0.74), pulmonary capillary volume (b=0.74), and total morphometric lung diffusing capacity for oxygen (b=0.69) correspond closely to the VO2max value. Allometric comparisons reveal that a number of key lung morphometric parameters of bats scale less favorably with increasing body mass than do those of birds; an observation which may help explain why the largest species of bat weighs almost an order of magnitude less than the largest extant species of bird which uses flapping flight. [Supported by a Fulbright Senior Scholar Research Fellowship (J.N.M), and by NSF grant PCM-8303050 (S.P.T)].

21.11

ROLE OF AIRWAY RESISTANCE IN SETTING THE LIMIT TO $V_{O2}max$: A TEST OF SYMMORPHOSIS. S.L. Lindstedt M. Eliasson* and J.F. Hokanson*. Northern Arizona University, Flagstaff, AZ 86011

Symmorphosis predicts optimal design in which structure "satisfies but does not exceed" functional requirements. We examined the match between structure and ventilation in humans. We measured $V_{O2}max$ on the bicycle ergometer in highly trained ($V_{O2}max$ > 70 $ml O_2 \cdot kg^{-1} \cdot min^{-1}$) and untrained ($V_{O2}max$ < 45 $ml O_2 \cdot kg^{-1} \cdot min^{-1}$) male subjects, with and without added airway resistance (AR). Peak inspiratory flow changed as an identical function of AR in both groups. When subjects worked at their peak aerobic workloads with AR, $V_{O2}max$ varied as a function of resistor area. $V_{O2}max$ in the untrained subjects was relatively unaffected by AR while the trained subjects were much more sensitive to AR. A single graph describes oxygen uptake as a function of resistor area in both groups. When extrapolated to the actual in vivo resistance in humans, predicted $V_{O2}max$ is about 90 $ml O_2 \cdot kg^{-1} \cdot min^{-1}$, roughly equal to the highest values reported in humans. These results suggest that airway resistance is not matched to $V_{O2}max$ in humans. Further that resistance to bulk flow in the airways might be an important factor setting the maximum (species-specific) aerobic performance in humans. Rather than symmorphosis, we feel that only those structures with high phenotypic plasticity will be matched to demand, those with minimal plasticity must be built to accommodate changes in the malleable structures. (NIH RO1HL41986; American Heart Association, Flinn Foundation Fellowship)

INFLAMMATION

22.1

RELATIONSHIP OF TISSUE LIPID PEROXIDATION TO THE LUNG AND SYSTEMIC RESPONSE FROM REPEATED ENDOTOXEMIA AND INTERLEUKIN-2 (IL-2) INFUSIONS. D. Zhu, C. LaLonde, T. Eberlein, R. Demling* Longwood Area Trauma Center, Boston, MA, USA, 02115.

Recurrent endotoxemia (E) and IL-2 both produce a hyperdynamic "septic" state and organ dysfunction, felt to be due to monokine induced O_2 radical release. Our purpose was to determine whether oxidant induced tissue lipid peroxidation, L.P., correlated with the injury state. 10 chronically instrumented sheep with lung lymph fistula were given (E)1mcg/kg or IL-2 (1.5 x 10^5 units) 2-3 times per day x 5 days, then killed. L.P. was measured by MDA nMol/g tissue. Data comparing pre-study baseline with the last dose response is shown.

Mean±SD	$\dot{Q}_L$ % Inc.	L/P Ratio	Ppa (mmHg)	PaO_2 (mmHg)	C.I. l/min/M^2	VO_2 ml/min/M^2	PvO_2 (mmHg)
(B)	-	.56	17±3	89±4	5.4±0.8	140±20	40±5
(E)	136±50*	.55	24±5*	82±6*	10.5±1.7*	220±30*	36±6
IL-2	450±140*	.56	31±5*	74±5*	8.3±1.2*	150±50	43±5*

* = significantly different from baseline

Lung inflammation and MDA were markedly increased after (E), MDA being 117±48 compared to (B) of 45±4 and IL-2 of 48±6. Liver MDA after (E) increased to 369±95 compared to (B) of 110±8 and IL-2 of 104±14. We conclude that the physiologic lung changes did not correspond with the magnitude of tissue inflammation and L.P. However, O_2 consumption, $\dot{V}O_2$, was increased with increased L.P.

22.2

HISTAMINE PROTECTION AGAINST PARAQUAT INDUCED LUNG TOXICITY IN THE MALE MOUSE. S.A. Novacek*, and S.D. Mercurio* (SPON: M. Frank).

Dept. of Biology, Mankato State University, Mankato, MN 56001.

Previous studies indicate that histamine plays a role in paraquat-induced pulmonary injury. This study investigated histamine and histamine antagonists' action on paraquat mortality in male Swiss-Webster mice. Histamine at 5.0 mg/kg in sterile saline (1.0 ml/kg) was injected i.p. while simultaneously administering 325 mg paraquat/kg p.o. in 1.0 ml/kg distilled water. There was significant protection of histamine on the mortality of male mice compared with paraquat controls. Oral administration of 325 mg/kg paraquat and i.p. injection of the specific H1 histamine receptor antagonists chlopheniramine maleate (5.0 mg/kg) or diphenhydramine HCl (5.0 mg/kg) significantly increased mortality compared to paraquat controls. In addition, the histamine H2 receptor antagonist cimetidine injected i.p. at 100 mg/kg did not exhibit any noticeable effect on paraquat toxicity in mice. Since studies of paraquat employing perfused lung preparations indicate that anti-inflammatory agents reduce inflammation induced by oxidative damage, new hypotheses concerning the role of inflammation in oxidant toxicity in lung or endothelial tissue should evidently come from the use of whole animal model systems in conjunction with tissue analysis. Supported by grant 1R15ES05109-01TOX U.S. Public Health Service.

22.3

Leukotriene B_4 (LTB_4) Increases Hydroxyl Radical (·OH) Production in Sheep Polymorphonuclear Leukocytes (PMNs). W.M Abraham and I.T. Lauredo*. Mt. Sinai Medical Center, Miami Beach, FL 33140.

The effect of LTB_4 on ·OH generation by PMNs was studied. PMNs were isolated from venous blood by density gradient centrifugation and ·OH production was measured by a spectrophotometric reaction based on the degradation of deoxyribose (Free Radical Biol. Med. 6:385, 1989). Mean (±SE) basal release of ·OH was 48.8 ± 17.7 ng/10^6 cells (n=11). PMN (1x10^6 cells/tube) stimulation with phorbol-12-myristate-13-acetate (PMA) produced dose dependent increases in ·OH: 0.5, 1.0 and 10.0 ng PMA resulted in 4-, 8- and 10-fold increases in basal ·OH production, respectively. Incubation (1h, 4°C) of PMNs with LTB_4 alone (0.03 to 30 μM) increased basal ·OH production by 50%, but the increase was seen with all LTB_4 doses. Pre-incubation (1h) of PMNs with LTB_4 enhanced the PMA-stimulated (1 and 10 ng) release of ·OH by 25%, but the increase was also independent of the LTB_4 concentration used. Thus, the generation of ·OH may be enhanced in inflammatory conditions, where activated PMNs are exposed to LTB_4. Since this condition exists during late asthmatic responses and allergen-induced airway hyperresponsiveness, ·OH could contribute to these pathophysiologic events. NIH-33897.

22.4

SOME STRUCTURAL-FUNCTIONAL CHANGES IN THE LUNG WITH PULMONARY HYDATID CYSTS. S. Alnoor, I. Hussain*, N. AL-Jiboori* and A.W. Mehdi*. Physiology Department, College of Veterinary Medicine and Pathology Department, College of Medicine, Baghdad University, Bagdad, Iraq.

The structural changes in the lung with pulmonary hydatid cyst and the expected impact on gas exchange were analyzed in human and sheep lungs. Simple and infected cysts with surrounding lung tissue were isolated and placed in fixative solution. Histological sections from both lungs were prepared and stained with H&E. Microscopic examination revealed reduction in alveolar space and bronchiolar luminal space, distorted blood vessels in the surrounding lung tissue, thickening of the alveolar septa, detached bronchiolar epithelium and accumulation of exudate were seen in both human and sheep lungs with infected cysts. Distortion of pulmonary vessels and bronchiolar integrity might be due to lack of mechanical interdependence between infected and surrounding tissue. These morphological changes may cause severe mismatching of ventilation and pulmonary blood flow resulting into gas exchange abnormality. Such gas exchange disturbance might be accentuated by diffusion impairment caused by thickening of the alveolar septa and exudate accumulation.

22.5

LOBAR DISTRIBUTION OF EXPERIMENTALLY-INDUCED PNEUMONIC LESIONS IN THE LUNG OF GNOTOBIOTIC PICLETS. R. Klemm,[1] J. Johnson,[1*] N. Anderson;[1*] A. Doster[2*]. Kansas State Univ. Manhattan, KS 66506;[1] Univ. of Nebraska, Lincoln 68583.[2]

Actinobacillus pleuropneumoniae-induced virulent swine pleuropneumonia, under naturally-occurring conditions, can be complicated by super-infection with Bordatella bronchiseptica. As our objective was to study the early effects of A. pleuropneumonia infection on the lung, therefore, we used gnotobiotic piglets. Ten Hampshire piglets, age = 6-7 wks, wt = 2.10 ± 0.17 kg (Mn±SD), were divided into two groups and inoculated intratracheally either with 1.0 ml PBS (Controls; N=2) or with a 1.0 ml inoculum containing 10^6 CFU of A. pleuropneumoniae (Treatment; N=8). Four animals each of the treatment group were sacrificed at 1 and 4 hrs post-inoculation (PI) and tissues taken for microscopic study. Alveolar macrophages were greater in number at 1 hr only, while numbers of interstitial and bronchiolar PMN's increased continuously up to 4 hrs PI. Lesion formation, was already visible at 1 hr PI in the peribronchiolar region of the dorsal aspect of the right caudal lobe of experimentally infected lungs. Compared with controls and 1 hr PI, the right middle and right and left caudal lobes at 4 hrs PI showed a significant ($P<0.05$) increase in degree of lung involvement; involvement of the left cranial lobe was slight, and the right cranial lobe was completely unaffected.

LUNG DEVELOPMENT

23.1

EFFECTS OF PRENATAL UNILATERAL PULMONARY ARTERY LIGATION (PAL) ON INTRAUTERINE LUNG GROWTH. Jeff Wagener and Kevin Pringle*. University of Iowa, Iowa City, Iowa 52242

Previous studies of post-natal unilateral PAL show little change in lung development. Since the majority of non-alveolar lung development occurs prior to birth, we performed left PAL in mid-trimester (78-86 day) lamb fetuses. Ten animals underwent intrauterine surgery (5 left PAL and 5 thoracotomy(T). Five healthy newborns were used as controls(C). At 1-3 days of age, animals were sacrificed, lungs were inflation fixed and morphometry was performed.

		PAL	T	C	p
Lung volume (ml)	right	186±45	183±45	159±44	ns
	left	28±8	114±22	112±25	<.01
Parenchyma (%)	right	91±2	92±1	90±1	ns
	left	80±10	91±1	90±5	ns
Mean Linear intercept (um)	right	6.4±.5	6.4±.6	6.3±.5	ns
	left	6.9±.7	5.9±.4	5.6±1.0	ns
Internal surface area (m2)	right	.89±.27	.87±.24	.89±.09	ns
	left	.12±.03	.72±.10	.83±.25	<.01
Small (<1mm) airways (#/cm2)	right	67.0	67.4	63.4	ns
	left	42.7	74.6	75.3	<.05

These results indicate that intrauterine unilateral PAL decreases lung volume and internal surface area. The decreased development is occurring at mid-trimester and is influenced by pulmonary artery perfusion. (supported by an American Lung Association grant)

23.2

EFFECTS OF BOVINE RESPIRATORY SYNCYTIAL VIRUS INFECTION ON AIRWAY FUNCTION IN NEONATAL CALVES. Patrick H. LeBlanc*, John C. Baker, Peter R. Gray, N. Edward Robinson and Frederik J. Derksen. Michigan State University, College of Veterinary Medicine, East Lansing, MI 48824

Respiratory synctial virus (RSV) infection causes severe lower respiratory tract disease in infants and calves. Neonatal respiratory infection in children often produces persistent changes in lung function. The specific objective of this study was to determine if neonatal calves experience transient and/or persistent alterations in pulmonary function and airway reactivity following RSV infection. Six (2-3 day old) Holstein bull calves were inoculated with 10 ml of bovine respiratory syncytial virus (BRSV) inoculum ($10^{2.7}$ to $10^{3.8}$ cell culture infective doses (CCID)/ml) intranasally and 10 ml of BRSV inoculum ($10^{4.8}$ to $10^{5.9}$ CCID/ml) intratracheally for 4 consecutive days, while 5 other calves were sham inoculated. Prior to inoculation (day 0) and days 4, 14, and 30 after the last inoculation body weight (kg), dynamic compliance (C_{dyn}), pulmonary resistance (R_L), and two indices of airway reactivity ($ED_{65}C_{dyn}$ and $ED_{200}R_L$) were measured. Control calves gained weight progressively throughout the study, whereas RSV-inoculated calves failed to gain weight for 14 days but equaled control calf weight by 30 days post inoculation. The C_{dyn} of control calves increased significantly by 30 days but did not in the RSV-infected calves. Pulmonary resistance was increased significantly at 4, 14 and 30 days but was unaffected by sham inoculation. The $ED65C_{dyn}$ and $ED200R_L$ indicated an age-dependent increase in reactivity to histamine and an increase in responsiveness in the infected group beginning at 14 days and persisting until the end of the study period. The data indicate that BRSV causes airway obstruction and hyperreactivity in neonatal calves which persists for at least 30 days following viral exposure.

PLEURAL SPACE

24.1

APNEA ABOLISHES THE INTRAPLEURAL LIQUID FLOWS.
G. Miserocchi, D. Negrini and C.R. Bellina. Istituto di Fisiologia Umana, Università degli Studi, Milano, ITALY.
Previous experiments have shown that in anesthetized spontaneously breathing animals (JAP 56, 1984: 526; Respir. Physiol. 65, 1986: 13; JAP 64, 1988: 577) intrapleural liquid flows occur down hydraulic pressure gradients from the costal to the extracostal regions and from the less dependent towards the more dependent regions of the pleural cavity. In the present investigation we studied the effect of apnea on intrapleural liquid flows. Experiments were carried in 10 anesthetized, paralyzed, mechanically ventilated dogs. With a gamma camera placed either frontal or lateral to the chest, we followed the intrapleural spreading of tecnitium labelled albumin along the costo-extracostal or the gravity dependent direction respectively, while the animal was left apneic up to 15 min (0_2 delivered intratracheally). Label injections (n= 12) were done at various pleural sites via a 0.2 ml saline bolus. Intrapleural label distribution was evaluated from the regional counting surrounding the injection site, relative to the rest of the gamma camera image. 15 min after injection, activity at injection sites decreased only slightly (~15%) indicating a negligible intrapleural spreading of the label. The intrapleural hydraulic pressure head (as measured by intrapleural cannulas) averaged 0.3 and 0.7 cm H_20/cm in the gravity-dependent and in the costo-extracostal direction, namely equal to those occurring at FRC in spontaneously breathing dogs. We conclude that respiratory movements are essential for intrapleural liquid flows to occur: these may be due either to the sliding of pleural membranes and/or to the increase in pressure gradients occurring during inspiration.

24.2

PERMEABILITY-SURFACE AREA PRODUCT AND REFLECTION COEFFICIENT OF THE PARIETAL PLEURA IN DOGS.
D. Negrini, R.K. Reed and G. Miserocchi. Istituto di Fisiologia Umana, Università degli Studi, Milano, ITALY.
The permeability of the parietal pleura to proteins was studied in five anesthetized dogs. After dissection of the skin and superficial muscles, small areas (~ 1 cm^2) of parietal pleura were exposed by resecting the intercostal muscles. The prepared portions of the chest were removed and placed on a bath of autologous plasma. Small hemispheric capsules were glued to the parietal pleura and were connected to a pressure manometer and to a graduated pipette, respectively. Following a procedure recently developed to calculate the unique Peclet number and the permeability surface area product (PS) in the microvasculature (FASEB J. 3: 246, 1989), we measured the transpleural total proteins flux (Js) at progressively increasing transpleural liquid flows (Jv) values to identify the maximum diffusional flow component. From the slope of the linear phase of the Js vs Jv relationship obtained at Jv values higher than the maximum diffusional protein flux, the calculated total protein reflection coefficient of the parietal pleura was 0.11±0.04 (SD). The PS and the hydraulic conductivity were 35.4±12 µl/ (h cm^2) and 9±6.5 µl/ (h cm^2 cm H_20), respectively. The data indicate that the parietal mesothelium offers little restiction to protein movement: as the physiological pleural to plasma protein concentration ratio is about 0.2, we conclude that most of the protein seiving occurs across the parietal capillary endothelium.

25.1

UPTAKE OF (54)Mn^{2+} ACROSS THE BLOOD-NERVE BARRIER OF THE RAT PERIPHERAL NERVE IS FACILITATED AND CONCENTRATION-DEPENDENT. Kishena C. Wadhwani, Vincent A. Murphy*, Quentin R. Smith and Stanley I. Rapoport. NIH, Bethesda, Md. 20892.

Manganese is an essential trace metal and is required for certain physiological functions. Both deficiency and excess of manganese lead to neurological disorders. Because our laboratory recently demonstrated that manganese transport at the blood-brain barrier (BBB) in the rat central nervous system is facilitated and saturable, we thought it of interest to examine whether a similar system exists for manganese transport at the blood-nerve barrier (BNB) in the peripheral nerve. The influx of (54)Mn^{2+} from blood to the rat sciatic nerve was measured under different concentrations of nonlabeled Mn^{2+} in the plasma, using and i.v. infusion technique. (54)Mn^{2+} influx into the desheathed sciatic nerve exhibited a facilitated and saturable pattern when plasma Mn was maintained in the range from 4.18 to 4312 ng/ml. Similarly, (54)Mn^{2+} influx at the BBB also exhibited a facilitated and saturable characteristic. The saturable and nonsaturable constants for Mn at the BNB and BBB were determined to be: for BNB: Km=4.71±1.1 μM, Vmax=0.56±0.05 nmol/g.s x10^{-3} and Kd=6.3±0.8 ml/g.s x10^{-6} (mean±SE for n=5-6 animals). For BBB: Km=0.95±0.13 μM, Vmax=0.40±0.02 nmol/g.s x10^{-3} and Kd=0.3±0.2 ml/g.s x10^{-6}. The results show that, as at the BBB, the BNB of the rat peripheral nerve transports Mn from blood to nerve by a facilitated, saturable mechanism.

25.2

MYO-INOSITOL (MI) TRANSPORT IN THE OCULAR LENS OF RAT. F.P.J. Diecke, A. Beyer-Mears and K. Mistry.* Department of Physiology, UMD-New Jersey Medical School, Newark, N.J. 07103.

The ocular lens accumulates free intracellular MI at concentrations ranging from 3 to 10 mmol/kg wet weight in the presence of extracellular MI concentrations of 100 μM. The mechanism for this accumulation is a Na-dependent co-transport located in the epithelial cell layer covering the anterior surface of the lens. We have investigated the properties of this co-transport. MI-influx measured as a function of MI concentration consists of a hyperbolic component and a linear component. The hyperbolic component represents the co-transport and has a maximal transport rate (J_{max}) of 30 μM/kg/ hour and a transport coefficient (K_t) of 65 μM. The linear component indicates the presence of passive diffusion which is apparent only at high MI concentrations (>500 μM). MI transport at low MI concentrations is very sensitive to extracellular Na. The kinetics of Na activation of MI transport suggest a stoichiometry for Na and MI of 1:1 and a half-maximal activation of MI transport at 180 mM Na. K substitution for extracellular Na has an even greater effect indicating that MI transport is Na and membrane potential dependent. MI transport is inhibited by phlorizin and phloretin. Phlorizin has an inhibitory coefficient (K_i) of 29 μM while phloretin inhibits at much higher concentrations (K_i=300 μM). MI transport in the lens has properties similar to MI transport described for other vertebrate epithelial tissues. (Supported by NIH grant EY-03226)

25.3

TRANSFORMING GROWTH FACTOR β STIMULATES Na^+-DEPENDENT UPTAKE OF ASCORBIC ACID BY RAT OSTEOBLASTIC CELLS. S. J. Dixon*, E. M. Jaworski*, A. Kulaga*, E. Pruski* and J. X. Wilson. University of Western Ontario, London, Canada N6A 5C1.

The mechanisms by which transforming growth factor β (TGF-β) stimulates matrix synthesis by osteoblasts and other connective tissue cells are poorly understood. The purpose of this study was to examine the effects of TGF-β on the uptake by osteoblastic cells of ascorbic acid, a cofactor essential for the production of collagenous extracellular matrices. Uptake of L-[^{14}C]ascorbate by quiescent cultures of UMR-106 rat osteosarcoma cells proceeded linearly with time for at least 10 min at 37°C. At concentrations of ascorbate in the physiological range, uptake was Na^+-dependent and saturable. Within 6 h, exposure to TGF-β (porcine TGF-β1, 3 ng/ml) stimulated initial rates of Na^+-dependent ascorbate uptake. When cultures were pretreated with TGF-β (3 ng/ml) for 24 h, the initial rate of uptake of L-[^{14}C]ascorbate (10 μM) increased from basal levels of 26 ± 3 to 40 ± 3 nmol ascorbate/g protein/min (means ± SE, n = 11). Half-maximal stimulation of uptake was observed at 0.5 ng/ml TGF-β. Simultaneous exposure of cultures to cycloheximide (10 μM), an inhibitor of protein synthesis, abolished the stimulatory effect of TGF-β. These data suggest the possibility that TGF-β stimulates osteoid production by enhancing osteoblastic uptake of ascorbic acid. (Supported by the Medical Research Council of Canada)

25.4

KINETICS OF pH EQUILIBRATION DURING MIXING IN A CLOSED SYSTEM. A. Bidani, C.G. Vanoye*, V.J. Cardenas* and T.A. Heming. Univ. Texas Medical Branch, Galveston TX 77550.

Regional variations in tissue CO_2 exchange will produce capillary blood streams with different pH and P_{CO_2} values. Subsequent mixing of these blood streams in the postcapillary vasculature will result in transient changes in blood pH and P_{CO_2}. We analyzed the kinetics of such changes, experimentally and theoretically. Experimental pH time courses were followed in a stop-flow apparatus under closed conditions, after mixing red cell suspensions and salines of different pH and P_{CO_2} values. Mixture pH time courses were determined, in the presence or absence of extracellular carbonic anhydrase (CA), CA inhibitors, and inhibitors of red cell HCO_3^-/Cl^- exchange. These data were used, together with mathematical models, to calculate changes in pH_o (extracellular), pH_i (intracellular), $[HCO_3^-]_o$, $[HCO_3^-]_i$, and P_{CO_2}. Significant pH disequilibria were observed after mixing the different fluids. The magnitude and time course of these disequilibria were markedly influenced by CA and red cell HCO_3^-/Cl^- exchange. Our results suggest the following: (1) extracellular CA on the luminal surface of vascular endothelial cells is important for equilibration of blood pH in the postcapillary vasculature. This complements the proposed role of extracellular endothelial CA in blood pH equilibration during capillary gas exchange; (2) HCO_3^-/Cl^- exchange is crucial for ensuring rapid pH equilibration across the red cell membrane.

25.5

DISTRIBUTION OF SOURCES AND SINKS AS A MECHANISM FOR METABOLIC REGULATION. Dean P. Jones and Tak Yee Aw. Emory University, Atlanta, GA 30322.

The requirement for diffusion of solutes from a site of entry or generation to the site of exit or consumption is a fundamental constraint upon the structural design of living cells. The magnitude of a diffusion-induced solute concentration gradient (ΔC) from entry to exit is defined by a form of the Fick equation: $\Delta C=(J/D)*G$, where J is flux, D is diffusion coefficient and G is a term or function appropriate for the geometry. Because a solute concentration gradient is biologically important as ΔC approaches the mean solute concentration, it follows that substantial gradients can occur only for species where the ratio of flux to mean concentration is large. These include ADP, O_2, inorganic phosphate, oxaloacetate, glc 1-phosphate and glc 6-phosphate. For a radial geometry, G is a function of the square of the distance from source to sink; consequently, ΔC is more sensitive to a change in distance than to a change in J or D. Thus, for species where flux is high and the mean concentration is low, spatial redistribution of the source and/or sink provides an effective means to regulate metabolic functions. Supported by NIH grant GM-36538.

26.1

ARTERIAL BLOOD OXYGENATION AND ACID-BASE CHANGES DURING MAXIMAL EXERCISE IN RATS ACCLIMATED TO SIMULATED ALTITUDE. Norberto C. Gonzalez and Richard L. Clancy, Department of Physiology, Univ. of Kansas Med. Ctr., Kansas City, KS 66103

Acclimation to high altitude (HA) leads to hypocapnia, intra- and extracellular bicarbonate depletion and a decrease in buffer capacity. The present experiments were carried out to determine if these changes influence arterial blood oxygenation during exercise in rats acclimated to simulated HA. Male rats were acclimated to simulated HA (PB: 370-380 mmHg) for 3 weeks (3WHx) and run in a treadmill at a PIo_2 of ~70 mmHg. Controls were run either in normoxia (Nx) or at PIo_2 of 70 mmHg (acute hypoxia: AHx). Maximum oxygen uptake (Vo_2max, mlSTPD/min*kg) was 70.4±1.0 in Nx, 46.4±1.9 in AHx and 52.6±1.1 in 3WHx. Exercise resulted in acidosis and hypocapnia in all groups. Exercise blood lactate (mM) was 10.9±0.2 in Nx, 10.8±0.5 in AHx and 6.5±0.4 in 3WHx. Exercise pH was similar in all groups. Pao_2 in exercise increased 12±1.8 mmHg in Nx, 6±1.9 mmHg in AHx and 7±2.1 mmHg in 3WHx. O_2 saturation of Hb (HbO_2sat), however, decreased with exercise in AHx and 3WHx. Oxyhemoglobin equilibration curves indicate that the decrease in HbO_2sat can be accounted largely by the Bohr effect due to the acidosis. Vo_2max correlated linearly with the arterial oxygen concentration at the end of exercise. These results suggest that the acidosis induced by exercise may influence Vo_2max in hypoxia by affecting arterial oxygenation. (Supported by NIH grant HL 39443)

26.2

DECREASED RELIANCE ON LACTATE DURING EXERCISE AFTER ACCLIMATIZATION TO 4,300 M. G.A. Brooks, G.E. Butterfield, R.R. Wolfe, B.M. Groves, R.S. Mazzeo, J.R. Sutton, E.E. Wolfel, and J.T. Reeves. Univ. California, Berkeley, CA 94720.

Seven healthy males (23±2 yr, 72.2±1.6 kg, mean ±SEM) on a controlled diet were studied in the post-absorbtive condition at sea level (SL), upon acute exposure (AA) to 4,300 m, and after 3 weeks of acclimatization (CA) to 4,300 m. Subjects received a primed-continuous infusion of [3-^{13}C]lactate and rested for a minimum of 90 min, followed immediately by 45 min of exercise at 101±3 W, which elicited 51.1±1% of the SL VO_2max (65±2% of CA VO_2max). Resting arterial lactate concentration at sea level was 7.4±0.3 mg/dl, and increased to 18.8±1.6 mg/dl during exercise. During rest at SL, lactate appearance rate (Ra) was 0.52±0.03 mg/kg/min; this increased 6 fold during exercise to 3.24±0.19 mg/kg/min. Upon AA, resting and exercise lactate Ra's rose to 2.2 ±0.2 and 18.6±2.9 mg/kg/min, respectively. Resting lactate concentration after CA (12.2±0.56 mg/dl) and Ra (1.77±0.25 mg/kg/min) were intermediate between SL and AA values. During exercise after CA, lactate concentration (26.3±1.6 mg/dl) and Ra (9.2±0.7 mg/kg/min) rose from resting values, but were intermediate between SL and AA values. During rest and exercise mean lactate Ra and epinephrine values were highly correlated (R=1.0). Increased arterial lactate concentration during exercise during acute altitude exposure is due to increased Ra. Decreased arterial lactate concentration during exercise at altitude after acclimatization is due to a less exaggerated Ra. Sympathetic-adrenergic responses appear to be important in regulating the metabolic response to high altitude.

26.3

SELECTIVE INCREASES IN CHOLINE ACETYLTRANSFERASE ACTIVITY AFTER SYMPATHETIC DENERVATION IN GUINEA PIGS WITH RIGHT ATRIAL AND VENTRICULAR HYPERTROPHY. Donald D. Lund, Carol A. Whitels, Alberto R. Subieta, Benet J. Pardini, and Phillip G. Schmid. Veterans Affairs Medical Center, Cardiovascular Center, University of Iowa College of Medicine, Iowa City, IA.

Choline acetyltransferase (CAT) activity is a neurochemical marker of cardiac parasympathetic innervation. Our goal was to investigate the role of the sympathetic nervous system in modulating CAT activity in response to right atrial and right ventricular hypertrophy produced by hypobaric hypoxia. Guinea pigs first received either sham surgery (I, Innervated) or a left unilateral stellate ganglionectomy (D, Denervated). One week later, groups of animals (n=10) were either sacrificed (4 Week Control), or maintained in hypobaric hypoxia at a simulated altitude of 18,000 feet, 376 TORR (7 Week Hypoxia), or normal atmospheric conditions (7 Week Control) for three weeks. CAT activity nmol/chamber/hr is shown in the following table (mean ± SEM; *p<0.01 vs 4 Week Control):

GROUP	4 Week Control	7 Week Control	7 Week Hypoxia
Right Atrium (I)	3.57 ± 0.59	6.10 ± 0.91	5.12 ± 0.55
Right Atrium (D)	4.63 ± 0.82	4.73 ± 0.99	*7.76 ± 1.27
Right Ventricle (I)	16.00 ± 2.28	25.20 ± 4.42	24.29 ± 2.38
Right Ventricle (D)	19.34 ± 2.90	23.72 ± 2.47	*30.51 ± 2.19

Animals with a left unilateral stellatectomy and right ventricular pressure overload induced by hypobaric hypoxia had significant increases in CAT activity in the hypertrophied chambers. Animals with intact innervation did not have detectable changes in CAT activity. These results may indicate an inhibatory influence of the cardiac sympathetic innervation on the parasympathetic innervation during cardiac hypertrophy produced by pressure overload. Supported by Department of Veterans Affairs, NIH HL14388 and HL38187.

26.4

EFFECTS OF ANEMIC HYPOXIA ON ERYTHROPOIETIC ACTIVITY IN TWO STRAINS OF RATS. L.C. Ou, J. Chen, T. Brinck-Johnsen, R. Smith. Departments of Physiology, Pathology, Pharmacology and Toxicology. Dartmouth Medical School, Hanover, NH 03756.

Hypoxic hypoxia resulted in much larger increases in erythropoietin (EPO) production in Hilltop (H) than Madison (M) rats, resulting in excessive polycythemia and pulmonary hypertension (signs of Chronic Mountain Sickness) in H rats. The present study was initiated to determine if there is any strain difference in EPO production and the erythropoietic activity in response to anemic hypoxia. Hemolytic anemia was induced by a single injection of phenylhydrazine (Phz; 6 mg/Kg, i.p.). Control animals received saline. Ninety six hrs after drug injection, the following parameters were measured: hematocrit (Hct), total nucleated RBC in bone marrow (B-NRBC) and in spleen (S-NRBC) per 100g bw, reticulocyte counts (Retic#) and plasma and renal tissue EPO titers. There was no strain difference in any of these parameters in control groups. phz treatment induced moderate anemia in H and M rats (Hct = 24.7 and 24.1) and increased plasma and renal tissue EPO, B-NRBC and retic# to similar extents in both strains of rats. Similar results were obtained in splenectomized animals. However, phz treatment increased S-NRBC by 260 fold in H but only 150 fold in M rats. The present study demonstrates that anemia resulted in no difference in EPO production and medullary erythropoietic activity but a pronounced difference in splenic erythropoietic activity between H and M rats. Supported by NIH grant HL 21159.

26.5

LOWERED HYPOXIC THRESHOLD FOR ERYTHROPOIETIN (EPO) PRODUCTION IN RATS WITH CHRONIC MOUNTAIN SICKNESS (CMS). J. Chen, T. Brinck-Johnsen, R. Smith, L.C. Ou. Departments of Physiology, Pathology, Pharmacology and Toxicology. Dartmouth Medical School, Hanover, NH 03756.

Exposure to simulated altitude (0.5 Atm) resulted in a much greater increase in both plasma and renal tissue EPO titers in Hilltop (H) than Madison (M) rats, leading to excessive polycythemia and pulmonary hypertension (signs of CMS) in H rats. The present study was undertaken to assess the roles of plasma EPO clearance, extrarenal EPO production and altered capability of EPO production in this strain difference. The following measurements were made: plasma clearance of ^{125}I-EPO under sea level (SL) and hypoxic (0.5 Atm) conditions; plasma EPO in bilaterally nephrectomized rats under SL and severe hypoxia (0.4 Atm); and plasma EPO and kidney mRNA in "maximally" stimulated rats (single cobalt injection (60 mg/Kg bw, i.p.) followed, 12 hr later, by severe hypoxia (0.4 Atm) for 4 hr). The plasma clearances of ^{125}I-EPO were comparable in H and M rats at SL and remained unchanged with hypoxic exposure. Severe hypoxia elevated significantly plasma EPO titers in nephrectomized rats, which was indicative of extrarenal production, but there was no strain difference. "Maximal" stimulus induced 100 fold increase in plasma EPO titers and marked accumulation of kidney mRNA for EPO in both H and M rats with no detectable strain difference. The present results suggest that the exaggerated EPO production in H relative to M rats under moderate hypoxia may result from a lowering of the hypoxic threshold for EPO production. Supported by NIH grant HL 21159.

26.6

Measurement of Blood Oxygen Saturation and Partial Pressure in the Presence of a Gas Mixture of Ethane, Cyclopropane and Sulfur Hexafluoride. V.A. Forte, Jr. and A. Cymerman. U.S. Army Research Institute of Environmental Medicine, Natick, MA 01760-5007.

Some anesthetics and halogenated gases have been shown to interfere with the measurement of blood oxygen saturation or partial pressure. We evaluated the potential interference of an experimental mixture of 70% ethane, 20% sulfur hexafluoride, and 10% cyclopropane, currently used to measure the ventilation-perfusion ratio in the lung. Blood from a young, healthy, male non-smoker was tonometered at three O_2 concentrations (10, 16 and 21%), with and without adding 20.8% of the experimental mixture. Oxygen saturations were then measured with three different instruments: (1) polarographic electrode ABL-300 (ABL), (2) spectrophotometric Co-Oximeter (COOX), (3) and galvanic cell Lex-02-Con (LEX). The results were then compared with the oxygen saturations calculated from the Siggaard-Anderson equation. The experimental mixture did not affect the O_2 values measured by the COOX and ABL methods, but lowered the LEX saturations from 2.5 to 3.6% (mean = 3.1%). Of the three methods, the ABL was found to most closely approximate the calculated saturation values, both with and without the experimental gas mixture.

26.7

CIRCADIAN TEMPERATURE RHYTHMS ARE DIFFERENTIALLY PHASE-SHIFTED BY CAFFEINE DEPENDING ON TIME OF ADMINISTRATION.
L. A. Farr, C. M. Todero,* L. Boen,* S. Hayes,* M. Kline,* M. Kowal,* and A. J. O'Neil.* College of Nursing, University of Nebraska Medical Center, Omaha, NE 68198-5330.

Theophylline and caffeine have been reported to phase-shift circadian temperature and activity rhythms in rats although the direction of shift reported by Farr et al. (1985) is at odds with that of Ehret et al. (1981). To resolve these differences, 72 male rats were implanted with radio transmitters, allowed to recover for one month, and then core temperature and locomotor activity were measured by telemetry under a 12:12 LD cycle (lights off at 2000). Following 5 days baseline, three groups (n = 12) received 7.5 mg/kg caffeine citrate orally by feeding syringe at either 2000, 0200, or 0745 hours for 5 days. Control rats (n = 12) received distilled water at each time. Circadian rhythms of rats that received caffeine at 2000 advanced, at 0745 delayed, and no change in timing was seen at 0200. Amplitude of circadian cycles was increased when caffeine was given at 0200. Controls showed some shifts due to handling, but these were not as great as those of caffeine. Similar patterns were observed in activity rhythms although more intragroup variation was observed. Results suggest that timing of caffeine ingestion may be important in adaptation to changing schedules (supported by DHHS grant #1R01 NU01098-03).

26.8

SLEEP DEPRIVATION EFFECTS ON THERMOREGULATION MAY BE PARTLY DUE TO DISRUPTED CIRCADIAN TIMING
L.A. Stephenson and M.A. Kolka. U.S. Army Res. Inst. Env. Med., Natick, MA 01760.

The purpose of this study was to determine whether the lower core temperature (T_c) threshold for onset of cutaneous vasodilation observed after 33 h of sleep deprivation (SD) can be accounted for by a change in circadian timing of the T_c rhythm. Four men were studied during two control experiments when T_c was at its peak (T_{HI}) and at its nadir (T_{LO}). After one day of SD the men were studied again when T_c was near its peak (SD_{HI}). A fourth experiment was done after recovery sleep when T_c was near its nadir. The men exercised at 55% peak $\dot{V}O_2$ on a cycle ergometer (T_a=35°C; T_{dp}=13°C). Esophageal temperature and forearm blood flow (FBF, plethysmography) were measured every 0.5 min. The slope of FBF:T_{es} (ml•100ml^{-1}•min^{-1}•°C^{-1}) during control experiments was greater ($p<0.05$) at T_{HI} (40.0±5) than T_{LO} (23.9±5) and SD_{HI} (27.4±10). Although the T_{es} threshold for onset of cutaneous vasodilation was higher during T_{HI} (37.0°C±0.1) than T_{LO} (36.4°C±0.1), there was no difference between T_{HI} and SD_{HI} (36.8°C±0.2) when T_c was used as a circadian marker. Likewise, there was no difference in the FBF threshold after recovery sleep between T_{LO} (36.4°C±0.2) and the nadir of the T_c rhythm during recovery (36.7°C±0.2). During T_{LO} the change in T_{es} during exercise averaged 1.1(±0.2)°C which was greater ($p<0.05$) than T_{HI} (0.8±0.2°C) and SD_{HI} (0.9±0.2°C). These data present evidence that the threshold shift in onset of cutaneous vasodilation during SD is due to disruption of circadian timing.

26.9

CORTISOL RESPONSES TO EXERCISE DURING AND AFTER SLEEP DEPRIVATION.
P.W. Burgoon*, M.A. Kolka, and L.A. Stephenson. U.S. Army Res. Inst. Environ. Med., Natick, MA. 01760-5007.

Four healthy, young subjects were studied during a normal sleep/wake cycle (CON), sleep deprivation (SD, 40-56 hours), and recovery (R, following a period of uninterrupted sleep). During these periods, subjects underwent an exercise test during core temperature peaks and nadirs (T_{HI} and T_{LO}) at 55% peak V_{O_2} in a hot environment (T_a = 35°C, T_{dp} = 11°C) while seated on a modified cycle ergometer. Blood samples were collected after 20 minutes of rest and 25 minutes of exercise. Overall CON cortisol levels were greater at T_{LO} than at T_{HI} (16.74 and 6.30 $\mu g \cdot dl^{-1}$, $p \leq 0.05$). Cortisol responses were not different within T_{LO} experiments. At T_{HI}, overall SD cortisol (11.79 $\mu g \cdot dl^{-1}$) increased compared to CON (6.30 $\mu g \cdot dl^{-1}$, $p \leq 0.05$). Exercise cortisol during CON and SD (10.32 $\mu g \cdot dl^{-1}$) was higher than rest (7.77 $\mu g \cdot dl^{-1}$, $p \leq 0.05$). Cortisol concentration for SD and R (12.27 and 7.18 $\mu g \cdot dl^{-1}$, $p = 0.12$) suggested that cortisol decreased with recovery, but high cortisol persisted even after uninterrupted sleep. These observations were made possible by utilizing core temperature rather than clock time as a circadian marker. These data indicate: 1) cortisol responses to sleep deprivation, exercise, and recovery from sleep loss were dependent upon circadian cortisol levels and 2) core temperature provides a marker to assess cortisol responses to sleep status and exercise.

26.10

EFFECTS OF ADRENALECTOMY AND DEXAMETHASONE REPLACEMENT ON CIRCADIAN RHYTHMS OF GI PEPTIDES IN RATS.
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The role in circadian variations of gastrointestinal peptides is not known. In this study we examined the influence of the adrenal gland on 24 hour fluctuations of plasma and tissue gastrin and cholecystokinin (CCK) in adult male Sprague-Dawley rats. METHODS: 140 rats underwent either bilateral adrenalectomy (ADX) or sham-adrenalectomy (SHAM). One group of ADX rats received dexamethasone (DEX) replacement (71 μg/day) the others were maintained on a sodium/dextrose drinking solution. All animals were kept in sound attenuated environmental chambers under a 12:12 L/D cycle for a period of 4 weeks. The rats were then fasted for 24h, removed, anesthetized, and blood and tissues were collected at 3h intervals for 24h. Plasma and tissue levels of gastrin and CCK were determined by specific RIA. Completeness of adrenalectomy was verified by plasma corticosterone RIA. The data were analyzed by ANOVA and single cosinor analysis. RESULTS: Significant circadian fluctuations for plasma gastrin and CCK were not detected in ADX rats ($P<0.2$) compared to the 24h fluctuations observed in SHAM animals ($P<0.05$). DEX treatment in ADX animals, however, tended to restore these rhythms in plasma. Duodenal CCK levels exhibited a significant fluctuation ($P<0.02$) in SHAM and ADX+DEX rats but not in ADX rats ($P<0.1$). Antral gastrin levels did not exhibit significant fluctuations. CONCLUSIONS: ADX tends to abolish circadian rhythms of plasma gastrin and CCK in rats. DEX replacement in ADX animals tends to restore rhythms extinguished by ADX. Thus, the adrenal may play an important role in governing the 24 hour oscillations of GI peptides in rats. (Support: NIDDK P01 DK35608-04)

CONTROL OF BREATHING

27.1

INFLUENCE OF N-METHYL-D-ASPARTATE (NMDA) BLOCKADE ON INSPIRATORY REFLEXES.
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This study determined the effect of NMDA blockade on the short-latency excitation, transient inhibition, or inspiratory termination elicited by superior laryngeal nerve (SLN) or intercostal nerve (ICN) stimulation, plus the transient inhibition elicited by phrenic nerve (PN) or brainstem respiratory group stimulation. Adult cats were anesthetized (pentothal, 50 mg/kg, i.p.), decerebrated, paralyzed and ventilated. Both PNs, a SLN, and an ICN were isolated and placed on electrodes. A stimulating microelectrode was positioned in the brainstem. After recording control PN responses to stimulation, the NMDA channel blocker MK-801 was given (i.v., 0.1 mg/kg doses). MK-801 at low doses produced apneusis upon no-inflation tests. The short-latency excitations produced by SLN or ICN stimulation were present after MK-801 with no change in onset latencies or durations. Thresholds and onset latencies of the transient inhibitions produced by brainstem, SLN, ICN, or PN stimulation were not significantly altered at any dose. The durations of the inhibitions elicited by ICN, SLN, or brainstem stimulation were unchanged, while that produced by PN stimulation was slightly prolonged. SLN or ICN stimulation continued to elicit inspiratory termination at all doses. We conclude that these reflexes do not depend on NMDA-receptor mediated neurotransmission. (Supported by NIH HL40369)

27.2

UPPER AIRWAY COOLING AND *L*-MENTHOL ON DIAPHRAGMATIC ACTIVITY AND AIRWAY RESISTANCE.
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Both laryngeal cooling and exposure of the upper airway to *l*-menthol, a specific stimulant of cold receptors, can depress ventilation by prolonging expiratory duration (T_E). The aim of this study was to establish whether post-inspiratory activity of the diaphragm (PIIA) contributes to this prolongation of T_E as well as to measure total airway resistance. Respiratory airflow, laryngeal temperature, esophageal pressure and diaphragmatic EMG were recorded in 5 anesthetized guinea pigs, breathing through a tracheostomy, while a 30 ml/s flow of cold air (25°C) or warm air (37°C, with or without *l*-menthol) was passed through the isolated upper airway. Airway resistance was not affected by any of the challenges. The cooling-induced prolongation of T_E (125 ± 2 SE, % of control) was not associated with any change in PIIA while the *l*-menthol-induced prolongation of T_E (255 ± 24%) was accompanied by an increase of PIIA (142 ± 8%). This increase in PIIA was inversely related to the mean expiratory flow ($r = -0.62$). The PIIA response was abolished by topical anesthesia of the nasal mucosa. We conclude that nasal cold receptors, through their reflex effects on PIIA, can play a role in the regulation of expiratory airflow. (Supported by HL-20122)

27.3

DIFFERENTIAL PERIPHERAL CHEMOREFLEX EFFECTS BY CO_2 AND CYANIDE ON SYMPATHETIC AND RESPIRATORY NEURONS. W-X. Huang, S. Lahiri, A. Mokashi,* and D. Spergel*. Department of Physiology, University of Pennsylvania School of Medicine, Philadelphia, PA 19104-6085.

Effects of carotid chemoreceptor stimulation by CO_2 and cyanide on internal intercostal expiratory nerve (IICEN), recurrent laryngeal nerve (RLN) and cervical sympathetic nerve (PSN) discharges were tested simultaneously with phrenic nerve (PN) activities in the anesthetized and paralyzed cats in which the aortic and vagus nerves were cut bilaterally. Inspiratory discharges (PN or RLN) were usually stimulated by the intracarotid injections of both cyanide (10 μg) and CO_2-saturated saline (0.5 ml) solutions. Most IICEN and expiratory RLN fibers (in 18 cats) responded only slightly to cyanide injection. In two cats, IICEN and RLN fibers responded to CO_2 more than to cyanide, although PN and PSN activities responded to both cyanide and CO_2 injections. Carotid sinus nerve transection abolished all the responses to intracarotid CO_2 and cyanide injections, indicating chemoreflex origin of the responses. The results that some of the expiratory neurons were stimulated by CO_2 but only slightly by cyanide injections suggest that the carotid chemoreceptor afferents may consist of two types, one responding to CO_2 more strongly than to cyanide and that these fibers have synaptic distribution to expiratory neurons; the reflex pathway of the other type preferentially leads to inspiratory neurons. (Supported in part by grants NS-21068 and HL-19737)

27.4

EARLY EXPIRATORY DIAPHRAGMATIC AND LARYNGEAL MUSCLE ACTIVITIES IN AUGMENTED BREATHS IN NEWBORN LAMBS. A.A. Hutchison, J.W. Wozniak*, T.L. Watts*, H-G. Choi*, P.C. Kosch. University of Florida, Departments of Pediatrics & Physiological Sciences, Gainesville, Fl. 32610.

Following augmented inspirations after birth, incremental increases in lung volume occur with laryngeal retardation (braking) of expiratory airflow (V_E). The degree of change in absolute lung volume depends, in late expiration, upon the timing of the onset of diaphragmatic (DEMG) activity relative to laryngeal opening (Clin Res 1990; 38:63A) and, in early expiration, will depend upon the degree of V_E. To examine the early expiratory events, airflow, thyroarytenoid (TA), posterior cricoarytenoid (PCA) and (DEMG) activities were recorded in 8 previously instrumented fetal sheep delivered by C-section. 100 augmented breaths were studied in the first 20 minutes after birth. Braking of early V_E was related primarily to varying degrees of post-inspiratory inspiratory DEMG activity, decreasing PCA and increasing TA activities. In addition, after cessation of the main PCA and DEMG inspiratory bursts, second smaller PCA and DEMG bursts could occur. These were associated with retardation of V_E and could result in inspiratory flow. Finally, a complex form, combining laryngeal and DEMG braking, occurred. It is postulated that different patterns are employed to achieve a certain level of lung mechanical afferent feedback at which point more prolonged TA retardation of V_E commences. (Supported by NIH grant HL 39858)

27.5

RESPIRATORY VERSUS POSTURAL ROLE OF THE ABDOMINAL EXPIRATORY MUSCLES. E.A. Phillipson, F. Yasuma*, J.R. Kimoff*, L.F. Kozar*, T.D. Bradley, and S.J. England. University of Toronto, Toronto, Ontario, M5S 1A8.

We examined the respiratory and postural activities of the abdominal expiratory muscles in 4 trained dogs in whom recording electrodes had been implanted chronically in the costal diaphragm (DP), external oblique (EO), and transversus abdominis (TA) muscles. During quiet wakefulness or non-REM sleep, progressive hypercapnia resulted in progressive augmentation of DP, EO, and TA EMG activity. However, when afferent vagal inputs were blocked by cooling exteriorized cervical vagal loops, EO and TA activity was markedly reduced despite hypercapnia and the addition of expiratory flow-resistive loads. Similarly, during REM sleep there was abolition of respiratory-related EO and TA activity, even with hypercapnia, resistive loading, and the vagi intact. Since vagal inputs convey information regarding lung inflation (i.e. "posture"), and REM sleep inhibits postural muscle activity, the results suggest that the abdominal muscles are influenced more by postural than by chemical respiratory stimuli.

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27.6

INTERACTION BETWEEN PERIPHERAL AND CENTRAL CHEMORECEPTORS IN THE CONTROL OF VENTILATION IN THE TOAD, *BUFO MARINUS*. Allan W. Smits* and Neal J. Smatresk. Univ. of Texas, Arlington, TX 76019

We recently provided evidence of central chemoreceptor control of ventilation in amphibians. Intracranial perfusion with mock CSF of varying pH and P_{CO2} significantly altered ventilation in *Bufo*, even when blood gases and pH were held constant with unidirectional lung ventilation (UDV). The goals of the present experiment were to 1) localize central chemoreceptors, 2) evaluate contributions of peripheral and central chemoreceptors to ventilation and 3) determine the adequate stimulus (pH vs CO_2) for these intracranial receptors. Thus, ventilation in toads was characterized during exposure to multiple combinations of peripheral and central chemoreceptor stimulation. Perfusion of hypercapnic, acidic CSF in brain areas other than near the ventral medullary surface (VMS) had no effect on ventilation. Peripheral hypercapnia stimulated ventilation much more than peripheral hypoxia at all levels of central stimulation. Central stimulation had a much greater effect on the number of breaths/bout than did peripheral stimulation, and also reduced the time between breathing bouts. Superfusion of the ventral medullary surface with either hypocapnic acidic or hypercapnic alkalotic mock CSF stimulated breathing, but neither of these solutions was as effective as a hypercapnic acidic mock CSF. These data indicate that toad central chemoreceptors are in or near the VMS, respond to either pH and CO_2, and upon stimulation tend to convert periodic to continuous breathing patterns. Further, the greater ventilatory response to hypercapnia suggests the presence of superficial and deeper chemoreceptor loci. Supported by NSF grant DCB-8801846 to NJS.

27.7

THE ROLE OF ADENOSINE IN THE VENTILATORY RESPONSE TO HYPOXIA: A COMPARISON OF AMINOPHYLLINE, ENPROFYLLINE, AND PLACEBO. J. Randall Thompson* and N. K. Burki, University of Kentucky, Lexington, KY 40536.

A biphasic response of minute ventilation ($\dot{V}_E$) to sustained hypoxia has been reported(J Appl Physiol 1986; 61:906), consisting of an initial increase in $\dot{V}_E$ followed by a decline to an intermediate level. Aminophylline (A) is reported to prevent this secondary decline in $\dot{V}_E$, possibly mediated by its adenosine antagonist effect. We studied 9 healthy, non-smoking, male subjects (ages 23-32 years), comparing A and Enprofylline (E), which is a xanthine derivative similar to A, but lacking the adenosine antagonist effect. Each subject was studied on 3 separate days; on each day, 1 hour after ingesting a capsule of either placebo (P), A (500 mg) or E (200 mg), ventilatory measurements were made with inspired oxygen gas mixtures of 0.11 for 30 mins. SaO_2 with A was significantly ($p<0.05$) lower immediately and 15 mins after induction of hypoxia than with E or P (P=78.6±4.7%, E=77.2±7.0%, A=74.3±5.9%). In all three treatment groups, $\dot{V}_E$ rose initially; with P and E, there was a tendency towards a decrease in $\dot{V}_E$, despite marked hypoxemia. With A, $\dot{V}_E$ remained elevated. Both V_T and f were higher with A compared to P or E. We conclude that the effects of A may be mediated via its adenosine antagonist action, since the increase in $\dot{V}_E$ was maintained when compared to P or E.

27.8

BREATHING MOVEMENTS (FBM) OF FETAL SHEEP *IN UTERO* ARE STIMULATED BY CENTRALLY ADMINISTERED MUSCARINIC AGONISTS. A.R. Hohimer, J.M. Bissonnette, G.B. Willeke* and S.J. Knopp*, Oregon Health Sciences University, Portland, Oregon 97201-3098.

We sought to determine if central muscarinic receptors were involved in ventilatory control of the fetal sheep. We measured the incidence and magnitude of FBM (repetitive transient, negative intra-thoracic pressures associated with diaphragmatic contractions) to assess respiratory drive in chronically catheterized, unanesthetized fetal sheep at about 125-130 days of their normal 145 day gestation. FBM are normally episodic, occurring about 40% of the time and virtually only during the low voltage EEG state associated with REM sleep. FBM, of course, do not alter gas exchange. We found that administration of 1 μg of the cholinergic agonist carbachol into the CSF via a cisternal catheter rapidly increased the incidence of FBM to virtually 100%. This effect lasted for more than 1 hour and FBM occurred during the normally apneic high voltage EEG or "quiet" sleep state. The peak pressure generated by these respiratory efforts was dramatically increased (>2X) relative to control. A muscarinic (M1) agonist (McN-A-343) also stimulated FBM (albeit at a much higher dose). We conclude that muscarinic receptors (perhaps the M1 type) located near the cisternal CSF may be important modulators of respiratory drive in fetal sheep. (Supported by NIH HL 38039).

27.9

AFFERENT NERVE ACTIVITY IN THE LARYNGEAL NERVES OF THE GUINEA PIG. H. Tsubone* and G. Sant'Ambrogio. Department of Physiology, University of Texas Medical Branch, Galveston, TX 77550.

We have studied the afferent activity originating from the larynx of guinea pigs anesthetized and breathing spontaneously. A special cannula inserted into the cervical trachea allowed the diversion of breathing from a tracheostomy to the upper airway. Recording from the whole SLN revealed an inspiratory augmenting discharge that became expiratory when the animal made efforts against the upper airway. Single unit action potentials were recorded from 34 laryngeal receptors. Thirteen of them showed a respiratory modulation even during tracheostomy breathing, indicating an activation by laryngeal motion; they were inhibited by negative pressure and stimulated by positive pressure. Other 13 receptors responded only to pressure: 7 to negative pressure and 6 to positive pressure. The rest of the receptors did not show any activity related to the respiratory cycle, but could be activated by mechanical probing of the laryngeal lumen and by water instillation. The prevailing effect of collapsing pressure was an inhibition of the laryngeal afferent activity, at variance with that observed in the dog, but consistent with that reported for the rabbit. The relative abundance of "irritant" type activity is consistent with the high sensitivity of this species.
With the financial support of Proctor and Gamble.

27.10

RESPONSES OF DIFFERENT CAROTID CHEMORECEPTOR AFFERENTS TO CYANIDE AND CO_2 ARE NOT ALWAYS PROPORTIONAL. Q. He*, W-X. Huang and A. Mokashi*. Department of Physiology, University of Pennsylvania School of Medicine, Philadelphia, PA 19104-6085.

Effects of close intraarterial injections of cyanide and CO_2-saturated saline were tested on 54 pairs of carotid chemosensory activities in the anesthetized and paralyzed cats. Each pair consisted of two fibers (fiber A and fiber B) the activities of which were simultaneously recorded. The impulse frequencies of 108 chemoreceptor fibers in 6 cats during normoxic normocapnia were 2.51 ± 1.62 Hz (mean ± S.D.). The peak responses in 0.5 sec to cyanide were 29.07 ± 10.87 Hz, and to CO, were 28.04 ± 13.27 Hz. There was no statistical significance between the two responses. However, the responses of the fibers in each pair to the two stimuli were not always proportional. Of 54 pairs, fiber A of a pair showed greater responses in 23 and less in 31 to cyanide stimulation than another fiber. The responses of fiber A to CO_2 were greater than that of fiber B in 22 and less in 32 pairs. In 8 out of 10 cases, the simultaneously studied fiber A and fiber B did not show proportional responses to hypoxia and hypercapnia. Thus we conclude that individual carotid chemoreceptor fiber do not always collect proportional signals for sensing CO_2, hypoxia or cyanide and accordingly, the results support the hypothesis that the sense mechanisms of carotid chemoreceptors to CO_2 and O_2 (or cyanide) are different. (Supported in part by grants NS-21068 and HL-19737)

27.11

REFLEX VENTILATORY EFFECTS OF ELECTRICAL STIMULATION OF INTRATHORACIC NON-VAGAL AFFERENTS. R.L.Coon, P.S. Clifford, and F.A. Hopp, Med. College of WI and VA Med. Center., Milwaukee WI 53295.

A recent study (Coon *et al.*, Physiologist 32:A166, 1989) demonstrated that stimulation of lung receptors with non-vagal afferent nerves by KCl applied to the surface of the lungs produced reflex increases in the ipsilateral triangularis sterni electromyogram (TS-EMG). The purpose of this study was to investigate the probable pathway for this reflex. Five dogs were anesthetized with sodium pentobarbital and placed on positive pressure ventilation. The chest was opened through a mid-sternal incision. Diaphragm EMG and left TS-EMG were recorded along with systemic arterial blood pressure and tracheal pressure. Measurements of these variables were made, post-vagotomy, before and during electrical stimulation of the central end of the left vagosympathetic trunk (VST), ventrolateral and ventromedial cardiac nerves (CN), stellate cardiac nerve, when present, and the left ventral ansa subclavia (VA). Stimulation parameters were 30 Hz, 3.0 msec and from 0.3 to 3.0 mA. The primary reflex effect of the nerve stimulations was an increase in TS-EMG. Stimulation of the close CN and the VST produced maximum increases of 21 to 100% from control peak TS-EMG whereas stimulation of the VA produced a maxium increase of 150% ± 36 (mean ± SEM, N=4). Stimulation amplitudes as low as 0.3 mA were effective in producing a response. The results of this study suggest that the afferent fibers for the previously described reflex travel with the sympathetic efferent pathways and that the afferent nerves are A fibers. (Supported by the Medical Research Service of the VA)

27.12

A MODEL OF FICTIVE COUGH IN THE CAT. D.C. Bolser, Dept. Allergy and Immunology, Schering-Plough Research, Bloomfield, NJ 07003.

Little is known about the central mechanisms of cough. The purpose of this study was to develop a model of cough which would allow study of the central components of this motor task in a stable preparation. I hypothesized that stimuli known to elicit cough in spontaneously breathing animals would activate phrenic and abdominal muscle motoneurons in paralyzed animals in a pattern consistent with cough. Experiments were performed on five midcollicular decerebrate cats. The animals were artificially ventilated on a cycle-triggered pump, paralyzed and subjected to a bilateral pneumothorax. Phrenic (C5) and cranial iliohypogastric (L1) nerve efferent activities were recorded. Cough was elicited by electrical stimulation of the left superior laryngeal nerve (SLN) (1-4 V, 10 Hz, 1.0 ms pulse duration) or probing the intrathoracic trachea. Fictive coughs consisted of large amplitude bursts in phrenic motoneuron activity (≥ 150% of control) immediately followed by large bursts in abdominal motoneuron activity (≥ 500% of control). Probing stimuli elicited 265 fictive coughs during 31 trials (8.5 ± 1 coughs per trial) and SLN stimuli elicited 48 fictive coughs during 30 trials (1.6 ± 0.3 coughs per trial). I conclude that fictive cough can be produced in paralyzed cats ventilated on a cycle-triggered pump. This model will be useful in studies examining the neurogenesis of cough.

27.13

COMPARATIVE BREATHING PATTERN REGULATION. D.F. Boggs, B. Williams*, C. Colby*, D.L. Kilgore, Jr., U. of Mt., Missoula, Mt.59823.

While most mammals spend about 35% of each breath in inspiration and 65% in expiration, the mean T_I/T_{TOT} of 6 awake coati mundis is 0.44(± 0.017), and of 4 woodchucks, 0.24 (±.003). These species have similar inspiratory drives (V_T/T_I) of 49 (±5) and 41(±4) respectively, but very different 'total' respiratory drives indicated by low resting $PaCO_2$ values in coatis (23.4± 0.5 torr) vs high $PaCO_2$ in woodchucks (48±1 torr). The shorter T_E/T_{TOT} in coatis is associated in some individuals with less laryngeal expiratory 'braking' than in other species; i.e. Posterior Cricoarytenoid m. activity persists through 34-75% of T_E; whereas preliminary data on woodchucks indicate no post-inspiratory PCA activity. Yet there is little P-I diaphragmatic activity either. Much of the prolongation of T_E is due to delay in inspiratory onset. The ventilatory response to CO_2 differs in these species (slope of $\%\Delta\dot{V}/\Delta PaCO_2$ = 23 in coatis, 12 in woodchucks). The response pattern also differs. Coatis are closer to the model based on cats, rabbits, dogs and man, with the increased V_T accompanied by some reduction in T_I and more in T_E. But the woodchuck tends to increase T_E with increased V_T - a pattern shared by another CO_2 'insensitive' species, the syrian hamster (Walker et al, 1982). These interspecific patterns tend to confirm an independence of control over volume and timing components of respiratory system output and the probable role of peripheral CO_2 sensitivity in regulating T_E. (NSF grant #DCB-8608661)

27.14

ETIOLOGY OF PERIODIC BREATHING DURING SLEEP IN ELDERLY STROKE PATIENTS. David W. Hudgel, Mustafa Quadri*, Case Western Reserve University, Cleveland Metropolitan General Hospital, Cleveland, Ohio, 44019.

Patients with cerebrovascular accidents (CVA) often exhibit periodic breathing during sleep. Previously, we demonstrated that periodic breathing during sleep, induced in healthy subjects with mild hypoxia, was associated with fluctuations in upper airway resistance (UAR). When UAR was low, tidal volumes were large; and vise versa. The purpose of the present study was to test the hypothesis that the variation in sleep ventilation post-CVA is related to changes in UAR and not related to changes in central respiratory drive to chest wall inspiratory muscles. Four hemiplegic elderly subjects, 3 females and 1 male, age 67 ± 13 years were studied supine in Stage II NREM sleep. EEG, EOG, transmandibular EMG, and costal margin surface diaphragm EMG activity were monitored. Inspiratory flow and volume were measured by a pneumotachograph attached to a tight-fitting face mask. Airway pressure and recorded from a hypopharyngeal bias-flow catheter. Inspiratory resistance was calculated at peak pressure. 107 ± 13 consecutive breaths were analyzed in each subject when breathing was periodic. All four subjects demonstrated a hyperbolic relationship between inspiratory upper airway resistance and tidal volume, $Y = A + (B/X)$, such that as resistance increased tidal volume fell; and as resistance decreased, tidal volume increased, $r = 0.86 \pm 0.07$. Diaphragm EMG activity varied minimally. We conclude that the pattern of periodic breathing seen in these subjects is related to fluctuations in upper airway resistance, leading to a concomitant change in tidal volume. We speculate that periodic breathing in sleep may not be due to fluctuations in ventilatory drive to chest wall inspiratory muscles, but related to alterations in upper airway caliber.

28.1

PHOSPHOLIPIDS OF VASCULAR SMOOTH MUSCLE FROM NORMOTENSIVE AND HYPERTENSIVE RATS. C.C. Wu*, E. Clyde*, A.F. Dominiczak* and D.F. Bohr. N.D.M.C., Taipei P.O. Box 90048-504, Taiwan, R.O.C. and Univ. of Michigan, Ann Arbor, MI 48109

The functions of several membrane transport proteins have been found to be abnormal in hypertension. Because it seems unlikely that so many different transport proteins would be abnormal, we have hypothesized that the primary abnormality resides in the lipid bilayer and that this abnormality then alters the functions of each of the transport proteins. The purpose of this study is to determine whether a difference could be found in the phospholipid composition of the lipid bilayer from hypertensive vs. normotensive rats. Phospholipids were extracted from the aortic wall or from cultured vascular smooth muscle cells from normotensive (WKY) and hypertensive (SHRSP) rats. Individual phospholipids were separated by thin layer chromatography and quantified by total phosphate determination. Percent compositions of each phospholipid in WKY/SHRSP were: sphingomyelin, 13±2.8/14±1.1%; phosphatidylcholine, 33±5.6/38±0.6%; phosphatidylserine, 8.2±0.7/10±1.0%; phosphatidylinositol, 5.0±1.5/6.5±2.5%; phosphatidylethanolamine, 37±5.9/26±1.5%; phosphatidic acid, 3.9±0.1/4.2±0.3%. These preliminary results, indicating that there is less phosphatidylethanolamine in hypertension, are compatible with the possibility that in hypertension there are differences in the lipid bilayer of the plasma membrane that could alter the function of the transport proteins.

28.2

Increase in Endothelin Contraction in Renal Arteries, but not in Aortae, of the Dahl 'S' Hypertensive Rats. David D. Ku, Univ. of Alabama at Birmingham, AL 35294

In the present study, reactivity of Dahl salt-sensitive 'S' and salt-resistant 'R' rat aortae (AO) and renal arteries (RA) to endothelin (ET-1) was investigated. Seven 7-week old 'S' and 'R' rats were fed high (8%) NaCl diet for 5-6 weeks, at which time systolic blood pressure of the 'S' rats was markedly elevated. In freshly isolated 'R' AO with intact endothelium (EC), 0.1-30 nM ET-1 produced a dose-dependent contraction, reaching a maximum of 125±12% (M±SEM of 13 vessels) of the 70 mM KCl-induced contraction. Removal of EC did not alter the response to KCl, but markedly potentiated the ET-1 response to 218±15%. In the hypertensive 'S' aortae, the ET-1 contraction was significantly decreased (78±12%). Removal of EC enhanced the maximum response to that of the 'R' rats. The effects of ET-1 in the RA of the 'R' and 'S' rats, however, were not altered by the removal of EC. In addition, the 'S' RA showed a consistently greater response to ET-1 than the 'R' rats. Responses to 1 and 3 nM ET-1 in the 'S' RA were 25±8% and 57±15% as compared to 11±4% and 25±8% found in the 'R' rats. These results suggest that there is a regional difference in vascular responses to ET-1 and that the genesis of salt hypertension in Dahl 'S' rats is accompanied by an increased responsiveness of the renal arteries, but not aortae, to endothelin.

28.3

INCREASED SENSITIVITY OF THE CREMASTER MICROVASCULATURE IN SPONTANEOUSLY HYPERTENSIVE RATS WITH ELEVATED BODY TEMPERATURE (BT). J.M. Price and F.R. Wilmoth*. Dept. of Physiology, University of South Florida, Tampa, FL 33612.

The objective is to determine if differences in BT observed in SHR (39°C) and WKY rats (37.5°C) affect the cremaster microvascular response to phenylephrine (PHE). Scrotal temperature was found to be greater in 16 week old SHRs (35.4±0.5°C)than in WKY rats (33.2±0.3°C). Intravital TV microscopy was used to study the effect of bathing solution temperature on the response of primary arterioles (A1) and venules (V1) to topically applied PHE at either 34°±0.5°C or at 36°±0.5°C. Bath temperature had no effect on control period diameters or the maximum constriction of A1 and V1 vessels in 6 week old SHRs and WKY rats. Sensitivity (pD2) of V1 vessels was not affected by temperature. However, A1 values were significantly greater at 36°C than at 34°C in the SHR but not in the WKY rat. A1 sensitivity was greater in the SHR at 36°C than in the WKY rat at 36°C or 34°C. When compared at 34°C there was no difference in pD2 values of A1 vessels from SHR and WKY rats. The results suggest that a small difference in bath temperature can affect the microvascular response in the SHR and its cremaster microvasculature is more sensitive to phenylephrine stimulation than the WKY rat at their respective scrotal temperatures. (Supported by the American Heart Assoc. Florida Affiliate)

28.4

RESPONSES TO HYPOXIA AND SODIUM IN SPONTANEOUSLY HYPERTENSIVE RATS. W.N. Henley, L.L. Bellush*, D.A. Murray*, and M.A. Callaway*. Dpts.of Zool. & Psych., and Coll.of Osteo. Med., Ohio U., Athens, OH 45701

Sixteen 5-wk-old male SHR were exposed to continuous hypobaric hypoxia (H;simulated altitude=3658m) while 16 SHR remained in normoxia (N;lab altitude=1520m). SHR from both groups were subdivided to receive either 0.9% NaCl (S) or distilled water (W) as their sole fluid intake. All SHR were decapitated after 3 wks of experimentation. Hypoxia lowered systolic blood pressure (SBP;$p<0.05$) while S elevated SBP without evidence of interaction ($p>0.8$). Hematocrit was elevated, rt. ventricles were heavier and kidneys lighter in H- vs N-SHR. Saline caused hypertrophy of kidneys and both ventricles. Serotonin (5HT) was unchanged while 5-hydroxyindoleacetic acid (5HIAA) and turnover (5HIAA/5HT) were significantly decreased in brain stem of H-SHR while S had no effect on brain stem serotonergics. Brain stem norepinephrine was elevated in H- versus N-SHR with an interactive influence of saline. Saline reverses the protective influence of H in the young SHR. However, a general lack of interaction between saline and hypoxia indicates that their influences on blood pressure are elicited via different mechanisms. Supported by the Central Ohio Heart Chapter, Columbus, OH.

28.5

CHRONIC CARBON MONOXIDE EXPOSURE DOES NOT EXACERBATE HYPERTENSION WITH OR WITHOUT ADDED SALT IN THE BORDERLINE HYPERTENSIVE RAT (BHR). David G. Penney and Roman M. Skikun*. Wayne State University, Detroit, MI 48201

Our goal was to evaluate the effect of longterm CO exposure on blood pressure (BP) in a animal model reputed to show sensitivity to salt and other environmental stimuli. One-half of three groups of BHR (F_1 of SHR mother and WKY father) each were fed 8% added NaCl beginning at 56 ("Young", n=27), 103 ("Mid", n=24), and 172 ("Old", n=32) days of age; the other halves ate standard chow (0.6% NaCl). Twenty-five days later, half of each Hi-Salt and each Low-Salt group, began 30 days continuous exposure to 500 ppm CO: the others remained in room air (Air). The 8% added salt was discontinued at the same time as CO. Systolic BP and heart rate (HR) were monitored by tail-cuff. A 60% increase in water uptake and a sharp decrease in body wt. gain in the Old Hi-Salt groups indicated increased physiologic stress. Neither BP nor HR were altered by added salt in the Young, Mid, or Old BHR. BP was lowered 10-18 mmHg during CO exposure in the Young, Mid, and Old BHR ($P<.01$), both in the presence and in the absence of added salt. Hematocrit was increased approximately 35% by CO exposure. No significant differences in BP or HR were found between the Hi-Salt/Air, Hi-Salt/CO, Low-Salt/CO, and Low-Salt/Air BHR for as long as 125 days post salt and CO treatments. The results: 1) suggest no provocatory role for CO in the development of immediate or persistent hypertension, either in the presence or absence of added Na, in this animal model; 2) dispute reported CO-induced hypertension in the Dahl salt-sensitive rat; and 3) dispute reported salt sensitivity in the BHR. (Supported by St. John Hospital, Detroit)

28.6

INCREASED ANGIOTENSIN II LEVELS IN THE HEART OF THE HYPERTENSIVE RAT. Elisabeth A. Speakman* and M. Ian Phillips. Dept. of Physiology, College of Medicine, Gainesville, Fl. 32610.

There is growing support for the existence of an endogenous renin angiotensin system (RAS) in the heart. In this study we determined angiotensin II (AngII) levels in rat heart tissue during the development of hypertrophy and hypertension. Fourteen days after renal artery clipping, Ang II levels were measured in the left and right ventricle of renal hypertensive (2-kidney, 2-clip, 2K2C) and sham operated control rats. The 2K2C hypertensive rat model was selected as a normal plasma renin model with a high success rate of hypertension development. Blood pressure measured by the tail cuff method was significantly higher after renal artery clipping (148.3±4.9 (n=8) v. 114.1±3.7mmHg (n=6), p=0.002). Hearts excised from rats were retrogradely perfused with ice cold saline to remove plasma borne AngII. Both the right (80.3±3.5 v. 69.5±2.8, p=0.05) and left ventricular (LV) tissue weights (274.1±9.7 v. 225.8±1.9g/100g body weight, p=0.005) were increased in the 2K2C rats versus controls. AngII levels were unchanged in the LV (54.3±7.4 v. 54.5±6.1pg/g tissue), but were significantly increased in the RV of 2K2C rats (110.1±11.9 v. 67.8±5.9pg/g, p=0.019). This study suggests that there are measurable AngII levels in the rat heart, that these are increased during the development of hypertension and hypertrophy and that they may be independent of plasma borne AngII. (Supported by a grant from the AHA, Fl. Aff.)

28.7

EFFECTS OF DuP 753 OR QUINAPRILAT ON PRESSOR RESPONSES TO ANGIOTENSIN IN RATS. L. Davis, S. Haleen, J. Keiser. Parke-Davis Pharm. Res. Div., Warner-Lambert Co., Ann Arbor, MI 48105

The purpose of this study was to compare the abilities of DuP 753, an AII receptor antagonist, and quinaprilat, an angiotensin converting enzyme (ACE) inhibitor, to block pressor responses to angiotensin I (AI) and AII in anesthetized ganglionic-blocked rats. Antagonist activity was determined by comparing mean arterial pressure (MAP) responses to equipotent bolus-doses of AI (0.3 ug/kg iv) or AII (0.1 ug/kg iv) delivered before and after treatment with five rising doses of DuP 753 or quinaprilat. Control AI or AII challenges increased MAP by 59±4 and 40±4 mmHg, respectively; these responses are approximately half maximal. DuP 753 and quinaprilat right shifted AII or AI dose response curves, respectively, in a competitive fashion. DuP 753 inhibited both AI and AII pressor responses with ED50s of 0.38 and 0.61 mg/kg, respectively. Quinaprilat was 38 times more potent than DuP 753 at inhibiting AI responses (ED50, 0.01 mg/kg). The maximal inhibitory effect of DuP 753 was 91±4% for AI and 96±5% for AII. The maximal inhibitory effect of quinaprilat on AI responses was similar (89±2%). Quinaprilat did not inhibit AII pressor responses. These data indicate that ACE inhibitors and AII receptor antagonists are equieffective at inhibiting pressor responses to exogenous angiotensin.

28.8

WKY SUBSTRAIN EXHIBITING SALT-SENSITIVE HYPERTENSION AND STRESS-INDUCED HYPERREACTIVITY. R. Casto, R.T. Henry, & M.P. Printz. Dept. of Pharmacology, Univ. of Calif, San Diego, La Jolla, CA. 92093

In a repeated startle paradigm, Spontaneously Hypertensive (SHR) and Wistar-Kyoto (WKY) rats exhibit distinctive cardiovascular responses to mild stimuli. We have characterized cardiovascular reactivity in the SHR, two substrains of WKY, and F_1 generation hybrids by studying startle responses, circadian rhythm of blood pressure and heart rate (HR), and the effects of chronic salt treatment. Systolic (SYS) and diastolic (DIA) arterial pressure fell significantly (-8 and -9 mmHg respectively) in inbred WKY (from Charles River stock, CR) during the rest phase and was accompanied by a dramatic decrease in HR (-70±5 bpm). SHR had no diurnal variation in pressure and a blunted variation in HR (-29±3 bpm). This pattern was also observed in the F_1 generation. A substrain of WKY (from Taconic Farm stock, TF) with slightly elevated arterial pressure also exhibited little SYS or DIA variation with small HR changes (-17±2 bpm). In repeated startle, SHR and TF exhibit tachycardia to alerting stimuli while CR and F_1 show a stimulus-dependent bradycardia. Chronic NaCl (1%) drinking water produced a dramatic increase in SYS and DIA in the TF but not in CR. Startle responses were not altered by NaCl. Diurnal rhythm was abolished in salt-treated animals. Thus similarities between the strains were dependent on the test modality. CR and F_1 produced similar results in the startle paradigm, as did SHR and TF. Circadian patterns were similar in TF and F_1. Salt treatment in CR produced a circadian pattern similar to TF. These results indicate differential responses to stress and sodium loading in substrains of WKY.

28.9

DERIVATION OF MEDULLIPIN I BY PERFUSION OF ISOLATED NORMAL KIDNEYS WITH ALBUMIN SOLUTION UNDER PRESSURE. E. Eric Muirhead, Bennie Brooks*, Lawrence W. Byers*, Leonard Share and Kenji Toba*. Univ. of Tennessee and Baptist Memorial Hospital, Memphis, TN 38146

Isolated normal rat kidneys were perfused with 5% human albumin bubbled with O_2 at various pressures. The renal venous effluent was tested for antihypertensive activity by i.v. and stomach tube injections into hypertensive recipients. There were 2 sets of experiments. Set I (perfusion at 80, 110-120, 170-180 mm Hg). 80 mm Hg and control perfusates (perfusion of aorta at 180 mm Hg without kidneys attached) caused no change in BP. Perfusate at 110-120 mm Hg dropped BP from 183±6 to 161±8 ($p < .05$) and at 170-180 mm Hg dropped BP from 186±1 to 146±14 ($p < .002$), both remained depressed for 1 hour of observation. Early findings were different ($p < 0.025$). Set II (perfusion at 170-180 mm Hg, perfusate given by stomach tube, 10±0.8 ml, measurement of BP, heart rate and cardiac output). Results:

Parameter	Control	Nadir	p	Recovery	p vs Control
BP mm Hg	190±9	158±8	<.02	194±11	.75
HR beats/min	383±24	387±23	>.9	384±29	>.9
CO ml/100g wt	19±1.1	18.6±2	>.9	18.2±1.6	>.7

Conclusions: 1) Isolated kidney perfusion supports the view that renal artery perfusion pressure modulates secretion of Med I. 2) Med I, a vasodilator, is active by stomach tube. 3) Med I should be active by mouth.

28.10

EFFECTS OF NEUTRAL ENDOPROTEASE (NEP) INHIBITOR THIORPHAN ON HEMODYNAMICS AND RENAL EXCRETORY FUNCTION IN FOUR MODELS OF EXPERIMENTAL HYPERTENSION (HT) IN RATS. MB Pamnani, RD Ghai, C Yuan, S Chen, HJ Bryant, JF Schooley, FL Douglas and FJ Haddy, Dept. Physiol., USUHS, Bethesda, MD & Ciba Geigy Corp. Pharma. Div., Summit NJ.

Thiorphan, an NEP inhibitor, has been shown to enhance effects of atrial natriuretic peptide *in vivo*. We examined the effect of iv infused thiorphan on hemodynamics and excretion of UV, $U_{Na}V$, and $U_{K}V$ in 1) SHR, 2) 70% reduced renal mass-saline, 3) 1-K, 1C, and 4) 2-K, 1C hypertensive rats. Models 2 and 3 are low renin volume dependent and model 4 is renin dependent HT. Rats were divided into experimental (E) and control (C) groups. Under inactin (120 mg/kg bw) anesthesia, rats were instrumented to record BP and dp/dt (Millar catheter) and urine was collected through a suprapubic urinary bladder catheter. E animals received iv thiorphan 0.5 mg/kg/min for 120 min. C animals received vehicle only. In some animals VSMC potentials (E_ms) were recorded *in vivo* during infusion of thiorphan or vehicle. Cardiac output (CO) was also recorded in some SHR. The thiorphan infusion produced a similar progressive decrease in BP in all models. The contractility index dp/dt/P (P = ventricular pressure) did not change, but VSMC in tail arteries hyperpolarized in all four models. CO (SHR) did not change. In spite of the significant decrease in BP, UV and $U_{Na}V$ either increased or remained unchanged. These data show that thiorphan, an NEP inhibitor, is a potent vasodepressor agent in hypertensive rats. Vasodepressor activity seems to be independent of the HT mechanism and at least in SHR seems due to the peripheral effect. The absence of any decrease in UV or $U_{Na}V$ in some cases, in spite of significant vasodepression, suggests renal effects.

28.11

ACUTE BLOOD PRESSURE REACTIVITY TO STRESS IN BORDERLINE HYPERTENSIVE (BHR) AND NORMOTENSIVE (WKY) RATS ON A CHRONIC HIGH SALT DIET. J.E. Lawler, S.K. Naylor* and E.F. O'Connor*. Physiology Program and Department of Psychology, University of Tennessee, Knoxville, TN 37996.

A number of studies have suggested that blood pressure (BP) reactivity to various stressors is enhanced in a subpopulation of humans placed on a high salt load. Typically, salt loading is accomplished in a controlled fashion during a hospital stay of several days' duration. However, this does not represent the typical picture in the United States, where acute stressors are superimposed on a chronic high salt diet. To determine if reactivity to stress is affected by a chronic high salt load in rats with a positive family history of high BP, 47 male BHR and 49 male WKY were placed on either a normal or high salt (8% NaCl in chow) diet at 2 months of age. After either 2 or 6 months on the appropriate diet, femoral artery catheters were implanted for direct BP measurement while animals were at rest or receiving a 20 min tail-shock session (.4-.6 mA intensity, 1 sec duration, every 20 secs). For all groups, the correlation between reactivity and mean BP was negative. Furthermore, those 30 animals showing the most reactive BP responses to stress had significantly lower BPs than the 30 least reactive animals. Finally, high salt significantly reduced BP reactivity. We conclude that compensatory mechanisms operate to reduce the BP response to stress in the case of a chronic high salt diet. (Supported by HL19680)

28.12

A BETTER MODEL OF EXPERIMENTAL HYPERTENSION (HT) ASSOCIATED WITH STREPTOZOTOCIN (STZ) INDUCED INSULIN DEPENDENT DIABETES MELLITUS (IDDM). S. Chen, C. Yuan, J.F. Schooley, F.J. Haddy, M.B. Pamnani. Dept. of Physiol., USUHS, Bethesda, MD 20814-4799.

We have previously shown that STZ induced IDDM is associated with HT in normotensive rats with 60% or 25% reduction in renal mass (RRM). Normotensive 60% RRM rats were infused STZ, 65 or 40 mg/kg b.w. iv as a bolus injection. All 60% RRM rats receiving STZ, 65 mg/kg developed IDDM, and associated HT, but the HT developed at an accelerated rate which could not be sustained beyond 5 weeks due to a rapid loss of body weight. Whereas only 50% of normotensive 60% RRM rats receiving STZ, 40 mg/kg b.w. developed IDDM and HT. In contrast, all normotensive 25% RRM rats receiving STZ, 65 mg/kg b.w. as a bolus iv injection developed IDDM and HT which was sustained. Their systolic blood pressure progressively increased from control value of 120 ± 1.3 mm Hg before STZ injection to 158 ± 3.9 mm Hg by the 13th week following STZ injection, when it was confirmed by the direct method. In these rats, HT was associated with ventricular and renal hypertrophy, microalbuminuria, increased plasma volume and decreased hematocrit. Relative to control 25% RRM rats receiving vehicle only, rats receiving STZ also showed hypoproteinemia, hypochloremia, hyperkalemia and acidemia (anion gap acidosis), characteristics not unlike those seen in a clinical case. These data suggest that 25% RRM rat receiving STZ, 65 mg/kg, b.w. is a better model of experimental HT associated with IDDM.

29.1

Cryopreservation of human coronary arteries and endothelial cell function. Mark J. Winn*, Tracey A. Grigsby*, and David D. Ku. Dept of Pharmacol, UAB, University Station, Birmingham, 35294, Alabama.

Freezing canine coronary arteries in the presence of dimethylsulfoxide (DMSO) and fetal calf serum (FCS) preserves endothelium dependent relaxation. We have now determined whether cryopreservation also maintains human coronary arteries (HCA), and endotheilal cell dependent relaxation. A total of 83 vessel segments from 3 patients receiving cardiac transplantation were obtained. HCA were dissected free, cut into 5mm rings, and either used immediately (fresh), or were stored for 7-10 days at -75°C in the presence of 1.8 M DMSO and 20% FCS. Both substance P (SP) and histamine (HIS) produced EDRF-dependent relaxation (E_{max} -55.4 ± 5.02% SP; E_{max} -61.45 ± 4.07% HIS) in 23 of a total of 29 cryopreserved vessels, although relaxation was less marked than that seen in fresh vessels (E_{max} -72.0 ± 3.5% SP; E_{max} -86.5 ± 3.0% HIS). Relaxation was also recorded in response to thrombin. However, both the magnitude of relaxation (E_{max} -37.9 ±7.77% cryopreserved; E_{max} -87.4 ±4.1% fresh), and the number of responsive vessels, (n=14/29) were reduced; no significant thrombin induced relaxation occurred in the remaining vessels. In conclusion, cryostorage of HCA in the presence of DMSO and FCS preserved smooth muscle and endothelial cell responses, and may provide a valuable method of maintaining functionally viable vasculature.
This work was supported by NIH grants HL-17667 and HL-39945.

29.2

ENDOTHELIAL DYSFUNCTION INDUCED BY SPLANCHNIC ARTERY OCCLUSION WITH REPERFUSION. Xin-liang Ma* and Allan M. Lefer. Department of Physiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA 19107.

Splanchnic artery occlusion (SAO) with subsequent reperfusion results in a severe and lethal type of circulatory shock associated with significant reduction in mesenteric blood flow. To explain the poor re-establishment of splanchnic blood flow after reperfusion, we tested endothelial function of the superior mesenteric artery in rats subjected to ischemia/reperfusion. Pentobarbital-anesthetized rats were subjected to 90 min occlusion of both the celiac and superior mesenteric arteries followed by reperfusion. In isolated superior mesenteric artery rings from SAO shock rats, the endothelium-dependent dilator response to acetylcholine (ACh) was severely depressed (23 ± 2 vs. 97 ± 2% in rings from sham SAO shock rats, $p<0.001$) whereas the endothelial-independent dilator response to acidified $NaNO_2$ was unchanged. In contrast, superior mesenteric artery rings from the rats subjected to SAO and reperfusion, but treated with 5 mg of h-SOD just prior to reperfusion, showed relatively normal vasorelaxation to ACh (71 ± 4%) along with a normal relaxation response to $NaNO_2$. On the other hand, superior mesenteric artery rings from the rats subjected to 90 min SAO without reperfusion showed 82 ± 4% relaxation to ACh, a value only slightly below that of sham operated controls. These results indicate that reperfusion following splanchnic artery occlusion induces a severe endothelial dysfunction which is mainly due to superoxide radical generation associated with reperfusion.

29.3

THE POSSIBLE ROLE OF ENDOTHELINS BY SURGICAL STRESS M.Onizuka, T.Miyauchi,* S.Endo,* A.Fujiwara,* H.Yuasa,* E.Akaogi,* K. Mitsui,* N. Suzuki,* M.Fujino,* M.Yanagisawa, K.Goto, T.Masaki and M.Hori. Departments of Surgery and Pharmacology, Univ of Tsukuba and Takeda Chemical Res Lab. Tsukuba 305 Japan

We studied the involvement of endothelin-1 (ET-1), endothelin-3 (ET-3) and big endothelin-1 (big ET-1) in physiological response to surgical stress. Plasma consentrations of endothelins were measured. The blood samples were collected from the pulmonary artery (PA), the left atrium (LA) and the median cubital vein (MCV) in 6 patients (4 men and 2 women, aged 44-81 years) who underwent pulmonary lobectomy. The samples were taken appropriately before, during and after the surgery. The data are summarized in the table (mean ± SD, pg/ml).

	Time sampling				
	pre-operation	after open-chest	before close-chest	6h after operation	24h after operation
PA	1.06±0.37	1.24±0.22	1.81±0.41	1.67±0.40	1.03±0.19
LA		1.28±0.27	1.99+0.49		
MCV	1.25±0.47		3.06±1.64	3.74±1.20	1.64±0.59

Plasma ET-1 levels increased significantly in the blood from all the sampling sites. The levels were significantly higher in MCV samples than PA samples 6 h after surgery. This suggested ET-1 was released from the forearm. We speculate ET-1 might be involeved in a compensatory response by the reduction of local blood flow in non-vital organs. Big ET-1 increased similarly to ET-1, whereas ET-3 did't change throughout this study.

29.4

DIETARY COPPER DEFICIENCY INHIBITS ACETYLCHOLINE-INDUCED AORTIC RELAXATION. Jack T. Saari. USDA, ARS, Grand Forks Human Nutrition Research Center, Grand Forks, ND 58202.

Morphological and biochemical evidence indicates that the blood vessel wall, perhaps including the endothelium, is disrupted in dietary copper (Cu) deficiency. Male, weanling Sprague-Dawley rats were fed a purified diet that was either deficient (CuD, <0.5 ppm) or adequate in Cu (CuA, 5.0-5.5 ppm) for four weeks. Cu deficiency was verified by liver and serum Cu concentrations. Aortic rings (3-5 mm long) from paired CuD and CuA animals were isolated from the descending thoracic aorta, placed in tandem tissue baths and attached to force transducers. Aortas were precontracted with phenylephrine ($3x10^{-7}$ M) and relaxation response to successively increasing concentrations of acetylcholine (10^{-8} - 10^{-5} M) or to histamine (10^{-6} - 10^{-3} M) was measured. Two-way repeated measures ANOVA indicated that Cu deficiency significantly reduced the relaxation response to acetylcholine ($p<0.05$) and marginally reduced the response to histamine ($0.05<p<0.10$); each agent caused a 28% reduction in maximal relaxation. Because the relaxation responses to both acetylcholine and histamine are known to be dependent on endothelium, this study indicates a functional disruption of vascular endothelium in Cu deficiency.

29.5

GENDER-DEPENDENT RESPONSES OF ENDOTHELIUM TO Mg^{2+} AND Na^+ IONS IN RAT AORTIC SMOOTH MUSCLE. Aimin Zhang*, Bella T. Altura and Burton M. Altura. Department of Physiology, SUNY, Health Science Center, Brooklyn, NY 11203.

Evidence has accumulated to suggest that Na^+ and Mg^{2+} may participate in the ion transport mechanisms involved in Ca^{2+} homeostasis in both endothelial and vascular smooth muscle cells. The modulatory effects of sex hormones on these ionic mechanisms are unknown. The present studies were designed, using aortic rings isolated from adult Wistar rats, in order to compare gender differences of contractile responses to lowering extracellular concentrations of Mg^{2+} $[Mg^{2+}]_o$ (0 mM) and $[Na^+]_o$ (84 mM). As recently reported (Altura, et al. Magnesium, 1990), $[Mg^{2+}]_o$ withdrawal and lowering $[Na^+]_o$ concentration by replacement of NaCl with isosmolar amounts of sucrose in Krebs-Ringer bicarbonate solution induced significant increases of basal tone in aortic strips from male rats. In the present study, this increase in basal tension was not seen in intact female aortic rings. However, such tension development was observed in endothelial-deprived aortic preparations isolated from both sexes. The amplitudes of such Mg^{2+}-free, low-Na^+ induced tension increases reached about 140% of maximal K^+-induced contractions, which were attenuated by adding 1.2 mM $[Mg^{2+}]_o$ to the incubation media. Castration plus treatment with 17-β-estradiol (4 weeks) also attenuated the contractile tension in such treated male rats. These results show that: 1) $[Mg^{2+}]$ plays an important role in controlling Ca^{2+} movement across membranes in both endothelium and vascular smooth muscle, probably via Na^+-Ca^{2+} exchange; and 2) there is a sexual dimorphism of vascular responses to Mg^{2+}-regulated Na^+-Ca^{2+} exchange in endothelial cells, which may be modulated by female sex hormones.

29.6

EFFECTS OF ENDOTHELIN ON CARDIAC FUNCTION IN CONSCIOUS DOGS. M. Bigaud* and S.F. Vatner. Harvard Medical School, New England Regional Primate Research Center, Southborough, MA 01772.

Endothelin-1 exerts positive chronotropic and inotropic effects on cardiac muscle in vitro. To examine effects of endothelin-1 on cardiac function in conscious animals, 11 dogs were chronically instrumented with a solid state pressure gauge in the left ventricle (LV) and an aortic pressure (AP) catheter. In intact conscious dogs, endothelin-1 (1 μg/kg, iv) induced a transient fall followed by a sustained rise in AP (>30 min). Maximal increases in heart rate (HR)(+98 ± 17%) and LV dP/dt (+9 ± 2%) occurred early, i.e., within 2 min, and then returned to baseline. At 15 min, LV dP/dt was actually depressed by 25 ± 4% from baseline. In order to eliminate any autonomic and hormonal related effects, the endothelin injection was repeated on a separate day after pretreatment with combined propranolol, atropine, phentolamine, captopril and a vasopressin antagonist. After blockade, the early increases in HR and LV dP/dt were no longer observed. However, HR and LV dP/dt were increased gradually and, within 10 min, were significantly elevated by 33 ± 7% and 27 ± 9% respectively ($P<0.05$). Thus, in intact conscious dogs, it appears that autonomic and hormonal mechanisms are entirely responsible for the early increases in HR and LV dP/dt and also masked the expression of the delayed direct positive inotropic and chronotropic effects of endothelin.

30.1

GLUCOREGULATORY EFFECTS OF OXYTOCIN IN NORMAL AND DIABETIC RATS. Eric P. Widmaier, Parul Shah*, and Gabriel Lee*. Boston University, Boston, MA 02215

Oxytocin (OXY) may have glucoregulatory functions in rats and dogs. The present study examined the interaction between glucose (G) and OXY in normal and streptozotocin (STZ)-induced diabetic rats. Plasma G and OXY levels were significantly correlated in cannulated, fed or fasted lactating rats ($r=.44$, $p<0.01$). To test the hypothesis that OXY was acting to elevate plasma G, adult male rats were injected with 10μg/kg OXY and sacrificed 30 or 60 min later. OXY increased plasma G from 6.1±0.1 to 6.8±0.2 mM ($p<0.05$), and glucagon from 179±12 to 259±32 pg/ml ($p<0.01$, $n=18$). There was no significant effect of OXY on plasma insulin. To eliminate putative local inhibitory effects of insulin on glucagon secretion, male rats were made diabetic by i.p. injection of 100 mg/kg STZ, which increased G to >18 mM and glucagon to 249±25 pg/ml ($p<0.05$). In these rats, OXY failed to further increase plasma G, but caused a much greater increase in glucagon (to 828±248 pg/ml) and also increased plasma ACTH. A specific OXY analog, Thr^4, Gly^7-OXY, mimicked the effect of OXY on glucagon secretion in both normal and diabetic rats. Finally, the effect of glucose on OXY *secretion* from intact isolated rat hypothalami was tested *in vitro*. Increasing concentrations of glucose in the incubation medium significantly decreased basal OXY secretion within 30 min ($r=0.62$, $p<0.01$) with half-maximal inhibition at ~5mM. We conclude that OXY has moderate glucoregulatory actions in rats; glucose can feedback to inhibit further OXY secretion from the hypothalamus/median eminence; and the effects of OXY on pancreatic function are augmented in insulin-deficient diabetic rats. Supported by PHS NIH grant DK 41263.

30.2

INSULIN STIMULATES PHOSPHATE TRANSPORT IN OSTEOBLAST-LIKE CELLS. S.A. Kempson, K.J. Kunkler*, L.M. Everett*, and D.K. Breedlove*. Indiana University, Indianapolis, IN 46223.

The rat osteosarcoma cell line UMR-106-01 has an osteoblast-like phenotype. UMR cells in monolayer culture transport phosphate (Pi) via a Na^+-dependent carrier. This Na^+/Pi cotransport system is stimulated by parathyroid hormone (Selz et al. AJP 256:E93,1989). Insulin regulates Na^+/Pi cotransport in renal cells. Since there are insulin receptors on osteoblast-like cells, we determined if insulin influences Na^+/Pi cotransport in UMR cells. Incubation of UMR cells with 10^{-8} M insulin for 3 h produced a 73% increase ($p<0.025$) in Na^+/Pi cotransport. Na^+/alanine cotransport was not changed, and there were no changes in Na^+-independent uptake of Pi and alanine. The stimulatory effect of insulin was detected within 2 h, and was dose-dependent within the range 10^{-10} to 10^{-7} M. The change in Na^+/Pi cotransport was due to an increase in Vmax from 2.7 ± 0.2 (controls) to 4.7 ± 0.6 (+insulin) nmol/mg/5 min ($p<0.05$). The Km was not changed. Blockade of de novo protein synthesis with cycloheximide (70 uM) did not interfere with insulin action on Na^+/Pi cotransport. We conclude that insulin, like parathyroid hormone, directly stimulates Na^+/Pi cotransport in UMR cells. The mechanism remains to be determined. The increased Vmax could be due to either increased activity of existing Pi transporters or recruitment of additional Pi transporters from an intracellular pool.

30.3

DEFEROXAMINE-REVERSIBLE AND -UNREVERSED EFFECTS OF FLUORIDE ON ADENYLYL CYCLASE. D.F. Li*, Z.M. Nie* and R. J. Ho, Dept. of Biochemistry and Molecular Biology, University of Miami School of Medicine, Miami, FL 33101

Membrane bound or solubilized adenylyl cyclase (AC) from rat or rabbit adipocyte, or rat liver in response to fluoride (F) in the presence of epinephrine (E) or glucagon (Gl) or ACTH, GTP and GDP analogs, forskolin(Fo) and deferoxamine(D) were determined. The stimulatory action of F (NaF 5 mM and $AlCl_3$ 100 uM) can be reversed by D (0.1 to 5 mM) in a dose dependent manner. In the presence of E, or Gl, G and Fo, F caused a marked inhibition. This inhibition was not reversed by D. In the presence of GDPbS in addition to E or Gl, Fo and G, AC was inhibited approaching to the level due to Fo alone. Under those conditions, F became an activator again . Such stimulation by F again can be reversed by D. Therefore, there are two different actions of F: deferoxamine-reversible stimulatory activity (DRSA) and deferoxamine-unreversed inhibitory activity (DUIA). GDPbS inhibited and Mn^{2+} stimulated AC in the presence of E or Gl, Fo and G, both convert DUIA to DRSA. Therefore F, and Fo may be used to study the interactions of G- protein and the catalytic unit of adenylyl cyclase. (supported in part by cAMP Fund).

30.4

THE ROLE OF FORSKOLIN IN ADENYLYL CYCLASE'S RECEPTION OF G-PROTEIN ACTIVATION. R. J. Ho, Z. M. Nie* and J. S. Liu* Dept. of Biochemistry and Molecular Biology, University of Miami School of Medicine, Miami, Fl. 33101

Membrane bound and solubilized adenylyl cyclase (AC) of rat and rabbit adipocyte and rat liver in response to stimulatory hormone (epinephrine, glucagon and ACTH), GTP and forskolin (Fo) were determined under several conditions. Using the magnitude of G-stimulation of C indicated the interactions of C and G-proteins, C in adipocyte membrane preparation stimulated by G by only 10 pmol/mg/min. G-effect was increased to 142 and 46 pmol/mg/min, when membrane was incubated also with epinephrine (E), or AC was solubilized with Lubrol-px, respectively. Fo stimulated membrane C from a basal level of 20 to 578 pmol/mg/min, G has low effect over Fo-stimulated activity (+10 pmol/mg/min). When both E and Fo were present, the G-effect was increased up to 488 pmol/mg/min over that due to E and Fo. While G has low effect on Fo-stimulated C in a membrane assay, it increased the Lubrol-solubilized Fo-stimulated C over 1041 pmol/mg/min. Similar results were obtained with membrane and solubilized AC from rabbit adipocyte and rat liver. All indicate that the condition of C is a major factor in reception of Gs-stimulation.
(Supported in part by cAMP Fund).

30.5

PROTEIN METABOLISM DURING THE PROLONGED, NATURAL POSTWEANING FAST IN RAPIDLY DEVELOPING ELEPHANT SEAL PUPS. C. Leo Ortiz. Institute of Marine Sciences and Department of Biology, University of California, Santa Cruz, CA 95064.

In sharp contrast to most young mammals, elephant seal pups fast entirely for 8-12 wks after weaning. Although losing substantial mass, they undergo rapid physical development presumably requiring significant body protein turnover and tissue reorganization. However, the quantitative dynamics of overall protein turnover under these unusual conditions are unknown. We estimated whole body protein synthesis rates derived from ^3H leucine (and other amino acids) clearance kinetics(AAC) and serum albumin flux using ^{125}I albumin in 10 pups that had been naturally fasting > 6 weeks. AAC averaged 1410 ± 493 ml/min suggesting a conservative overall protein synthesis rate of 6.3 ± 1.4 g/kg·day or ~6 to 10 % of the total body protein. Leucine oxidation accounted for < 4% of its overall flux. Albumin turnover averaged 318±52 mg/kg·day when computed from either ^{125}I albumin clearance or ^3H leucine incorporation. We conclude that : 1) protein turnover in developing, but natural fasting seal pups is equivalent to or exceeds that of most immature mammals under complete nutritional regimes and 2) this species appears to have exceptional mechanisms of amino acid sparing and nitrogen conservation and thus may provide an excellent model for several important human pathologies. (Supported by Minority Biomedical Support Program- NIH RR-08132).

30.6

GLUCOSE DEPENDENCE OF THE ISOLATED TURTLE CEREBELLUM DURING ANOXIA. M. Pérez-Pinzón, M. Rosenthal, T.J. Sick and P. Lutz. Dept Neurology, Univ Miami Med Sch, Miami, FL 33101 and Div Marine Biology and Fisheries, Rosenstiel School of Marine and Atmospheric Science, Miami, Fl 33149.

Previous studies have shown that the turtle brain can survive long periods without oxygen during which extracellular potassium ion activity (K^+_o) is not markedly increased, evoked potential (EP) activity is depressed but not suppressed, and ATP levels are unchanged from control. Strategies to account for such anoxia tolerance likely include decreased ATP demand, such as by electrical depression, and increased anaerobic ATP production. Although plasma glucose levels were elevated in turtle during prolonged anoxia, the presence of a Pasteur effect (i.e. enhanced glycolysis) in the turtle brain remains controversial. To determine the glucose threshold during anoxia, we found that the isolated turtle cerebellum in normoxia maintained K^+_o baseline and EP activity with 5 mM glucose in its artificial cerebrospinal fluid (ACSF), but 20 mM was required during anoxia. As in intact brain, phosphocreatine decreased and lactate increased, but ATP levels were constant during 6 hours of anoxia when the isolated cerebellum was superfused with ACSF containing 20 mM glucose. When ACSF glucose was lowered during anoxia K^+_o rose to high (≥ 30 mM) values of anoxic depolarization. The latency to depolarization was related to declines in ACSF glucose. These results demonstrate the dependence of turtle cerebellum on glucose to maintain ATP levels and ion transport actively during anoxia. They also suggest the presence of a Pasteur effect at least during the transition to a hypometabolic state.

30.7

METABOLIC ACTIONS OF CATECHOLAMINE IN CONSCIOUS AND ANESTHETIZED PIGS. Janis A. Loveday* and John P. Hannon. Division of Military Trauma Research, Letterman Army Institute of Research, Presidio of San Francisco, CA 94129

Hypermetabolic states induced in conscious pigs by hemorrhage or morphine are characterized by increases in muscle activity and plasma concentrations of epinephrine (E) and norepinephrine (NE). To isolate metabolic effects attributable to catecholamine from those at attributable to muscle movement, metabolic variables were measured in chronically instrumented pigs (N=5) during a 15 min infusion of E or NE (5 ng/kg bolus followed by 1.25 ng/kg/min), first while the animals were conscious and subsequently while anesthetized with pentobarbital. E, but not NE, increased oxygen consumption (about 35%) in conscious pigs, a response that was associated with bouts of muscle activity; metabolic rate was not altered in anesthetized pigs. During anesthesia E raised and NE lowered the respiratory exchange ratio, effects that were not seen in conscious pigs. NE, but not E, produced an increase in core temperature (about 0.5C) in conscious animals while temperatures of both E and NE pigs decreased (about 1C) during anesthesia. In both awake and anesthetized animals, E infusion led to tachycardia and NE infusion to an elevated mean arterial pressure. We concluded: 1) that E leads indirectly to hypermetabolism by increasing muscle activity; 2) that NE increases core temperature by decreasing body heat loss; and 3) that E increases carbohydrate catabolism and NE increases fat catabolism, at least in anesthetized pigs.

30.8

VALIDATION OF INFRARED THERMOGRAPHY FOR DETERMINING EVAPORATIVE HEAT LOSS IN NEONATES. D.A. Ponzer, A.K. Adams, R.A. Nelson, Department of Internal Medicine, U of Illinois, Carle Foundation, Urbana, IL. 61801

A new method, infrared thermography (IRT), was used in conjunction with an already validated method, continuous weight loss measurement, to determine evaporative heat loss in infants. Infrared images and weight loss measurements were obtained in 10 normal birth weight (NBW) infants after 24 hours of life. IRT is a non-invasive, portable system which accurately measures mean body surface temperature (MBST). MBST is used in conjunction with heat loss theory to calculate insensible and respiratory evaporative heat losses. Using an infant scale, evaporative heat losses were measured by multiplying the weight loss over time by the latent heat of vaporization at the infant's core temperature. Evaporative heat loss calculated with IRT showed a mean $\pm$ SD of 0.99 $\pm$ 0.12 Kcal/kg/hr, and that measured using the scale was 0.70 $\pm$ 0.34 Kcal/kg/hr. When the calculated and measured values for evaporative heat loss were added to radiant and convective losses calculated by IRT, there was no significant difference between the total heat loss values. Based on the closeness of the evaporative and total heat loss values obtained by both methods, it can be concluded that IRT produces valid results for determining evaporative heat loss in NBW infants.

30.9

FUNCTIONAL DEMAND AND SUBSTRATE AVAILABILITY AS MODULATORS OF CELLULAR MITOCHONDRIAL O_2 DEPENDENCE IN MAMMALIAN CELLS. Tak Yee Aw* and Dean P. Jones. Dept Biochem., Emory Univ., Atlanta, GA 30322.

We have examined the O_2 dependence of mitochondrial function in a variety of adult and neonatal mammalian cell types to study the functional determinants of mitochondrial activity. In cardiac myocytes, electrical stimulation of quiescent cells increases the O_2 consumption rate and the half-maximal (P_{50}) value for oxidation of cytochrome $a + a_3$. Similarly, stimulating Na^+, K^+ ATPase activity in renal proximal tubule cells with nystatin increases O_2 consumption and the P_{50} value, while decreasing ATP demand with ouabain decreases both values. A similar relationship of changes in P_{50} with respiration rate occurs for neonatal liver cells. However, wide variations in O_2 consumption can be obtained by varying succinate supply, and comparison of the O_2 dependences at different substrate concentrations show that the P_{50} varies as a function of the succinate-dependent O_2 consumption rate. Thus, the cellular O_2 consumption rate is an important determinant of the O_2 concentration requirement for the mitochondria. These results suggest that mitochondrial O_2 dependence in excitable tissues, such as the brain, and in absorptive tissues, such as the small intestine, may be particularly sensitive to modulation by variations in workloads and availability of specific substrates. Supported by NIH grant GM 36538 and a grant from SIDS Alliance.

40.1

AEROBIC AND ANAEROBIC BACTERIAL ISOLATES AND THE ANTIMICROSUSCEPTIBILITY PATTERNS FROM HORSES WITH PNEUMONIA AND PLEUROPNEUMONIA. CR Sweeney, SJ Holcombe, SC Barningham, J Beech. University of Pennsylvania, School of Veterinary Medicine, 382 West Street Road, Kennett Square, PA 19348

The frequency of aerobic and anaerobic isolates in 327 tracheobronchial aspirates (TBA) and in 123 pleural fluid (PF) samples in 327 horses with pneumonia or pleuropneumonia and their antimicrobial susceptibility patterns were reported. Of the 327 horses, 75% survived, 20% were euthanized, and 5% died. TBAs were positive for growth in 91% of the horses while PF was positive for growth in 66% of the horses. Of 327 horses, 68% had only aerobic isolates, 23% had mixed aerobic and anaerobic isolates, 8% had no growth, and 2% had only anaerobic isolates. The survival rate for horses with only aerobic isolates was 81%, while the survival rate for horses with an anaerobic isolate was 41%. The aerobic bacteria most frequently isolated were β-Streptococcus sp (60% of horses), Pasteurella sp, (38%), and E. coli (25%), Enterobacter sp (20%), Klebsiella pneumonia (14%), and Pseudomonas sp (10%). The anaerobic bacteria most frequently isolated were Bacteroides sp (20%) of the horses, and Clostridium sp (10%) of horses. Knowledge of the prevalence and susceptibility of bacterial isolates from horses with pneumonia aids clinician in instituting rational antimicrobial therapy.

40.2

CYTOLOGICAL FINDINGS OF BRONCHOALVEOLAR FLUID IN 22 HORSES WITH PNEUMONIA OR PLEUROPNEUMONIA. Y Rossier, CR Sweeney, EL Ziemer, University of Pennsylvania, School of Veterinary Medicine, 382 West Street Road, Kennett Square, Pa 19348

The purpose of the study was to determine the cytologic findings of bronchoalveolar lavage (BAL) fluid in 22 horses with pneumonia or pleuropneumonia and to compare them to the results of the tracheobronchia aspirate (TBA). All horses had clinical evidence of pneumonia or pleuropneumonia on physical examination, radiology, ultrasonography, TBA, or postmortem examination. BAL fluid analysis included total cell count, differential cell count, and cytologic evaluation. Results showed the 22 horses could be grouped in 3 categories. In Group 1, (9 horses) BAL values were normal. In Group 2 (3 horses) BAL values had small differences from normal values. In Group 3 (10 horses) BAL values had elevations in the total cell count and neutrophils, and decrease in macrophages and lymphocytes. All horses having a TBA had cytologic evidence of acute inflammation. The results of this study showed that BAL fluid analysis may be normal in horses affected with pneumonia or pleuropneumonia. Therefore, the BAL may not be the diagnostic technique of choice to evaluate equine patients with pneumonia or pleuropneumonia.

40.3

CELLULAR CHANGES IN THE LUNG OF GNOTOBIOTIC PIGLETS EXPOSED TO ACTINOBACILLUS PLEUROPNEUMONIAE: EFFECTS OF DOSE AND TIME. Jane A. Westfall, Asita Chatterjee* and Neil V. Anderson*. Kansas State University, Manhattan, KS 66506

Infection of gnotobiotic piglets with pure cultures of A. pleuropneumoniae can be controlled experimentally so that cellular changes specific to that organism can be examined by electron microscopy. The effect of 10^6 and 10^8 CFU/ml of A pleuropneumoniae serotype 5, at 1 and 4 hours after transtracheal inoculation was studied ultrastructurally in lungs of 10 gnotobiotic piglets (mean weight + SD = 2.04 ± 0.78 kg). At a dose of 10^6 CFU/ml there was a generalized red mottling in the dorsal half of the caudal lobe at 4 hr. p.i. Electron microscopy revealed evidence of neutrophil infiltration into alveoli along with a few erythrocytes and fibrin. At a dose of 10^8 CFU/ml there was a bilateral lesion in the dorsal aspect of the caudal lobes at 4 hr. p.i. in addition to a generalized mottling. Electron microscopy revealed numerous bacteria and cellular debris in the alveoli. Capillary swelling, cytolysis and sloughing of epithelial and endothelial cells, occasionally leaving only a basal lamina enclosing degenerating erythrocytes and masses of fibrin, was present. Bacteria observed in pulmonary alveoli at 1 and 4 hr. p.i. with a 10^8 inoculum were not found with the lower dose. For experimental studies of early cellular changes associated with the early time course of pneumonia in piglets, we recommend that a dose of 10^6 CFU/ml of A. pleuropneumoniae be used.

40.4

BIOCHEMICAL AND MORPHOLOGICAL CHANGES IN LUNG MACROPHAGES FROM DOGS WITH G_{M1}-GANGLIOSIDOSIS. Glen L. Spaulding, Christopher D. Warren*, Rita DeGasperi*, John Torday*, and Joseph Alroy*. Tufts Univ. School of Veterinary Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02111.

Bronchopneumonia is a common complication in children with lysosomal β-galactosidase deficiency (i.e. G_{M1}-gangliosidosis), but the pathogenesis is unclear. We studied three dogs with G_{M1}-gangliosidosis and 3 corresponding controls to characterize their lung macrophages. From each dog an excised lung lobe was serially lavaged with 0.9% saline, and specimens were collected from other lung lobes for morphologic evaluation. The total lavage cell populations were determined by hemocytometer and differential cell counts; the cellular and extracellular fractions were separated by centrifugation. From each fraction the phospholipids were extracted with chloroform-methanol and measured spectrophotometrically; the glycolipids were analyzed with thin layer chromatography and the oligosaccharides were characterized by HPLC. Affected dogs bore threefold more pulmonary macrophages than controls ($p<.05$). The amount of cellular and extracellular phospholipids was similar in both groups. Oligosaccharide patterns characteristic of G_{M1}-gangliosidosis were demonstrated by HPLC in cellular lung lavage components. The macrophages contained numerous enlarged secondary lysosomes laden with fine fibrillar material, consistent with the ultrastructural appearance of oligosaccharides. These findings suggest that pulmonary defense mechanisms are altered in G_{M1}-gangliosidosis.

40.5

An Ultrastructural Analysis of Bronchoalveolar Lavage Fluid from Neonatal Foals. **Robert R. King and Donald A. Samuelson*. College of Veterinary Medicine, University of Florida, Gainesville, FL 32610.**

Dramatic changes in lower airway cell populations occur during the first week of life in foals. Alveolar macrophages and neutrophils predominate, however a lot of darkly staining "debris" is also present. In this study, we examined the morphological characteristics of bronchoalveolar lavage fluid "debris" at the light and electron microscope level from 4, 4 day old horse foals. Lung lavage consisted of 200 ml sterile 0.9% saline. An aliquot of fluid was cytocentrifuged and cellular morphology was evaluated after staining with Wright-Giemsa. The remaining fluid was centrifuged and the cellular pellet was fixed in 2% glutaraldelyde cacodylate - buffered solution. Samples were further fixed in 1% osmium tetroxide, washed, dehydrated, and flat-embedded in Epon-Araldite mixture. Ultrathin sections were stained with uranyl acetate and lead citrate and viewed by transmission electron microscopy. We found the lavage fluid "debris" to represent epithelial-type cells in various stages of degeneration. We conclude that rapid cell maturation is most likely responsible for the increased number of degenerating epithelial-type cells present in lung lavage fluid from neonatal foals. Supported by a grant from the Equine Neonatology Study Group, University of Florida.

40.6

PHARYNGEAL DILATION ASSOCIATED WITH CRICOTHYROID MUSCLE CONTRACTION IN DOGS. T.C. Amis, A. Brancatisano*, A. Tully* and L.A. Engel. Thoracic Medicine Unit, Westmead Hospital, Sydney 2145, Australia.

The mechanical function of phasic respiratory activity of the cricothyroid muscle (CT) of the larynx is poorly understood. Previously, we have observed piriform recess dilation in dogs during induced supramaximal CT contractions. In the present study we document changes in upper airway geometry during CT contraction using computerized axial tomography (CAT). Three adult mongrel dogs (weight=16-26 kg) were deeply anaesthetized with sodium pentobarbitone, mechanically ventilated via a tracheostomy and placed in a prone posture with the mouth open. Bilateral CT contraction was produced by supramaximal electrical stimulation (STIM) of the external branch of the superior laryngeal nerve. Upper airway CAT was obtained from the tip of the epiglottis to the caudal edge of the cricoid cartilage with and without STIM. Oropharyngeal (tip of epiglottis) and piriform recess (mid-epiglottis, n=2) cross-sectional area increased during STIM by 16-23% and 68-80%, respectively. Furthermore, the horizontal distance between the thyroid cartilage alae increased by 7-20%. These findings show that supramaximal CT contractions cause lateral movements of the thyroid cartilage alae with resultant widening of the piriform recesses. Thus the cricothyroid muscle may act as an inferior pharyngeal dilator and therefore contribute to control of oropharyngeal airway patency. Supported by NH & MRC of Australia.

40.7

THE INFLUENCE OF THIORPHAN, INDOMETHACIN AND CAPSAICIN ON THE RESPONSE OF GUINEA PIG AIRWAYS TO VASOACTIVE INTESTINAL POLYPEPTIDE (VIP). **D. Mason, N. Schultz-Darken*, M. Tengowski*, M.F. Leite*, R. Saban. School of Veterinary Medicine, University of Wisconsin, Madison, WI 53706.**

Removal of epithelium from segments of the proximal trachea of the guinea pig results in a leftward shift in the concentration response curve to VIP. To examine the role of epithelial factors that may contribute to the VIP response in guinea pig trachea, we studied VIP dose-response curves (DRC) in the presence of thiorphan, indomethacin and capsaicin. Propranolol (10^{-6} M), and phenoxybenzamine (3×10^{-5} M) were present in the tissue bath and tone was induced with prostaglandin F2-alpha (10^{-5} M) before cumulative concentration response curves to VIP were obtained. Relaxation was expressed as a percentage of the maximum degree of relaxation produced by papaverine (10^{-3} M) added at the end of the experiment. Pretreatment of the tissues with indomethacin (5×10^{-6} M)did not alter the leftward shift induced by epithelial removal, while capsaicin (10^{-6} M) reduced but did not eliminate the effect of epithelium removal. To examine the influence of an epithelial-derived neutral endopeptidase on the response to VIP, the tissues were pretreated with thiorphan (10^{-5} M) in the presence of indomethacin and capsaicin. Thiorphan did not cause a significant change in the DRC to VIP. Therefore, epithelium removal potentiates VIP-induced relaxation which is not dependent upon removal of an epithelial-derived prostaglandin, nor entirely to the removal of excitatory neuropeptides. This study does not exclude the possibility that other peptidases may be present in the epithelium of the guinea pig trachea which might account for the potentiation of VIP response due to epithelial denudation.

40.8

MECHANICAL BEHAVIOR OF THE EQUINE TRACHEA: AN IN VITRO STUDY. T.Art* and P.Lekeux. University of Liege, B-4000 Belgium

The dynamic behavior of the intra- and extrathoracic airways may be an important factor in modulating respiratory airflow and pulmonary resistance. Previous studies performed on horses during strenuous exercise have reported compressive transmural tracheal pressure as high as 5kPa. Therefore, the aim of this work was to study "in vitro" the mechanical properties of the equine trachea submitted at the compressive pressure observed "in vivo". The pressure-volume relationship was determined in isolated extra- and intrathoracic tracheal segments issued from 29 healthy slaughtered horses (1 to 15 years; 352 to 651 kg). At the same time the changes in cross-sectional lumen area (X-SA) at the mid-point of the segment was measured using a slit-lamp transillumination and photographic measurement by endoscopy. These measurements allowed the calculation of the tracheal specific compliance (Cs) as well as the relative changes in X-SA for intraluminal pressure from 0 to -5kPa.

The extrathoracic tracheal Cs was $0.138 \pm 0.002 kPa^{-1}$ and at intraluminal pressure of -5kPa X-SA was reduced at about 69% of its resting value. At similar compressive pressure, the intrathoracic segments had a Cs of $0.115 \pm 0.008 kPa^{-1}$ and their X-SA was reduced at 58% of the resting values.

These data showed that the equine tracheal compressibility is high and suggested consequently that the large increase in pulmonary resistance observed during strenuous exercise could be explained by a partial collapse of the extrathoracic -during inspiration- or intrathoracic -during expiration- trachea.

40.9

FREQUENCY DEPENDENT RESPONSE OF EQUINE TRACHEALIS TO ELECTRICAL FIELD STIMULATION IN VITRO. L.E.Olson, V.P. Wright*, and L.M. Tobin*. The Ohio State University, Columbus, OH, 43210-1092

Strips of equine midcervical trachealis were studied at optimal length in 25 ml organ baths filled with Krebs-bicarbonate solution at 37° C. Data were normalized to the response to an electrical field stimulation of 18 V, 25 Hz, 0.5 ms administered prior to the addition of drugs. Muscles were treated with 10^{-6}M atropine, then contracted with 10^{-4}M histamine (n = 4). Field stimulation at 18 V, 25 Hz, 0.5ms contracted muscles and at 18 V, 100 Hz, 0.5ms relaxed muscles, with or without epithelium. Muscles with or without epithelium (n = 9) were treated with 10^{-6}M propranolol, 10^{-6}M Regitine, and 10^{-6}M atropine, then contracted with 10^{-4}M histamine. Field stimulation at 18 V, 25 Hz, 0.5 ms (n = 7) had no effect and at 18 V, 100 Hz, 0.5 ms caused a 3x10^{-6}M tetrodotoxin insensitive relaxation. In an additional set of experiments, the addition of 10^{-5}M methylene blue (n = 7), 510 Units catalase, 110 Units superoxide dismutase, and 10^{-4}M ascorbic acid (n = 7), or 5 x 10^{-5}M gossypol (n = 7), to muscles with the epithelium removed that were treated with 10^{-6}M propranolol, 10^{-6}M Regitine, 10^{-5}M indomethacin and 10^{-6}M atropine did not alter the relaxation response to 100 Hz. These results suggest that either the inhibitory nerves are nonadrenergic, noncholinergic and tetrodotoxin insensitive, or that the 100 Hz relaxation is not neurally mediated and not mediated by nitric oxide-like factors, superoxide radicals, or arachidonic acid metabolites.

40.10

USE OF TIDAL BREATHING FLOW-VOLUME LOOPS FOR THE EVALUATION OF FELINE CHRONIC BRONCHIAL DISEASE. E.A. Rozanski, B.C. McKiernan, J.A. Dye, Veterinary Medicine Teaching Hospital, College of Veterinary Medicine, University of Illinois, Urbana, IL 61801

Tidal breathing flow-volume loop (TBFVL) analysis has been used for the evaluation of obstructive airway disease in the conscious dog. TBFVLs from 6 bronchitic cats (diagnosed via history, physical, radiography and measurements of lung resistance) were compared to TBFVLs from 19 healthy cats (diagnosed via history and physical examination). Using BUXCO FVL^{R} software, analyses of representative loops (6/cat) were performed as previously described. Measurements of volumes at and areas under portions of the flow-volume curves, and volumes at specified expiratory times were also obtained. Measurements of TBFVL indicies (e.g. PEF/PIF) were reproducible (mean CV= 4.2-14.5%). Compared to healthy cats, the mean values for loops from bronchitics demonstrated prolonged expiratory time, decreased expiratory flow rates and decreased area under the expiratory flow-volume curve (from peak to end of expiration). TBFVL analysis appears to be useful as an objective, yet non-invasive method of assessing cats with bronchial disease.

40.11

PRELIMINARY EVALUATION OF FLOW- AND PRESSURE-VOLUME LOOPS IN HORSES WITH RECURRENT AIRWAY OBSTRUCTION SYNDROME (HEAVES). D.B. Tesarowski, L. Viel and W.N. McDonell. Clinical Studies, O.V.C., Guelph, ON, N1G 2W1.

This study was designed to characterize flow- and pressure-volume (F-V, P-V) loops obtained in unsedated horses associated with the development of clinical signs of heaves. Three horses, ages 5, 9 and 20 were tested prior to challenge with mouldy hay and dusty straw (HSC) and retested 1-3 days later when they exhibited clinical signs. A Buxco Pulmonary Mechanics Analyzer and computer were used to record data. Loop analysis was performed using software from Buxco. Parameters recorded at rest and after 4 min of challenge with inhalation of a mixture of 10% CO_2 in air included F-V parameters: inspired tidal volume, respiratory rate, minute ventilation, inspiratory and expiratory times, peak inspiratory and expiratory flow rates, expiratory flow rate at 25% and 50% of tidal volume, expired volumes at 0.5, 0.75 and 1s; P-V parameters: resistance, dynamic compliance, work of breathing, minimum and maximum pleural pressures and transpulmonary pressure. Statistical analysis included SAS GLM with means analysis using LSD when appropriate. Inhalation of CO_2 significantly changed ($p < 0.05$) all parameters both pre- and post-HSC with respect to resting with the exception of resistance and dynamic compliance. There was no significant effect of HSC on any F-V parameters either at rest or after CO_2 inhalation although there were significant effects on pressure-volume parameters (work of breathing, maximum pleural pressure and transpulmonary pressure). These preliminary data suggest that analysis of the P-V loop may be more appropriate in studying horses with heaves. (Supported by OTS and CLA).

40.12

CLINICAL SAFETY AND EFFICACY OF VENTIPULMIN® ORAL SYRUP IN HORSES WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD). Deborah F. Erichsen, Boehringer Ingelheim Animal Health, Inc., St. Joseph, MO 64502.

The efficacy of Ventipulmin (clenbuterol HCl) was demonstrated in a controlled field study in 239 horses with COPD. Severity of COPD (heaves) was determined primarily from clinical evaluation of expiratory effort and was assigned a numerical score for the Overall Heaveiness Rating (OHR). Horses began an individual incremental dose titration of Ventipulmin to effect, beginning with 0.8 mcg/kg b.i.d. On the 10th day of treatment at the effective dose (0.8, 1.6, 2.4, or 3.2 mcg/kg), horses were assigned to 1 of 2 treatment schedules. Treatment was withdrawn from horses on Schedule A and the heavey condition monitored over an 8-day withdrawal period. Horses on Schedule B continued on the effective dose for a total of 30 days.

Ventipulmin provided significant improvement in OHR of 75% of the horses with a lower 95% confidence limit of 71%. Treatment provided highly significant improvement from baseline OHR at all doses and at all treatment observation times (Days 10, 20, & 30). Withdrawal OHR for horses on Schedule A was significantly increased (worsened condition) from OHR on treatment day 10 at all doses.

Side effects of sweating, muscle tremor, and attitude change were infrequent and of low intensity with this treatment regimen of incremental titration to effect.

COMPARATIVE RESPIRATORY SOCIETY II

41.1

INDOMETHACIN AND SRI 63-441 MODIFY TUMOR NECROSIS FACTOR (TNFα)-INDUCED ALTERATIONS IN PORCINE HEMODYNAMICS. K.T. Kruse-Elliott, L. Johnson, and N.C. Olson. North Carolina State University, Raleigh, NC 27606.

TNFα, released during endotoxemia, may elicit pathophysiologic effects indirectly through release of platelet-activating factor (PAF) and cyclooxygenase products. We infused human recombinant TNFα (5 x 10^{6} U/mg) into anesthetized pigs at 1 μg/kg (IV) for the first 30 min followed by 5 ng/kg/min for 5.5 h in the presence and absence of indomethacin (cyclooxygenase inhibitor; 5 mg/kg + 3 mg/kg/h) or SRI 63-441 (PAF receptor antagonist; 5 mg/kg + 1 mg/kg/h). Control pigs were given inactivated (boiled) TNFα. TNFα approximately doubled mean pulmonary arterial pressure and pulmonary vascular resistance (PVR) by 15 min. Cardiac index decreased and total peripheral resistance and PVR increased from 2-6 h of TNFα infusion. TNFα did not increase postmortem bronchoalveolar lavage fluid albumin concentration, indicating no increase in alveolar-capillary membrane permeability. Both SRI 63-441 and indomethacin blocked the early (15 min) and attenuated the later (2-6 h) pulmonary hypertension and increased PVR. SRI 63-441 and indomethacin did not attenuate the TNFα-induced decrease in cardiac index, systemic hypertension, or granulocytopenia. Thus, PAF and cyclooxygenase products of arachidonic acid metabolism interact in effecting the pulmonary hemodynamic responses induced by TNFα in pigs. Supported by NIH 1F32 HL05923 and HL 32726.

41.2

ROLE OF LEUKOTRIENE D_4 (LTD_4) AND LTE_4 DURING ENDOTOXIN-INDUCED LUNG INJURY IN PIGS. N. C. Olson, K. T. Kruse-Elliott, and L. Johnson. North Carolina State University, Raleigh, NC 27606.

We evaluated the role of sulfidopeptide leukotrienes as mediators of endotoxin(E)-induced respiratory failure in a porcine model of the adult respiratory distress syndrome. E was infused IV into anesthetized pigs at 5 μg/kg the first h, followed by 2 μg/kg/h for 3 h in the presence and absence of LY171883, a specific LTD_4/LTE_4 receptor antagonist. E caused hemoconcentration, granulocytopenia, decreased cardiac index, systemic hypotension, pulmonary hypertension, increased pulmonary vascular resistance, bronchoconstriction, hypoxemia, increased permeability of the alveolar-capillary membrane, pulmonary edema, and increased plasma concentrations of TXB_2, $PGF_{2\alpha}$, and 6-keto-$PGF_{1\alpha}$. LY171883 did not modify E-induced cardiopulmonary and hematologic abnormalities, except for a modest attenuation of pulmonary hypertension (at 1 h) and increased pulmonary vascular resistance (at 1-2 h). Ex vivo stimulation of whole blood with calcium ionophore caused large increases in plasma concentrations of TXB_2, $PGF_{2\alpha}$, and LTB_4. These increases were not significantly modified in blood derived from pigs treated with LY171883. We conclude that LTD_4 and LTE_4 are not important mediators of E-induced lung injury in anesthetized pigs, albeit they may contribute modestly to pulmonary vasoconstriction. Supported by NIH HL 32726.

41.3

HISTAMINE INHALATION CHALLENGE IN NORMAL HORSES AND IN HORSES WITH SMALL AIRWAY DISEASE. Michèle Doucet, André Vrins and Anthony W. Ford-Hutchinson. GREMEQ, Faculté de Médecine vétérinaire, Université de Montréal, St-Hyacinthe, Qc, J2S 7C6.

The purpose of this study was to describe hyperreactivity reactions to histamine inhalation challenge (HIC) in horses. Following a complete clinical respiratory exam, lung biopsies were performed on 9 light breed mares aged 7 to 15 years. Pulmonary mechanics parameters were monitored at baseline following an aerosol of 0.9% saline for 2.5 minutes and up to 30 minutes after HIC with a 0.5% w/v solution aerosol for 2.5 minutes, administered by an ultrasonic nebulizer through a face mask. Tidal volume (Vt) and airflow (V) were obtained with a pneumotachograph mounted on the face mask, pleural pressure (Ppl) was measured by the oesophageal balloon catheter method. Dynamic compliance (Cdyn), total pulmonary resistance (RL) end expiratory work (EEW) and minute volume (MV) were calculated via a pulmonary mechanics computer. A characteristic pattern of bronchoconstriction was observed to various degrees in all animals tested. Horses with clinical signs and histological biopsy lesions of SAD responded with greater changes in EEW, Ppl, RL and Cdyn whereas normal horses responded to HIC mainly with an increase in RL. Two horses with no apparent clinical signs or SAD lesions at biopsy, showed a marked hyperreactivity to inhaled histamine as seen by an increase in EEW, Ppl, RL and a decrease in Cdyn. These results suggest that the HIC procedure described can be useful in detecting hyperreactivity in horses in clinical remission or subclinical states.

Financial support: Fonds du Centenaire, Merck Frosst Inc., FCAR and GREMEQ.

41.4

MODULATION OF BRONCHIAL REACTIVITY IN THE HORSE BY PHENYLBUTAZONE AND FUROSEMIDE. **E. Aguilera-Tejero, J.R. Pascoe and M.J. Woliner*. Department VM Surgery, University of California, Davis, CA 95616.**

Racehorses are often treated with Phenylbutazone and/or Furosemide before racing. The role of Phenylbutazone in regulating bronchial reactivity in the horse is unknown. Furosemide has been shown to alleviate recurrent airway obstruction in ponies (FASEB J 4:133; A289, 1990). Four healthy horses were studied using a latin square design. Intravenous histamine provocation tests (0.5, 1, 2 and 4 μg/kg/min) were done: 1) without pretreatment, 2) 1/2 hour after Phenylbutazone (8 mg/kg IV), 3) 1 hour after Furosemide (1 mg/kg IV), and 4) after Phenylbutazone+Furosemide. Esophageal pressure and respiratory flow-volume were measured; dynamic compliance (C_{dyn}) and respiratory resistance (R) were calculated. Histamine caused a dose dependent decrease in C_{dyn} and increase in R in all horses. Pretreatment with Phenylbutazone significantly attenuated the changes in C_{dyn} and R induced by histamine, whereas Furosemide had minimal protective action. Pretreatment with both Phenylbutazone and Furosemide was less effective than Phenylbutazone alone. We conclude that Phenylbutazone mitigates histamine-induced bronchoconstriction in horses. In contrast to recurrent airway obstruction in ponies, Furosemide has very little effect on the bronchoconstriction caused by histamine.

41.5

THE INFLUENCE OF FUROSEMIDE ON HEMODYNAMIC MEASUREMENTS DURING HIGH SPEED TREADMILL EXERCISE IN HORSES. S.C. Olsen*, B.S. Lowe*, N. Pelletier*, C.P. Coyne* and H.H. Erickson. Dept. Anatomy & Physiology, Kansas State University, Manhattan, KS 66506

Furosemide, a loop diuretic, is reported to be beneficial in the prevention of Exercise-Induced Pulmonary Hemorrhage (EIPH) by unknown mechanisms. Previous work with horses in our laboratory has indicated that 1 mg/kg of furosemide, administered 3 hours previously, decreases pulmonary arterial pressure and right atrial pressure during high speed exercise. The purpose of this study was to determine the influence of various dosages of furosemide (.25, .50, 1.0 and 2.0 mg/kg) on hemodynamic measurements in horses during a standardized treadmill exercise protocol. Using six horses, the four furosemide treatments and control (saline injection) were administered intravenously four hours prior to exercise. Our data suggests that furosemide decreases pulmonary arterial pressure and right atrial pressure in a dose-dependent manner over the concentrations studied. Furosemide also increased lactic acid concentration during exercise in a dose-dependent manner. No influence by treatment on hematocrit, plasma volume or heart rate was noted. Furosemide may mediate it's beneficial effect by a vasodilatory action which reduces hydrostatic pressure in the pulmonary vasculature. (Supported by the American Quarter Horse Association)

41.6

TOTAL THORACIC COMPLIANCE MEASUREMENTS: A PRACTICAL, SAFE, NON-INVASIVE MEASURE OF PULMONARY FUNCTION IN DOGS. LG King and JC Hendricks. Dept. Clinical Studies, School of Veterinary Medicine, Univ. of Pennsylvania, Phila., PA 19104

Total thoracic compliance (TTC) measurements are used in human intensive care units to assess lung function in ventilated patients. We used this test in dogs and found that the procedure was easy, took 5-10 minutes, and caused no ill-effects. Twenty normal dogs (1-16 years, 2.3-49.5 kg) were anesthetized. They were first hyperventilated to reduce pulmonary atelectasis, check for leakage, and eliminate voluntary respiratory efforts. The lungs were then inflated to positive pressures of 15, 20 and 25 cmH_2O. TTC measurements were calculated as the ratio of the difference in exhaled volumes (measured by a pediatric spirometer), to the change in static inspiratory pressures (measured by a water manometer), between 15 and 20 cmH_2O. The corrugated anesthetic tubing was replaced by non-distensible tubes. Mean TTC was 42.25 ± 32 $ml s/cmH_2O$ and was significantly correlated with weight (P=0.0001, r=0.88), but not with age (p=0.27) or gender (p=0.58). The mean weight-adjusted TTC was 1.85 ± 0.56 $ml s/cmH_2O/kg$. In studies of 10 dogs with respiratory disease, only one dog was within the normal range, and 5 dogs were below 2 standard deviations of normal. Changes in TTC in a ventilated canine patient paralleled the clinical course and PaO_2. This test may show promise for diagnosis and monitoring of respiratory disease.

41.7

SENSORY RECEPTORS IN THE RAT LUNG. D.R. Bergren and D.F. Peterson. Creighton Univ. Sch. Med. Omaha, NE 68178 and Oral Roberts Univ. Sch. Med. Tulsa, OK 74171. The use of the rat as a model for the study of certain pulmonary diseases has increased. However little is known of the sensory receptors in its airways. The sensory receptors of the rat were recently characterized by Tsubone, who reported "irritant like", inflationary and deflationary stretch receptors. Therefore, the profile of sensory receptors in the rat appears to differ from other species. We have further studied the airway receptors in the rat by recording from single fibers carried in the vagus nerve during mechanical ventilation. Pulmonary receptor activity was monitored during various ventilatory maneuvers. Location of the receptive ending and the fiber conduction velocity was determined. Slowly adapting receptors dominate the vagus nerve including abundant deflationary stretch receptors. Rapidly adapting receptors were extremely rare. Unmyelinated fibers were present which were capsaicin sensitive. Activation of these C fibers by capsaicin (1-4 ug, iv) occurred without changes in pulmonary mechanics. Therefore the composition of sensory receptors in the airways of rats differs from that of other species studied thus far.

42.1

RUNNING CHEAPLY: AN ADAPTATION FOR DESERT LIFE? J. R. Merkt*, J. E. Peters* and C. R. Taylor. CFS, Museum of Comparative Zoology, Harvard University, Old Causeway Rd., Bedford, MA. 01730

Food, like water, is in short supply in the desert. The purpose of this study was to find out whether desert mammals possess special physiological adaptations for running cheaply, reducing their food needs, just as they possess physiological adaptations for reducing water needs. Two possibilities were investigated: 1) a low cost of operating muscles; and 2) a low cost of operating non-muscular systems. The energetic cost of running was calculated from measurements of oxygen consumption in a highly adapted desert species, the golden spiny mouse (*Acomys russatus*), avg. weight 46 g. This species has a resting metabolic rate which is only 65% of that predicted for a mammal of its size. Furthermore, it dramatically reduces resting rate when food intake is restricted. We compared the cost of running when food was available *ad libitum* to the cost when intake was reduced by 50% -- resulting in a 43% reduction in resting metabolic rate. We found that the cost of operating the muscles was the same in the desert spiny mouse as in its non-desert relatives (1.45 ml O_2/g·km), and the 43% reduction in resting metabolic rate had no effect on this cost. However, the cost of operating non-muscular systems during running was 39% lower in the spiny mouse. To our surprise, the reduction in resting metabolism with food restriction had no effect on the non-muscular cost. The low cost of running enables the spiny mouse to travel one and a half times as far as its non-desert relatives on the same amount of energy. It seems likely that adaptations of energy conservation during running will be found generally among desert species.

This work was supported by NSF grant DCB-8918371.

42.2

TUNED MUSCLE-TENDON SPRINGS AND STRIDE FREQUENCY. Claire T. Farley*. (SPON: C.R. Taylor). Harvard University, Museum of Comparative Zoology, Cambridge, MA. 02138.

Running animals use their muscles and tendons as springs to bounce off the ground. These springs are not passive; the muscles must be activated and consume metabolic energy. I propose that the preferred stride frequency for human running is the frequency where the storage and recovery of elastic energy is maximized, and the cost of generating the muscular force to operate the springs is minimized. If recovery of elastic energy is incomplete, metabolic rate will increase because the muscles must do more work. I modelled a running human as a simple spring-mass system rebounding from the ground, and measured properties of the spring using a treadmill-mounted force platform. Oxygen consumption was measured simultaneously. Four subjects ran at 2.5 m/s while using stride frequencies from 26% below to 36% above their normal frequencies. At lower than normal frequencies, the subjects did not act like spring-mass systems and metabolic rate increased dramatically. Much of the elastic energy stored during the beginning of the landing phase was lost and could not be used for take-off. At higher than normal stride frequencies, the subjects did behave like good spring-mass systems, recovering almost all of the elastic energy stored during landing yet oxygen consumption increased. This indicates that the cost of generating muscular force to operate the spring must have increased. The metabolic rate was inversely proportional to the time of foot contact, t_c. When t_c is shorter (at higher frequencies), muscular force must be generated faster, requiring faster fibers whose crossbridges cycle and consume ATP at higher rates. Recent work has shown a similar inverse relationship between metabolic cost and t_c for both changing speed and size in quadrupeds. I conclude that running humans use stride frequencies that maximize storage and recovery of elastic energy and minimize the cost of generating force. This work was supported by NIH grant 5 RO1 AR18140-14.

42.3

ARE WALKING ELEPHANTS ROLLING EGGS? R. Kram*, G.M.O. Maloiy*, T.J. Roberts*, J. Black*, V.A. Langman, N.C. Heglund, J.-M. Weber and C.R. Taylor. Harvard University, Concord Field Station, Old Causeway Rd., Bedford, MA 01730.

Walking has been modelled as a rolling egg where forward kinetic energy and gravitational potential energy are exchanged with each step thus minimizing the fluctuations in total mechanical energy. In humans, the most economical walking speed coincides with the speed where maximal mechanical energy exchange takes place. Since larger animals have longer legs, the gravitational potential energy fluctuations per step per kg body weight are greater. Do large walking animals exchange potential and kinetic energy and is this a means of minimizing the metabolic energy required? To address these issues, we videotaped three female African elephants (1540 kg) as they walked across a calibrated area over a range of walking speeds. The most economical speed was about 1.0 m/sec. At this speed, the hip joint rose a distance of 0.17 m during the first half of the support phase. This amount of gravitational potential energy is more than three times the maximal forward kinetic energy available for transfer (if the elephant came to a complete stop). Thus, it appears that walking elephants are not rolling eggs and the exchange of mechanical energy may not be an important mechanism of minimizing energy consumption in long legged walking animals. This work was supported by NIH grant 5 RO1 AR18140-14.

42.4

DIVERSITY OF WATER BALANCE ADAPTATIONS AMONG ADULT MALE AND FEMALE ONE-HOST AND THREE-HOST IXODID TICKS. Marvin D. Sigal. The Ohio State University, Columbus, Ohio. 43210.

Parameters of water balance such as body size and water content, the presence of an active water vapor uptake system, and whole-body permeability (WBP) to water loss were determined for four species of hard ticks (Acari: Ixodidae) that differed in their on-host (versus off-host) period during the life cycle. The three-host ticks, *Amblyomma americanum* and *A. maculatum*, were found to actively gain water vapor from subsaturated air to maintain a critical equilibrium activity (CEA). The mechanism of water uptake in *A. americanum* was determined using freezing point depression analysis to be a solute-driven mechanism associated with a specific site in the gnathosoma. Neither of the two one-host ticks, *Boophilus annulatus* and *Dermacentor albipictus*, had a significant CEA, suggesting a secondary loss of active water uptake capability. There was a distinct sexual dimorphism in body size and water content between males and females of all the species examined. A sexual dimorphism of WBP's was also seen in all species except the three-host, *A. maculatum*. WBP's ranged from as low as 0.1064 % per hour among males of *A. maculatum*, to as high as 1.5415 % per hour among females of the one-host *B. annulatus*. A correlation analysis between body size and WBP among adults indicated that WBP's were significantly related to body size among females, and not correlated among males in *A. americanum*, *A. maculatum*, and *D. albipictus*. Conversely, in the more derived one-host tick, *B. annulatus*, males had a significant correlation of body size to WBP compared to females which did not.

42.5

CORTISOL STIMULATES HYPOOSMOREGULATORY ABILITY IN ATLANTIC SALMON, *Salmo salar*. G.A. Bisbal and J.L. Specker*. Dept. of Zoology, Univ. of Rhode Island, Kingston, RI 02881.

Juvenile Atlantic salmon, *Salmo salar*, acquire hypoosmoregulatory ability in advance of their entrance into seawater (SW). The aim of this investigation was to determine what aspects, if any, of these preparatory physiological changes might be induced by cortisol. Two-year-old Atlantic salmon were implanted with a cortisol-containing vegetable shortening pellet in December. This treatment elevated plasma cortisol titers from about 20 ng/ml in control fish (shortening implants without cortisol) to 160-170 ng/ml at days 6 and 12 after the implantation. By day 55, cortisol was 51 ng/ml in the treated and 19 ng/ml in the control salmon. As a result of this treatment, fish in fresh water developed a two-fold increase in gill Na^+/K^+-ATPase activity at days 6 and 12, and a three-fold increase by day 55. Intestinal mucosa Na^+/K^+-ATPase activity was not affected by cortisol. Cortisol-implanted fish exposed to 28 ppt SW for 48 h tended to show an improved ability to regulate their plasma osmolality and reduce their ionic load. Osmoregulatory ability was further evaluated by exposing fish to 37 ppt SW for 96 h. Survival of cortisol-implanted fish to these conditions was 10% at day 12, and 20% in the test conducted at day 55, whereas control fish showed no survival. Furthermore, there was a marked difference in mortality rates between control and cortisol-implanted fish during these tests. These results indicate that cortisol can induce biochemical and organismal changes during winter months that typify preadaptive changes normally occurring in the spring.

42.6

SALINITY ADAPTATION IN THE MILKFISH, CHANOS CHANOS: ENERGETIC PATTERNS AND POSSIBLE PHYSIOLOGICAL MECHANISMS. Christina Swanson. University of California, Los Angeles, CA 90024.

I studied aspects of the energetics of osmoregulation in the milkfish, Chanos chanos, an extremely euryhaline teleost. I measured metabolism (RMR) and growth in fish chronically acclimated to 15, 35 and 55 ppt. At equivalent activity levels, RMRs were significantly higher in 35 ppt than in either 15 or 55 ppt. RMRs in 15 and 55 ppt were comparable. At uniform food intake rates, growth rates were lowest in 35 ppt. Low RMRs and high growth rates in 15 ppt may reflect reduced osmoregulatory costs in this salinity which is near isomotic with milkfish blood. The equally low RMRs and high growth rates for fish in 55 ppt, a markedly hyperosmotic medium, were unexpected. Two possible hypotheses are that milkfish minimize the energetic cost of osmoregulation in 55 ppt by reducing the influx of ions by reductions in permeability of gill epithelia or gill surface area. Gill tissues from fish acclimated to each salinity were examined for evidence of changes in epithelial thickness and surface area. Preliminary examination shows that the gills of fish from 55 ppt exhibit fusion of adjacent secondary lamellae and decreased secondary lamellar length, both of which reduce gill surface area. These results indicate that osmoregulation costs are not simply a function of osmotic gradients.

42.7

LIPID PHASE TRANSITIONS IN INSECT CUTICLES STUDIED USING FT-IR. Allen Gibbs and John H. Crowe. University of California, Davis, CA 95616

Surface lipids, mainly long-chain hydrocarbons, constitute the main passive barrier to water loss in terrestrial arthropods, and the physical state of these lipids is important in determining their water-proofing properties. We used Fourier Transform Infrared spectroscopy (FT-IR) to study lipid phase transitions in insect cuticles. Gel-to-liquid crystalline phase transition temperatures in individual moults (exuvia) corresponded closely to those of *cuticle lipid* extracts. Melting temperatures were higher in cuticles from insects inhabiting warmer and drier environments, correlating with the need to minimize water loss under these conditions. We conclude that FT-IR provides a rapid, simple, sensitive, non-destructive method to examine the properties of cuticle lipids, and that FT-IR will be a valuable new technique for studies of water balance in arthropods. Supported by NSF grant DCB 89-18822.

42.8

EFFECTS OF NEST ARCHITECTURE AND INSULATION ON EGG COOLING RATES IN THE ORANGE TUFTED SUNBIRD: Israel Sidis and Amos Ar. Tel-Aviv Univ., Ramat-Aviv, 69978 Israel.

The Orange Tufted Sunbird (Nectarinia osea) is a 6g passerine (nectariniidae) with a uniparental incubation mode and a domed hanging nest. Cooling experiments were conducted by placing a warmed steel ball similar in diameter (12.7mm) to a real egg, outside of and in normal and dome removed nests, all in still air (SA), 1.5m/s head wind (facing the opening; HW) and tail wind (TW). The cooling rate of the "egg" in the normal nests was 1.5, 3.3 & 4.7 times lower than that of an exposed egg under SA, HW and TW conditions, respectively. Dome removal increased egg cooling rates only by 5% under SA and by 45% under TW. No significant difference was found under HW. The internal diameter of the nest was the second most effective architectural feature after the dome, mainly under HW conditions. The heat conductance of the nest wall had no effect on egg cooling rates under SA and TW, but showed relatively high partial correlation under HW in both normal and domeless nests. Analysis shows that in the absence of radiation convection was the major heat exchange mode of the "egg". Our results suggest that the windscreening effect is the major function of the nest in respect to egg energetics during parental absence, and may play a significant role in the evolution of nest design in small birds.

42.9

ACYL CHAIN REGROUPING IS A RAPID RESPONSE TO COLD EXPOSURE IN RAINBOW TROUT (Oncorhynchus mykiss). E.E. Williams and J.R. Hazel. Arizona State University, Tempe, Az. 85287

Cold acclimation in poikilotherms is characteried by alterations in membrane phospholipid composition. We have investigated the role of phospholipid acyl chain regrouping as a very early event in cold acclimation of rainbow trout. Hepatocytes from 20°C acclimated fish were isolated by collagenase perfusion. The cells were incubated with exogenous di-14C-palmitoyl phosphatidylcholine (*16:0,*16:0-PC) for one hour and then were transferred to 5°C for a predetermined period. Afterwards, the plasma membranes were isolated on a Percoll gradient and the PC fraction was resolved into molecular species by reverse phase HPLC. Each species was assayed for radioactivity. After only five hours, cells exposed to the novel temperature contained significantly higher amounts of radioactivity in 16:0,16:1-PC, 16:0,18:1-PC, and 18:0,20:4-PC than cells remaining at the acclimation temperature. Interestingly, radioactivity associated with 18:1,18:1-PC, present as a minor contaminant of the *16:0,*16:0-PC, decreased dramatically in the cold exposed cells. Acyl chain regroupings such as these would be a very rapid, and possibly metabolically inexpensive, means of altering membrane physical properties to offset the immediate effects of reduced temperature.
Supported by NSF grant DCB 89-01469 to JRH.

42.10

BASAL AND EPINEPHRINE-STIMULATED GLUCOSE RELEASE ARE HIGHER IN COLD- THAN WARM-ACCLIMATED TROUT LIVER. S.J. M'Kinley * and J.R. Hazel. Arizona State University, Tempe, AZ 85287

Since fish are poikilothermic, changes in temperature may perturb hormonal activation of cell function. To test this hypothesis, and determine the extent to which hormonal responses are thermally-compensated, the effect of temperature on epinephrine-stimulated glucose release in perfused trout liver was studied. Thermally-acclimated (5°and 20°C) rainbow trout (Oncorhynchus mykiss) were responsive to epinephrine (0.5 x 10^{-6}M) at 5°and 20°C. This effect was not inhibited by phentolamine, but was diminished by propranolol, this identified the response as β-mediated. Both the basal (19 and 84 mmoles/min/gm liver in 5°- and 20°-C trout, respectively) and epinephrine-stimulated (95 and 249) rates of glucose release were 3- to 5-fold higher in 5°C- than 20°C-acclimated fish regardless of perfusion temperature. In neither acclimation group was there a significant effect of temperature on the rate of epinephrine-stimulated glucose release. Q_{10} values ranged from .88 to 1.2. In summary, although rates of epinephrine-stimulated glucose release are temperature independent, acclimation to 5°C resulted in an enhanced capacity for basal and stimulated glucose release. (Supported by NSF grant #DCB 8901469.)

42.11

ANOXIA AND HYPOXIA LOWER THE SELECTED TEMPERATURE OF GOLDFISH. R.N. Rausch* and L.I. Crawshaw. Portland State University, Portland, OR 97207

The effect of reduced oxygen tension on selected temperature (Tsel) of goldfish was quantified. 25C acclimated fish used learned behavior to raise or lower the temperature of a sealed chamber. Severe environmental hypoxia led to graded decreases in Tsel. The response threshold was near 33 Torr. Goldfish are able to survive anoxia; Tsel of 15C acclimated fish under this condition was assessed by two methods. First, fish were placed in a sealed chamber after 1h anoxia (N2:1h; CO:5min). PO2 in the chamber was maintained below 3 Torr. Mean Tsel for fish in the chamber during the third hour of anoxia was 12C. Alternatively, 3h anoxic fish and normoxic fish were placed in a normoxic, aquatic thermal gradient device in which they could swim directly to warmer or cooler water. Tsel for anoxic fish was significantly lower than for normoxic fish only during the first 30min in the gradient. After 2h, mean Tsel for both groups was about 19C. Hypoxic hypothermia is an adaptive response which is rapidly reversed when oxygen tension increases.
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42.12

CHARACTERIZATION OF THE HEAT-SHOCK RESPONSE IN A THERMOPHILIC ALGA. S.R. Nieto* and B.M. Sanders. California State University, Long Beach, CA 90840.

The heat-shock response (HSR) is a cellular response involving the increased expression of the highly conserved heat-shock proteins (HSPs) which are known to increase cellular tolerance to heat and other physiological stressors. In this research, we examine the role that HSPs may play in adaptation to high temperatures in the thermophilic, eukaryotic alga, Cyanidium caldarium. Metabolic labelling with ^{35}S-methionine and electrophoresis demonstrated that cells grown at 30°C exhibit an increase in the synthesis of the 90-, 70-, 60-, 37-, 28-, and 20-kD HSPs when exposed to temperatures between 45°C and 55°C. Further characterization with a monoclonal antibody raised against mammalian HSP70, indicates a significant accumulation of the 70-kD HSP in cells at temperatures above 40°C. Studies show that many cell types given a mild pre-conditioning heat-shock can acquire 'thermotolerance' to a subsequent severe heat exposure. Furthermore, thermotolerance has been shown to correlate with a reduction in the period of translational inhibition after heat-shock. Experiments are now under way to characterize translational activity and to determine if a pre-conditioning heat-shock can confer translational thermotolerance in this thermophile at high temperatures. These results will contribute to our understanding of the role of HSPs in thermotolerance in organisms adapted to a unique high temperature environment. (Funded by the Richard B. Loomis Research award).

42.13

ACID-BASE STATE AND CONTROL OF VENTILATION IN THE TORPID BAT, *EPTESICUS FUSCUS*. Joseph M. Szewczak* and Donald C. Jackson, Brown University, Providence, Rhode Island 02912.

The effects of intermittent breathing upon acid-base (A/B) state and the control of ventilation were characterized in the torpid bat, *Eptesicus fuscus*. Arterial pH decreased as much as 0.24 pH units (mean=0.16; n=12) during the 8 to 12 minute apneic periods at a body temperature (T_b) of 20°C. The end-ventilatory A/B state for T_b=10-37°C was more faithful to an alphastat strategy, with a $\Delta pH/\Delta T_b$ slope of -0.011; r^2=0.98; n=26, based on grouped T_b means. But air convection requirements ($\dot{V}_e/\dot{M}_{O2}$) remained constant over this range, suggesting a net pH-stat regulation. *E. fuscus* remained sensitive to inspired gases throughout torpor. Hypercapnic stimulated breathing was rhythmic in pattern, and distinguishable from the less rhythmic pattern of hypoxic stimulation. These responses are incorporated into a proposed control theory model of ventilation in which a controller intermittently activates ventilation in response to the integrated effects of pH, P_{CO2}, P_{O2}, blood gas capacitances, and chemoreceptor response times. At $T_b \leq 10°C$, O_2 uptake is primarily non-ventilatory, and apparently occurs by diffusion down the airway, enhanced by cardiogenic mixing. Supported by NSF grant DCB 88-02045.

42.14

ACID-BASE DISTURBANCE AND VENTILATORY RESPONSE TO CHANGES IN PLASMA OSMOLALITY IN PEKIN DUCKS. Claudia E. Kasserra, D.R. Jones and M.R. Hughes. Univ. of British Columbia, Vancouver, B.C. V6T 2A9

The effect of acute changes in plasma osmolality on acid-base status and ventilation were investigated in the Pekin duck, *Anas platyrhynchos*. Hyperosmolality due to i.v. infusion of NaCl or sucrose (7.5 mmol/kg) caused a prolonged plasma acidosis (ΔpH=-0.08 units), but did not increase minute ventilation (V_I). An equivalent acidosis in ducks caused by infusion of lactic acid increased V_I 225% (Jones and Shimizu, unpubl.). $PaCO_2$ and PaO_2 increased and decreased 3.5±1.5 and 4±2 Torr, respectively, over the 2 hr experimental period. The acidosis was due to a decrease in the plasma $[Na^+]:[Cl^-]$ ratio, resulting in a decrease in strong ion difference. Plasma K^+ remained constant indicating total K^+ increased extracellularly. Infusion of KCl in amounts calculated to increase extracellular K^+ 50% caused only a transient increase in V_I. Hypo-osmolality had no effect on acid-base status or V_I. The lack of ventilatory compensation to acidosis caused by hyperosmolality may be due to paradoxical intracellular pH changes which suppress chemoreceptor stimulation.
Supported by NSERC of Canada

42.15

EFFECT OF CHANGING $[H^+]_a$ ON THE METABOLIC RATE OF ANAESTHETIZED, PARALYZED, PUMP VENTILATED GROUND SQUIRRELS (*SPERMOPHILUS LATERALIS*). Supriti Bharma* and William K. Milsom. Univ. of Brit. Col., Vancouver, B.C. V6T2A9

This experiment was designed to determine whether a change in arterial $[H^+]$ would affect a change in metabolic rate ($\dot{V}O_2$) in golden mantled ground squirrels, when the cost of breathing was excluded from metabolic rate and T_b was kept constant (37±1°C). In one group of anaesthetized, paralyzed and pump ventilated animals, F_ICO_2 of the ventilation gas was randomly changed every hour within the range of 0.03% - 7% CO_2 (respiratory acidosis). $\dot{V}O_2$ decreased as $[H^+]_a$ increased (~0.1 ml/min increase in $\dot{V}O_2$ for every 5mmoles/L increase in $[H^+]_a$) and vice versa. In another group of similarly prepared animals, lactic acid was loaded through intravenous infusions of 0.08mmoles/ml @0.19-0.38 mls/min for 20-30 minutes (metabolic acidosis). In this group, $\dot{V}O_2$ increased as $[H^+]_a$ increased (~0.1ml/min for every 5 mmoles/L increase in $[H^+]_a$). Similar results were obtained with the infusion of other weak acids such as acetic acid and Ringer's solution. The relationship between changes in Pa_{CO2} and pH_a were similar in both groups. Thus, respiratory acidosis and metabolic acidosis have opposite effects on metabolic rate. In conclusion, $[H^+]_a$ does not seem to be directly or strongly correlated to $\dot{V}O_2$. It may however, be indirectly correlated to $\dot{V}O_2$ by its' effect on some other factor which must be altered in different ways by respiratory and metabolic acidosis. Supported by NSERC of Canada.

42.16

EFFECTS OF ACETAZOLAMIDE ON THE VENTILATORY RESPONSE TO NASAL CO_2 IN THE TEGU LIZARD. E. Lee Coates* and Donald Bartlett Jr. Dartmouth Medical School, Hanover, NH 03756

Reptiles and amphibians decrease their ventilation when 0.4 - 5.7% CO_2 is introduced into the nasal cavities. This response requires intact olfactory nerves and presumably reflects CO_2 detection by olfactory receptors. The purpose of this study was to determine whether carbonic anhydrase plays a role in the ventilatory inhibition by nasal CO_2 in the tegu lizard, *Tupinambis nigropunctatus*. The trachea was intubated, and ventilation was monitored with a pneumotachograph. While the animal breathed room air, nasal CO_2 concentrations were rapidly altered using computer controlled solenoid valves in-line with small polyethylene tubes inserted into the external nares. The ventilatory response to 2 min presentations of 4% nasal CO_2 was measured before and after bathing the nasal cavities for 10 min with saline or 10^{-4}M - 10^{-2}M acetazolamide. The control response to nasal CO_2 was a transient fall in ventilatory frequency ("on response"), followed after removal of the CO_2 by a transient increase in frequency ("off response"). Neither response was affected by nasal saline. However, 15-30 min after nasal acetazolamide the "off response" was consistently attenuated or abolished. This effect of acetazolamide was reversed after 90 min. The results indicate that carbonic anhydrase plays a role in the ventilatory response to nasal CO_2, probably by participating in olfactory CO_2 detection.

Supported by Grants HL19827 and HL07449 from the National,Heart,Lung and Blood Institute.

42.17

HCO_3^-/Cl^- EXCHANGE IN KEMP'S RIDLEY SEA TURTLE ERYTHROCYTES. E.K. Stabenau, C.G. Vanoye* and T.A. Heming. Univ. Texas Medical Branch & Nat. Marine Fish. Ser., Galveston TX 77550.

HCO_3^-/Cl^- exchange was examined in turtle red blood cells (RBC), under conditions in which anion exchange was rate-limiting for transmembrane H^+-equilibration. Unidirectional exchange was measured at 10°C, by monitoring extracellular pH (pH_o) when a RBC pellet (HCO_3^--free, Cl^-_o~165 mM, pH_o~7.6) was mixed with an isotonic medium (HCO_3^- 0.1-2.0 mM, Cl^--free, pH ~7.6). Net exchange was determined at 30°C (turtle body temperature) by measuring pH_o after a RBC suspension (HCO_3^- 10 mM, Cl^-_o~165 mM, pH_o~7.4) was mixed with an acidic buffer solution (HCO_3^--free, Cl^-~165 mM, pH~6.7) in a stop-flow apparatus. Rate of HCO_3^-/Cl^- exchange was calculated from the initial $\Delta pH_o/\Delta$time, RBC volume and surface area, hematocrit, and extracellular buffer capacity. SITS (4-acetamido-4'-isothiocyanato-stilbene-2,2'-disulfonic acid), inhibited RBC HCO_3^-/Cl^- exchange, with I_{50} ~0.9 μM for unidirectional exchange and ~3.2 μM for net exchange. Maximum unidirectional exchange was 2.7 nmol-cm^{-2}-sec^{-1} at 10°C. Assuming the temperature-dependence of anion exchange in turtle RBC is comparable to that of human RBC, the unidirectional flux rate is equivalent to a total anion transport capacity at 30°C of ~40 nmol-cm^{-2}-sec^{-1}. Physiological net exchange at 30°C was 1.6 nmol-cm^{-2}-sec^{-1}, or 4% of the predicted total anion transport capacity. These data agree with computations for human RBC under physiological conditions (Wieth & Brahm, 1985). (Supported by NOAA grant NA89AA-D-SG139).

42.18

ACID-BASE CHANGES IN THE RUNNING GREYHOUND. Richard L. Pieschl*, Philip W. Toll*, L. Jane Peterson*, and M. Roger Fedde. Department of Anatomy and Physiology, Kansas State University, Manhattan, KS 66506-5602

To determine the factors responsible for changes in $[H^+]$ during and after sprint exercise in the racing greyhound, we applied Stewart's acid-base analysis to arterial blood samples taken at rest, at 8-sec intervals during exercise, and at various intervals after a 402-m sprint (29 sec) on the track. We measured $[Na^+]$, $[K^+]$, $[Cl^-]$, [Ca], [lactate], [total prot.], P_{CO2}, and pH, and calculated the $[H^+]$ from Stewart's equations. This sprint caused all measured variables to change. Maximal changes were: [SID] decreased from 36.7 meq/l at rest to 18.3 meq/l; [total prot.] increased from 13.6 meq/l at rest to 16.7 meq/l; P_{CO2}, decreased from 39.6 torr at rest to 27.9 torr immediately prerace, increased during exercise to 42.8 torr, and then decreased to near 20 torr during most of recovery; and $[H^+]$ rose from 36.6 neq/l at rest to a peak of 74.2 neq/l. In most cases, the $[H^+]$ calculated using Stewart's analysis was not significantly different from that directly measured. However, in some individual samples there were large differences between the measured and calculated $[H^+]$, partially resulting from the sensitivity of the calculations to measurement errors in the independent variables, especially at low [SID]. These results show that in addition to the increase in lactate and the changes in P_{CO2}, changes in total protein, $[Na^+]$, and $[Cl^-]$ also influenced $[H^+]$ during and after sprint exercise in the greyhound. (Supported by Hill's Pet Products).

42.19

ASSESSMENT OF RESPIRATORY DRIVE FROM ELECTROMYOGRAPHIC (EMG) MEASURES. S.C. Scott*, R.W. Butsch*, J.G. Inman* and I.R. Moss. UT Southwestern, Dallas, TX 75235

Respiratory muscle activity has long served as an index of respiratory drive and is commonly quantified by peak amplitude or summed activity of the integrated electrical signal. These measures give valuable information about general respiratory drive, but they cannot detect more subtle aspects of respiratory muscle activation such as rate of muscle recruitment, changes in shape of the EMG envelope, or very small responses to respiratory stimuli. We have developed an easily implemented, microcomputer-based system for analysis of multiple EMG parameters. In addition to peak amplitude, total area and duration, these include the area within the first 100 ms of activity (initial area) and the rate of rise of the rectified EMG envelope within the first 100 ms of muscle activity (initial slope). Furthermore, coordination between the activation of multiple muscles can be easily determined. We have found this system to be especially valuable in that we are able to quantify sensitive indicators of respiratory drive which may not be reflected in the more traditional measures. This approach can be easily adapted to other integrated electrical signals such as electroneurograms. (Supported by NIH HL 36939 and HL 07362).

42.20

ROLES OF ADRENAL CATECHOLAMINES DURING FORCED SUBMERGENCE IN PEKIN DUCKS. **LACOMBE A.M.A. and David R. JONES.** Department of Zoology, University of British Columbia, VANCOUVER, V6T 2A9 CANADA.

Maximum underwater tolerance (MUT) of ducks in which adrenal catecholamine release was prevented by chronic adrenal denervation (7 min. 10 ±13s) was significantly lower than that of sham-operated controls (12 min. 10 ±28s). Infusion of catecholamines during submergence significantly increased MUT in adrenal denervated ducks (9 min. 46 ±20s). Thus, adrenal catecholamines and other adrenal secretions increase the tolerance to submergence. Adrenal catecholamines do not work through beta-receptor activated myocardial actions since injection of propranolol during submergence did not reduce MUT. Leg perfusion experiments demonstrated that hypercapnemia had a depressant effect on the neural component of peripheral vasoconstriction which was opposed by catecholamine infusion. Consequently, by maintaining peripheral resistance, adrenal catecholamines save O_2 stores for the O_2 dependant tissues (heart and brain) and thereby enhance MUT.
Supported by NSERCC; B.C. Health Care; B.C.& Yukon Heart Fundation.

42.21

ADRENERGIC AND CHOLINERGIC REGULATION OF TROUT GILL O_2 CHEMORECEPTOR ACTIVITY. Mark L. Burleson and William K. Milsom. Univ. of British Columbia, Vancouver, B.C., Canada. V6T 2A9.

Chemoreceptor afferent activity may be modulated by a number of neurochemicals in mammals, but little is known about their modulatory effects on Heymans type chemoreceptors in lower vertebrates. Because of their involvement in the cardio-respiratory responses to hypoxia in fishes, the effects of adrenergic and cholinergic agents on afferent neural activity of O_2 sensitive chemoreceptors from the glossopharyngeal nerve were measured in isolated, perfused first gill arches of rainbow trout. Epinephrine, norepinephrine and isoproterenol had no effect or slightly reduced receptor discharge. Dopamine caused a modest transient increase in discharge followed by a decrease. Acetylcholine, nicotine and muscarine were potent stimulants of chemoreceptor activity. Propranolol and atropine reduced resting discharge and the responses to NaCN and hypoxia. Thus, adrenergic stimulation of ventilation in fish does not appear to be mediated by O_2 receptors. Cholinergic receptors, however, may play a major role in the regulation of O_2 chemoreceptor activity in fish.
Supported by NSERC of Canada.

42.22

MITOCHONDRIAL ACTIVITY; A SPECTROPHOTOMETRIC APPROACH TO QUANTIFICATION. Pierre Blier * and Helga Guderley, Université Laval, Québec, P.Q. Canada G1K 7P4.

The complications associated with the polarographic study of mitochondrial activity (i.e. calibration, quantities of mitochondria required, time etc.) led us to evaluate the validity of the spectrophotometric measurement of ATP production by mitochondria from trout red muscle. By combining an ADP regenerating system, i.e. hexokinase and glucose, with an NADP reducing step, i.e. glucose-6-phosphate dehydrogenase, we monitored ATP production by mitochondria provided with pyruvate, malate and ADP. The activity with ADP and without substrate was completely inhibited by the adenylate kinase inhibitor,P1,P5-di(adenosine-5')pentaphosphate. ATP production by adenylate kinase was 10 to 20% of the maximal rates. In the presence of substrates (pyruvate and malate) and ADP, ATP production was completely blocked by carboxyatractyloside or sodium azide. This suggests that the measured ATP production is completely associated with the adenylate transporter and the electron transport chain. The high sensitivity of this method should greatly facilitate comparative studies of mitochondrial metabolism.

42.23

THE ROLE OF CATECHOLAMINES AND CORTICOSTERONE DURING LONG-TERM COLD SUBMERGENCE ANOXIA AND RECOVERY IN TURTLES. K.M. Keiver, J. Weinberg* and P.W. Hochachka. Univ. of British Columbia, Vancouver, B.C. V6T 2A9

The ability of some species of freshwater turtles to withstand prolonged periods of anoxia is well known. The role that hormones play in this anoxia tolerance, however, is poorly understood. This study investigated the role of catecholamines and corticosterone during anoxic submergence (1 month) and recovery (1 month) in painted turtles (Chrysemys picta) at 5°C. Changes in plasma catecholamine and corticosterone levels in these turtles differed both quantitatively and qualitatively from those observed in other studies of anoxic submergence and recovery at warm temperatures. In contrast to the situation at warm temperatures, catecholamines and corticosterone did not appear to initiate changes in fuel mobilization or utilization in turtles during anoxia and recovery at 5°C.
This work was supported by NSERC.

42.24

DIURNAL VARIATION IN KIDNEY FUNCTION AND CLOACAL URINE EXCRETION OF SONG SPARROWS (MELOSPIZA MELODIA). Elisabeth Rothschild* and David L. Goldstein. Wright State Univ., Dayton, OH 45435

In birds, the ureters empty directly into the cloaca, making sequestering of urine in the lower intestine possible. The objective of this study was to assess the contributions of the kidney and cloaca to the excretion of urine. We captured song sparrows (Melospiza melodia) in Greene County, Ohio. We infused a kidney function marker, ^{3}H-polyethylene glycol (PEG), intraperitoneally using surgically implanted osmotic pumps. We collected the birds' excreta during intervals over 52 hours. Integrated over 52 hours, excreted PEG closely matched the amount of PEG infused by the pump. However, birds consistently excreted significantly less PEG during overnight periods than the amount infused by the pump, indicating either urine sequestering in the cloaca, a decrease in glomerular filtration rate (GFR), or both. We observed changes in plasma PEG levels indicating that GFR decreased by as much as 50% during the overnight period. Based on this changing GFR, the specifications of the osmotic pump, and PEG concentration of the marker solution, we developed a computer model to predict the total amount of PEG excreted during the overnight period. We collected a significantly lower amount of excreted PEG during the overnight period than predicted by the model, indicating cloacal sequestering of urine during these hours. In contrast, cloacal excretion of PEG typically exceded the predicted rate during the first hours of light. This is the first study to demonstrate a diurnal rhythm in birds of either kidney function or intestinal sequestering of urine.

42.25

MATURATION OF RENAL FUNCTION AND RESPONSE TO PARATHYROID HORMONE IN YOUNG CHICKENS. Jian Q. Feng and Nancy B. Clark, Univ. of Connecticut, Storrs, CT 06269

The glomerular filtration rate (GFR), urine flow rate and renal excretion patterns of phosphate, calcium, sodium and potassium were measured in chickens (Gallus gallus) one, five and nine days posthatching. Renal clearance experiments were performed. After a one-hour control period, 50 mM calcium gluconate was perfused, which inhibits the endogenous secretion of parathyroid hormone (PTH). Two hours after the start of calcium load, a bolus injection of PTH (10 µg / 100 g body wt; pH 2.8) was given via venous cannula. The results were compared with values obtained from four-week old chickens (Clark, unpublished).

Urine flow rates of 1, 5 and 9 day old birds were 0.34, 0.54 and 0.42 ml / kg.min, respectively. The GFR gradually increased from 2.12 ml / kg.min (day 1) to 4.28 ml / kg.min (day 5) to 5.19 ml / kg.min (day 9). The latter two values are similar to that of 4-week old chickens (5.0 ml / kg.min). The relative clearance of calcium in control periods averaged 29% at day 1, 10% at day 5 and 4%, the adult level, at day 9. Calcium clearance was elevated in all age groups in response to calcium loading; this was not affected by PTH. One day old birds lost significantly more urinary sodium (5% of filtered load) than did 5 or 9 day old birds (< 3%). The relative clearances of sodium and potassium increased significantly following PTH administration to 5 and 9 day old birds, but were not altered in 1 day old birds. The phosphate excretion of the 9 day old birds fell to near zero in response to calcium loading and rose to net phosphate secretion after PTH replacement, similar to results obtained in 4 week old chickens. The phosphate excretion pattern of one day old birds, in contrast, was unaffected by either calcium load or PTH administration. Five day old birds were sensitive to PTH administration but not to calcium loading.

We conclude that the kidney of the chicken is physiologically immature at hatching, and that its ability to respond the presence or absence of PTH gradually develops during the first week after hatching. (Supported by Grant DCB 88-12131 from the National Science Foundation.)

42.26

LOCALIZATION OF THE COLLAGENOUS ORGANIC MATRIX FRACTION FROM THE OCTOCORAL LEPTOGORGIA VIRGULATA. Jeffery L. Dupree*, Norimitsu Watabe, Roni J. Kingsley. Univ. of Richmond, VA 23173

Calcareous body inclusions are commonly found throughout the invertebrate taxa. Elaborately structured calcium carbonate spicules are the major mineralized body inclusions of the gorgonian, Leptogorgia virgulata. Spicule formation in this octocoral, as well as other calcium carbonate invertebrate structures, is apparently regulated by the intra-spicule organic matrix. Recent findings show that the insoluble fraction of the spicule organic matrix is collagenous. Collagen, although integral to calcium phosphate structures is not usually associated with the formation of invertebrate calcium carbonate structures. Interestingly, collagen is present in the organic matrix of summer specimens but absent in winter specimens. This suggests that there is a seasonal turnover of collagen. Antibodies were made directed against the purified collagenous fractions from summer samples. Immunocytochemical techniques were subsequently employed at both the light and electron microscope levels and localization of this collagen fraction was determined in animals collected throughout the year. The location and development of the collagenous fraction of the organic matrix was determined in the scleroblasts (spicule-forming cells) from the time of degradation in the Fall and Winter, to its reassemblage in the Spring and Summer.

42.27

HYDROGEN SULFIDE: A NOVEL INORGANIC SUBSTRATE FOR MITOCHONDRIAL RESPIRATION IN MARINE FISHES. Teodora Bagarinao* and Russell Vetter. Scripps Institution of Oceanography, A-002 UCSD, La Jolla CA 92093

Hydrogen sulfide at nanomolar concentrations is a potent inhibitor of cytochrome *c* oxidase. Nevertheless, many fish species including the California killifish (*Fundulus parvipinnis*) thrive in tidal marshes where sulfide levels can be quite high. We are investigating adaptations to sulfide in fishes. The cytochrome *c* oxidase of sulfide-tolerant fishes shows no increased resistance to sulfide inhibition. In the California killifish, oxygen consumption of isolated intact mitochondria is inhibited by sulfide greater than 50 µM. However, low sulfide concentrations up to 20 µM actually stimulate mitochondrial respiration, i.e., sulfide acts as a substrate. With the use of the monobromobimane-HPLC technique and radiolabeled ^{35}S-sulfide, we show that sulfide is oxidized exclusively to thiosulfate by mitochondria. Electrons liberated from sulfide oxidation enter the transport chain at site III, are then passed on to oxygen (stoichiometric ratio one mol O_2 consumed per mol sulfide oxidized) and result in ATP production (1 to 1.25 mol ATP per mol sulfide in the presence of 10-20 µM sulfide). Mitochondria of the California killifish have a much higher capacity to oxidize sulfide than those of the sulfide-intolerant speckled sanddab (*Citharichthys stigmaeus*). This is a clear demonstration of biochemical adaptation to sulfide in fishes.

42.28

MECHANISMS AND CONTROL OF CATECHOLAMINE RELEASE IN VIVO AND IN SITU IN THE ATLANTIC COD (GADUS MORHUA) DURING HYPOXIA. R. Kinkead, R. Fritsche, S.F. Perry and S. Nilsson. Dept. of Zoophysiology, Univ. of Göteborg, Sweden.

Gradual exposure of Atlantic cod (Gadus morhua) to different levels of hypoxia (75, 55 or 40 Torr) for 30 min stimulated mobilization of adrenaline (ADR) only. In order to stimulate a simultaneous increase of noradrenaline (NA) in the plasma, it was necessary to induce hypoxia more rapidly (within 5 min). Bilateral sectionning of spinal nerves 1-4 to the head kidney, with or without injection of fish with the adrenergic neurone release inhibitor bretylium, prevented NA increase in response to hypoxia. Neither treatment prevented or diminished the mobilization of ADR during the rapidly induced hypoxia (40 Torr). These results suggested a local direct effect of blood hypoxemia on ADR release from the chromaffin tissue of the head kidney. This hypothesis was confirmed using an in situ blood-perfused head kidney preparation in which hypoxemia stimulated ADR overflow into the efferent perfusate. Further experiments showed that overflow of a particular catecholamine during cholinergic stimulation of the head kidney was controlled independently probably by a negative feedback mechanism that may serve to maintain the plasma concentrations of that catecholamine within a 'target' range during hypoxia in vivo.

(This work was supported by a Swedish N.S.R. grant to S.N. and N.S.E.R.C. of Canada grant to S.F.P.)

42.29

AMMONIUM, TOTAL URATE, AND TITRATIBLE ACID EXCRETION IN ACID-LOADED LOCUSTS. Jon F. Harrison, Andrew P. Stagg*, and John E. Phillips. Univ. of British Columbia, Vancouver, B.C. V6T 2A9

We examined titratible acid and nitrogen excretion in HCl (10 µmol) injected locusts to evaluate the role of the renal system in hemolymph acid-base regulation. In a control group of NaCl injected locusts, the pH of the urinary pellet was below 5 and the ammonium content was very high (0.4 mol kg^{-1}). Because the water content of the feces was low (25%), ammonium excretion is clearly compatible with water conservation in the desert locust. Acid injection had no effect on excretion of titratible acid, ammonium, or total urate. If ammonium and total urate excretion represent equivalent excretion of acid, unfed locusts excrete 7.5 µequiv of net acid per day, of which 13% is titratible acid, 53% ammonium, and 33% uric acid. A portion of the net acid removed from the hemolymph during recovery from HCl injection was transferred to the lumens of the crop and midgut as titratible acid. The hemolymph-to-midgut net acid transfer was partially mediated by the Malpighian tubules; the decrease in hemolymph pH was correlated with a similar decrease in the pH of fluid secreted by tubules cannulated in vivo. Acid injection had no effect on tubular bicarbonate reabsorption. Supported by an NSERC operating grant to JEP and a Killam PDF to JFH.

42.30

SKELETAL BUFFERING POTENTIAL OF ACIDOSIS TOLERANT FRESHWATER TURTLES. Stephen J. Warburton and Donald C. Jackson. Brown University. Providence, RI 02912 USA.

We investigated the potential for shell and skeletal contributions to whole-body buffering in the freshwater turtle, *Chrysemys picta bellii*. Samples of femur and shell were analyzed for slowly-exchanging and labile CO_2. CO_2 was extracted from samples in a microdiffusion dish and analyzed in a Cameron chamber. Total CO_2 was measured in fresh samples, while the labile fraction was determined by drying samples to constant weight and using the relationship developed by Poyart et al. (Resp. Physiol., 25:101,1975):

labile CO_2 = 2(CO_2 fresh bone - CO_2 dried bone)

slowly-exchanging CO_2 = total CO_2 - labile CO_2.

There were no differences in either total CO_2 (1,600 umol/g ww) or labile CO_2 (480 umol/g ww) in bone versus shell in turtles. Both forms were present in greater quantities in turtle bone than are reported for mammal bone (total CO_2:800-900 umol/g ww; labile CO_2:approx. 255 umol/g ww). The proportion of labile CO_2 to total CO_2 is similar (30%) in turtles and mammals. The large skeletal mass of turtle shell combined with higher levels of CO_2 confer a potentially large buffer source in comparison to a mammal. The total rapidily-exchanging CO_2 pool in a mammal is approximately 43 mmol/kg bw, while in *Chrysemys picta bellii* the pool is approximately 190 mmol/kg bw. Experiments are underway to determine to what extent the rapidily-exchanging CO_2 pool in turtles is depleted during chronic acidosis.

Supported by NSF DCB 8802045

42.31

MUSCLE DEVELOPMENT AND ONTOGENY OF THERMOGENESIS IN RED-WINGED BLACKBIRDS. John M. Olson. Univ. of Michigan, Ann Arbor, MI 48109.

The capabilities of young red-winged blackbirds for regulatory thermogenesis improved markedly during the first 8 days of postnatal life. The metabolic expansibility of 8-day old nestlings during exposure to gradually decreasing ambient temperatures was substantially higher than that of their 6-day old counterparts, despite relatively small differences in overall body size between nestlings at these two ages. Shivering by the pectoralis muscles was apparently the primary mechanism of thermogenesis in both nestling and adult red-winged blackbirds. Shivering was detected with electromyography in nestlings as young as 3-days of age, however, the absolute intensity, dominant frequencies, and the duration of shivering in response to a given cold exposure increased markedly over the next few days. These improvements in thermoregulatory performance were accompanied by substantial increases in the size of individual muscle fibers and in the aerobic and contractile capacities of the pectoralis muscle. These results suggest that the morphological and biochemical maturation of the effector tissues for shivering is responsible for the development of thermogenic competence in the altricial red-winged blackbird. Supported by the Rackham Graduate School.

42.32

ONTOGENETIC APPEARANCE OF NEUROFILAMENT PROTEIN IMMUNOREACTIVITIES IN THE EMBRYONIC CHICK'S STATOACOUSTIC GANGLION. John E. Love* and Glenn M. Cohen* (SPON: J.G. Morris) Department of Biological Sciences and Space Research Institute, Florida Institute of Technology, Melbourne, Florida 32901

Neurofilaments are major structural elements of the neuronal cytoskeleton, and in mammals and birds consist of a triplet of intermediate-filament polypeptides with molecular weights of approximately 68 kDa (NFP-68), 160 kDa (NFP-160), and 200 kDa (NFP-200). We investigated the expression of NFP-160 and NFP-200 in the statoacoustic ganglion (SAG) of embryonic chicks of different ages. NFP levels were determined by immunoreactivity (peroxidase oxidation of 3,3'-diaminobenzidine tetrahydrochloride) within SAG neurons. Staining for NFP-160 was observed in the neurons of the SAG at stage 34 (8th embryonic day [ED]), the earliest stage examined in this study. By stage 46 (21st ED [hatching]), perikarya stained strongly for NFP-160, although with varying intensities. At stages 34 to 37 (8th to 11th ED), NFP-200 staining in the neurons of the SAG was ambivalent. By stage 38 (12th ED), when auditory nerves apparently begin to function, NFP-200 staining appeared in most perikarya. By stage 46, some perikarya stained strongly for NFP-200. Thus, it seems that NFP-160 and NFP-200 exhibit different temporal patterns of ontogenetic expression, with NFP-160 appearing earlier in the development of the avian SAG. [Funded by a grant from the Space Research Institute to GMC.]

42.33

THE FUNCTIONAL BASES FOR THE DEVELOPMENT OF ENDOTHERMY AND HOMEOTHERMY. Z.A. Eppley. Univ. of California, Irvine, CA 92717

The functional bases of endothermy and homeothermy were investigated during ontogeny of the Western Gull (*Larus occidentalis*), spanning the period from 2 days before hatching to 6 days after hatching. I measured thermoregulatory performance (T_b during cold exposure), and putative whole animal (metabolism and shivering EMGs) and biochemical determinants of performance (muscle aerobic capacity [citrate synthase] and contractile ability [myofibrillar ATPase activity]). I used a principal components analysis (PCA) to describe the pattern of variation in the data using a reduced number of independent factors. PCA of log-transformed variables gave a factor encoding growth (64.8% of the variance) and another factor encoding peak metabolism, shivering thermogenesis and myofibrillar ATPase activities (16.6% of the variance). I used these factors in a linear regression to predict thermoregulatory performance ($R^2 = 0.86$, $p < .0001$, partial correlations factor 1 = 0.77, factor 2 = 0.52). To detect other important factors whose role was obscured by their correlations with mass, I generated mass-residuals from the log-transformed data. PCA of the mass-residuals yielded 3 factors: 1-encoding metabolic intensity (37.4% of the variance), 2-encoding shivering thermogenesis (23.4% of the variance) and 3-encoding locomotor performance (9.6% of the variance). I used these factors and mass in a multiple regression to predict thermoregulatory performance. Factor 3 (locomotion) was not significantly correlated with thermoregulatory performance. The regression model predicted thermoregulatory performance well ($R^2 = 0.90$, $p < .0001$), with partial correlations of 0.69 for mass, 0.52 for factor 1 (mass-independent metabolic intensity), and 0.37 for factor 2 (mass-independent shivering thermogenesis). Heat balance models were used to further partition the separate contributions of thermogenesis and conductance to the development of endothermy and homeothermy for particular ages. I investigated the functional basis for the onset of endothermy among prehomoethermic age groups by correlating the development of particular systems with thermoregulatory performance. These studies generated a series of hypotheses which are being tested in other species. Supported by NSF Grants DCB 85-02218 and DPP 87-16005.

42.34

COMPARISON OF THE EFFECT OF AGE, BREED AND LEVEL OF TRAINING IN THE HORSE USING A STANDARDIZED EXERCISE TEST. E Morris and H J Secherman* Tufts University School of Veterinary Medicine, N. Grafton, MA 01536

The purpose of this study was to compare exercise measurements in several groups of racehorses. The effects of age and physical activity on exercise related parameters were examined by comparing the results of a standardized incremental exercise test in yearling, two-year old and adult Thoroughbreds. The effects of breed and training protocols were examined by comparing adult Standardbred and Thoroughbred racehorses. All of the adult horses were actively involved in racing or training at the time of the examination. Peak oxygen consumption ($\dot{V}O_2$peak), peak hematocrit and the maximum number of steps completed in the exercise test increased with increasing age and degree of physical activity ($p<0.05$). Peak venous lactate concentration and respiratory exchange ratio were significantly higher in both groups of younger Thoroughbred horses compared to the adult Thoroughbred racehorses ($p<0.05$). Peak heart rate did not change with age or training. Adult Thoroughbred racehorses achieved a significantly higher ($p<0.05$) peak hematocrit as compared to adult Standardbred racehorses. No other exercise measurements were significantly different in these two groups of horses. The results of the comparison between exercise measurements in yearling, two-year old and adult Thoroughbreds indicate that aerobic capacity and musculoskeletal strength increased with age and training. Anaerobic parameters were already well developed at a young age. The results of the comparison between adult Standardbreds and adult Thoroughbreds indicate that maximal aerobic power is not increased despite a notably greater emphasis on aerobic training in the Standardbred as compared to the Thoroughbred. The ability of the Standardbred to achieve a comparable $\dot{V}O_2$peak despite a lower peak hematocrit suggests increased oxygen extraction or increased oxygen delivery in this breed.

42.35

EFFECT OF PHYSICAL CONDITIONING ON THE SKELETAL AND CARDIAC MUSCLE MYOGLOBIN CONCENTRATION IN BAR-HEADED GEESE. David K. Saunders and M. Roger Fedde. Kansas State University, Manhattan, KS 66506

This study was performed to determine if physical conditioning of birds would result in an increased skeletal and cardiac myoglobin concentration, as has been shown to occur in mammals. Two bar-headed geese underwent 12 weeks of treadmill exercise (0.7m.sec^{-1}, 3° incline, 30 min/day, 5 days/week) while 2 other birds were not exercised and served as controls. Myoglobin concentration was determined in 6 leg muscles, 2 flight muscles, and in the left ventricle. In all birds, the highest myoglobin concentration was found in the left ventricle and the pectoralis major, the primary flight muscle. Physical conditioning resulted in an increase in myoglobin concentration in the 6 leg muscles, femorotibialis medius (31%), flexor cruris lateralis (28%), gastrocnemius lateralis (23%), tibialis cranialis (22%), iliotibialis medius (20%), gastrocnemius medius (13%), and in the left ventricle (17%). In contrast, there was little difference between exercised and nonexercised birds in the myoglobin concentration of the flight muscles, pectoralis major (2%) and supracoracoideus (3%). We conclude that skeletal and cardiac muscles of birds, like those of mammals, are capable of increasing myoglobin concentration in response to exercise.

42.36

PHYSIOLOGICAL CHANGES DURING RUNNING IN THE GREYHOUND: INFLUENCE OF RACE LENGTH. Joan L. Nold*, Richard L. Pieschl, Jr.*, Philip W. Toll*, L. Jane Peterson*, and M. Roger Fedde. Dept. of Anatomy and Physiology, Kansas State Univ., Manhattan, KS 66506-5602

Prolongation of strenuous sprint exercise may lead to progressive and damaging physiological changes. We investigated the changes in various physiological and biochemical variables in racing greyhounds before, during, and following races of three standard lengths (1/4 mile=402 m, 5/16 mile=503 m, and 7/16 mile=704 m). Mean race times for the three lengths were 29.5 sec (n=5), 36.8 sec (n=16) and 51.2 sec (n=5), respectively. Although the races were conducted during different months, average body temperature increase was similar (2.3, 2.6, and 2.6°C, respectively). The dogs did not hypoventilate during the race but PaO_2 decreased as much as 20 torr; they hyperventilated following the race with $PaCO_2$ falling to as low as 11 torr. pHa decreased below 7.0 and plasma lactate rose to 35 mmol/l in the longest race. Fluid movement from the vascular compartment progressively increased with race length resulting in an increase of 26% in plasma protein conc. Because of that and splenic contraction, hematocrit increased to 70%. Plasma potassium was not increased further by the longer race (3.5 meq/l over rest). Although long sprints accentuate lactate production and fluid shifts, these transient changes appear to be well tolerated by these animals. (Supported by Hill's Pet Products).

42.37

FLUID, ELECTROLYTE, AND RBC SHIFTS IN THE RACING GREYHOUND. Philip W. Toll*, Richard L. Pieschl, Jr.*, Peter Gaehtgens*, Dieter Neuhaus*, and M. Roger Fedde. Dept. of Anatomy and Physiology, Kansas State Univ., Manhattan, KS 66506-5602 and Institut für Physiologie, Freie Univ., Berlin, FGR.

Exercise causes fluids and electrolytes to shift among body compartments, and in some mammals, the number of circulating red blood cells increases. To investigate these changes, we drew arterial blood samples from six greyhounds at rest, just before, and five minutes after a 704 meter race. For the calculations below, we assumed that total plasma content of protein and the total content of Na^+ in extracellular fluid were constant; we defined blood volume (BV) at rest as 100%. Before the race, plasma volume decreased by 10% from its rest value, while total red cell volume increased by 60%, mainly due to an increase in red cell number rather than size. The result was a 24% increase in blood volume and an increase in PCV from 49 to 63%. By five minutes postrace, plasma volume was 24% below its rest value while total red cell volume did not change further; thus, blood volume fell but remained 18% above its rest value and PCV rose to 67%. Chloride content of the plasma compartment fell by the same fraction (24%) as the plasma volume, so $[Cl^-]$ was constant. Na^+ content fell by a smaller fraction (15%) so $[Na^+]$ increased from 151 meq/L at rest to 167 postrace. If $[Na^+]$ was the same throughout the ECF, then, presumably, H_2O moved into the intracellular compartment. A consequence of these changes is that the inorganic strong ion difference ($[Na^+] + [K^+] - [Cl^-]$) in plasma increased by about 15 meq/L, tending to minimize the acid-base effects of the 33 meq/L increase in lactate concentration. (Supported by Mark Morris Associates).

42.38

CONTRIBUTION OF PROTEIN CATABOLISM TO THE AVERAGE METABOLIC RATE OF FASTING NORTHERN ELEPHANT SEAL PUPS. Sean H. Adams, Lorrie D. Rea*, and Daniel P. Costa. Institute of Marine Sciences and Marine Sciences Board, University of California, Santa Cruz, CA 95064.

Studies with a variety of animals have shown that during extended periods of food deprivation, protein catabolism declines over time. This suggests that the relative contribution of protein catabolism to meet energetic needs drops over the duration of the fast. However, similar work which has considered changes in fasting metabolic rate has indicated that the decrease in catabolism is simply concomitant with a decline in metabolic rate. This study was initiated to examine the changes in the contribution of protein catabolism to the average metabolic rate of naturally fasting northern elephant seal pups. Daily urinary nitrogen output was determined after urine collections at the beginning (3-6 d), middle (26-29 d), and end (54-56 and 68-70 d) of the postweaning fast. Metabolic rate was measured via open circuit respirometry at various times throughout the fast. Both metabolic rate and daily nitrogen output declined as the fast progressed. The percent contribution of protein catabolism to average metabolic rate declined with time fasting: 2.74% (3-6 d), 1.99% (26-29 d), 1.37% (54-46 d), and 1.07% (68-70 d). Thus, in elephant seal pups protein catabolism contributes very little to metabolic rate, and its role as an energetic precursor lessens with time fasting.

42.39

DEVELOPMENT OF RESTING METABOLIC RATE IN NORTHERN ELEPHANT SEAL PUPS. Lorrie D. Rea* and D.P. Costa. Institute of Marine Sciences, University of California, Santa Cruz, CA. 95064.

From measurements of resting metabolic rate (RMR), body mass and body composition of northern elephant seal (Mirounga angustirostris) pups it is possible to quantify factors that influence the change of metabolic rate during the first four months of development. During the 4 week nursing period, body mass increased from 42.0 ± 3.5 kg to 127.3 ± 15.9 kg. Body fat increased from 4% of body mass near birth to approximately 48% at weaning. By the end of the 10-week post-weaning fast mean body mass declined to 83.1 ± 1.5 kg. Body composition remained relatively constant throughout the fast. Pups fed herring after 10 weeks of fasting increased mass to 98.7 ± 11.5 kg, with greatest increases seen in the lean body mass compartment. Dramatic changes in body mass and body composition such as these would be expected to influence RMR significantly. Oxygen consumption was measured in pups from birth to 18 weeks of age using open circuit respirometry. Body composition was estimated from total body water content determined by the dilution of tritiated water. There was no significant difference between metabolic rates of male or female pups at any age. Changes in metabolic rate were most strongly correlated with increases in lean body mass ($r=.71$, $p<0.01$). A 42% decline in mass specific RMR was seen over a 16 week period, independent of changes in body composition or in nutritional state (fasting or feeding). Together, changes in lean body mass and age accounted for 75% of the variability seen in RMR ($p<0.01$).

42.40

HYPOXIC PULMONARY VASOCONSTRICTION (HPV) DOES NOT CONTRIBUTE TO THE HIGH PULMONARY ARTERY PRESSURE (P_{PA}) IN EXERCISING HORSES. N. Pelletier* and D.E. Leith. Dept. Surgery & Medicine, Kansas State University, Manhattan, KS 66506, U.S.A.

Mean P_{PA} is higher in horses than in humans, both at rest (~30 vs 15 torr) and during exercise (≥ 80 vs ≤ 30 torr). The mechanisms are unknown. To see if HPV contributed to the high P_{PA} in exercising horses, we compared P_{PA}-flow ($\dot{Q}$) curves when inspired O_2 fraction (F_IO_2) was 0.16, 0.21, and 0.30, in 5 normal Thoroughbred horses (500 ± 42 kg) standing quietly and after 2 and 2.5 min galloping at 10 and 14 m/s on a level treadmill. We calculated O_2 consumption ($\dot{V}O_2$) from measurements of respired gas composition and flow, and then calculated $\dot{Q}$ from $\dot{V}O_2$ and measurements of arterial and mixed venous oxygen content (CaO_2 and $C\bar{v}O_2$) with the Fick method.

At 14 m/s, with $F_IO_2 = 0.16$, CaO_2 fell (to 14.7 from 20 mL/dL on air) and $\dot{Q}$ increased (to 0.86 from 0.65 L/min•kg on air) by increasing stroke volume (to 4.1 from 3.2 mL/min•kg on air). $\dot{V}O_2$ did not vary with F_IO_2 at any speed (3.8, 74 and 128 mL/min•kg, at rest and at 10 and 14 m/s), nor did the slope (90 torr•L^{-1}•min•kg) and intercept (20 torr) of $P_{PA}/\dot{Q}$ curves. We think it unlikely that HPV is an important mechanism in the high P_{PA} of exercising horses.

Funded in part by the Medical Research Council of Canada.

42.41

PHYSIOLOGICAL CORRELATES OF AIR-BREATHING BEHAVIOR IN THE BOWFIN (Amia calva). Michael S. Hedrick and David R. Jones. Univ. of British Columbia, Vancouver, B.C. V6T 2A9 CANADA

This study was designed to, 1) characterize the air-breathing (AB) pattern of conscious, undisturbed bowfin and, 2) determine the influence of respiratory gases on AB frequency and patterns. AB frequency and breath volumes were recorded using a video recorder from 7 bowfin placed in aquaria at 22±2 °C. Under normoxic conditions, bowfin exhibit two distinct AB patterns: Type I AB is characterized by exhalation followed by inhalation; Type II AB consists of inhalation only. A mixture of Type I and Type II AB (60:40, I:II) occurs in normoxia and the interbreath (IB) interval is 19.9 ± 0.9 (95% C.I.) min. In aquatic or aerial hypoxia, IB interval is less than in normoxia (13-14 min), and the Type I AB pattern is predominant. Bowfin exposed to 100% O_2 in the aerial phase do not decrease IB interval, but there is a switch to the Type II AB pattern; this occurs despite aquatic hypoxia. These results suggest that aquatic O_2 tension sets the AB frequency, but a behavioral switch in AB pattern occurs in response to high blood O_2 levels or stretch receptor feedback from the swim bladder. Supported by NSERC of Canada.

42.42

ACTIVE WATER VAPOUR ABSORPTION (WVA) IN TERRESTRIAL ARTHROPODS. Jonathan C. Wright and John Machin, Department of Zoology, University of Toronto, 25 Harbord Street, Toronto, Ontario, Canada.

Gravimetric monitoring of water exchange has identified WVA in 8 spp. of woodlice (Isopoda, Oniscidea), the first demonstrations in Crustacea. Uptake threshold - the minimum water activity from which water vapour can be absorbed - ranges from 0.87 to 0.94, correlating closely with ecotype, and allowing animals to overcome a water-debt in subsaturated humidities above these values. Uptake fluxes can be modulated to balance transpiratory losses in hydrated animals. Nano-osmometry has identified a solute-based absorption mechanism utilising cyclical production and resorption of a hyperosmotic fluid in the pleoventral chamber; prevention of WVA by wax blocking confirms this uptake site. Absorption dymanics are phasic, with a periodicity of 20-40 minutes and often abrupt interphase changes in uptake flux, indicating cyclical renewal (and changes in osmolality) of uptake fluid. The pleopods display ventilatory pumping (0.08-0.30 Hz) during absorption; ventilation frequency increases with external water activity, compensating for changes in the activity deficit between uptake fluid and air and maximising absorption rate. Both fluid production and resorption require movement against osmotic gradients. The compound transporting epithelia of the pleopodal endopods probably sustain both processes.

(Supported by grants from The Royal Society and Leverhulme Trust, U.K. and Natural Sciences and Engineering Research Council, Canada.)

43.25

EXTRACELLULAR AND INTRACELLULAR ACID-BASE EFFECTS OF SUBMERGENCE-ANOXIA AND NITROGEN BREATHING IN TURTLES. J.S. Wasser, S.J. Warburton, and D.C. Jackson. Brown Univ., Providence, RI 02912.

We compared acid-base state in turtles (*Chrysemys picta bellii*) at 20°C subjected to anoxia either by submergence or N_2-breathing. Measurements on control animals and on animals after 1, 2, 4, and 6 h of anoxia included blood pH, P_{O2}, P_{CO2}, and lactate and tissue pH_i, lactate, and glycogen concentrations. We hypothesized that anaerobic metabolism of submerged turtles would be depressed by their more severe extra- and intracellular acidosis . Submerged turtles had significantly lower arterial pH values than N_2-breathing animals (6.98 and 7.34 respectively after 6 h) due to a combined metabolic and respiratory acidosis. N_2-breathing animals experienced a pure metabolic acidosis. In spite of this disparity in pH_a, 6 h pH_i values for liver, heart, and brain were similar. Likewise, glycogen depletion and lactate accumulation at h 6 in these tissues and in skeletal muscle suggest no dramatic differences in anaerobic metabolic rate. However, skeletal muscle pH_i was somewhat lower at h 6 in the submerged group (6.73 vs 6.91 for N_2-breathers). Thus, at h 6, in spite of a 0.37 pH unit difference in pH_a, and a 70 mmHg difference in arterial P_{CO2}, pH_i and tissue lactate and glycogen were similar. These results can be explained if the apparent intracellular buffering capacities (β') of turtle tissues are very high. Although scatter in our *in vivo* data precludes an estimation of β', we have recently obtained a relatively high value of 88 slykes for isolated, perfused, anoxic turtle heart using ^{31}P-NMR spectroscopy. We conclude that extracellular acid-base state is not necessarily reflected intracellularly *in vivo* in turtles due perhaps to high apparent tissue buffer capacities and care must be taken in extrapolating between compartments when attempting to make inferences about metabolic depression or acid-base regulation. Supported by NSF DCB8802045, NIH HL07581, and RI Heart Assn..

43.26

LACTATE UPTAKE INTO INACTIVE SKELETAL MUSCLE DURING ACIDOSIS AND ALKALOSIS. George J.F. Heigenhauser, Yoni Yarom,* Robert S. McKelvie* and Norman L. Jones. Dept. of Medicine, McMaster University, Hamilton, Ontario, Canada. L8N 3Z5

Previous studies from this laboratory have shown that during exercise, plasma lactate concentration ($[Lac^-]_p$) was lower during induced acidosis (AC) than during induced alkalosis (ALK). We hypothesized that, compared to ALK, the lower $[Lac^-]_p$ during AC was due to a greater uptake of Lac^- into inactive skeletal muscle. To test the hypothesis, 5 healthy male subjects exercised on a cycle ergometer on two occasions at power outputs (PO) corresponding to 20, 40, 60, 80 and 100% of their previously determined maximal PO. The subjects exercised for 6 min at each PO. AC or ALK was induced in double blind, randomized order by ingestion of NH_4Cl (0.3 gm/kg) or $NaHCO_3$ (0.3 gm/kg) respectively. Blood samples were taken simultaneously from the brachial artery and a deep arm vein during the last minute of each PO. At each PO, compared to ALK, the $[Lac^-]_p$ during AC was lower. Venous-arterial Lac^- were similar at each PO. A greater proportion of Lac^- was taken up by the inactive skeletal muscle of the arm during AC, but this only partially accounts for the lower $[Lac^-]_p$ observed during induced AC compared to ALK.

Supported by the Medical Research Council of Canada and the Heart and Stroke Foundation of Ontario.

43.27

RESPONSE OF INTRACELLULAR pH IN THE BULLFROG CORNEAL EPITHELIUM DUE TO PROLONGED CHANGES OF BATHING SOLUTION pH. John I. Scheide. Department of Biology, Central Michigan University, Mt. Pleasant, MI 48859.

Chloride transport in the bullfrog corneal epithelium is dependent on bathing solution pH. The epithelial intracellular pH was determined in corneas that were bathed in a 10 mM HEPES-buffered saline (bicarbonate-free saline) under short circuit conditions using single-barrelled pH-sensitive microelectrodes. The intracellular pH of the corneal epithelia was 6.69 ± 0.06 (n=12 corneas) when corneas were bathed with a saline pH of 7.3. The measured cellular pH was different from bathing solution pH and the cell pH predicted from the cellular voltage, -50 ± 3 mV. Increasing the stromal bathing saline pH from 7.2 to 8.0 resulted in an increase in the short circuit current and tissue conductance indicative of an increase in chloride transport. The epithelial cell apical conductance increased with the increase in saline pH. The intracellular pH significantly increased 0.28 ± 0.09 (n=5 corneas), although this increase was not equal to the prolonged 0.7 increase in serosal bathing pH. A prolonged decrease in the stromal saline pH from 7.4 to 6.9 did not change the intracellular pH. The cornea epithelial cells appear to regulate cell pH within a narrow range.

Supported by the CMU Summer Fellowship Award.

COMPARATIVE PHYSIOLOGY: NMR SPECTROSCOPY

44.1

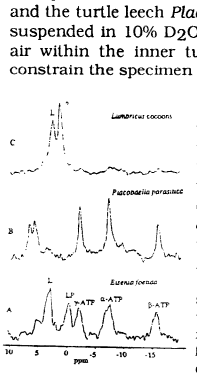
^{13}C NMR OF CITRIC ACID CYCLE ACTIVITY IN RESPONSE TO WORKLOAD IN INTACT HEARTS. E.D. Lewandowski. Baylor College of Medicine, Houston, TX 77030.

Oxidative metabolism was monitored with ^{13}C and ^{31}P NMR spectroscopy of isolated rabbit hearts. Citric acid cycle activity was observed at 3 workloads. Hearts were perfused with 2.5 mM [2-^{13}C] acetate (AC) at control (CON, n=5), with 10^{-7} M isoproterenol (ISO, n=4), and with 20 mM KCl arrest (KCL, n=4). Rate pressure products were: CON=23393±6069 (mean±SD); ISO=43721±10424; KCL= 0±0. Oxygen consumption was raised by ISO (4.82±0.39 μM/min/g wet, P<0.001) and reduced by KCl (1.49±0.31, P<0.05) as compared to CON (2.43±0.53). AC oxidation initially labeled glutamate (GLU) at C-4. Fractional enrichment with ^{13}C at C-4 was similar among groups. Recycling [4-^{13}C] GLU via the citric acid cycle placed label at C-2 and C-3 GLU. The ratio of ^{13}C at C-2 versus C-4 (C-2:C-4) reflected citric acid cycle stimulation by ISO and reduction with KCl. C-2:C-4 values at 4 min were: CON=0.35±0.09; ISO=0.69±0.19 (P<0.02); KCL=0±0 (P<0.001). Phosphocreatine:ATP ratios were similar at each workload. Thus, ^{13}C NMR demonstrated a workload dependent response of oxidative metabolism which was not reflected by ^{31}P NMR of high energy phosphates.

44.2

^{31}P NMR SPECTRA OF SINGLE, LIVE ANNELID SPECIMENS. Ronald G. Lawler and Elizabeth A. Arendt. Brown University, Providence, RI 02912.

Whole body 162 MHz. ^{31}P NMR spectra have been obtained from single, live specimens of the earthworms *Lumbricus terrestris* and *Eisenia foetida* and the turtle leech *Placobdella parasitica* (Figs. A & B). Animals are either suspended in 10% D_2O in a standard 10 mm NMR tube or positioned in air within the inner tube of a pair of coaxial tubes. Care is taken to constrain the specimen to the observing region of the sample using a teflon or cotton plug. Typical accumulation times for the spectra shown are 5-10 min. In the earthworms, well-resolved signals are observed from ATP, from the phosphodiester lombricine (L) and its phosphonamide derivative (LP) which serves as phosphagen. Leeches, on the other hand, do not exhibit a detectable phosphonamide peak, confirming the absence of such a phosphagen in that species. NMR spectra have also been obtained from a sample containing 11 *Lumbricus* cocoons (Fig. C, 2 hr. accumulation), 7 of which subsequently hatched. Unphosphorylated L and an unidentified peak with a chemical shift intermediate between L and LP are observed. Peaks from high energy phosphate species are barely detectable. It seems clear that whole body ^{31}P NMR spectra possessing sufficient resolution and sensitivity to be useful for nondestructive physiological studies may be obtained with relative ease from living specimens of appropriate size and shape.



45.1

THE QUANTIFICATION OF THE EFFECTS OF SUPPORTED AQUATIC JOGGING ON THE PERCENT OF ADIPOSE TISSUE AND OXYGEN UP- TAKE IN FEMALE VOLUNTEERS. James A. Richardson. The University of South Dakota, Vermillion, SD., 57069.

The purpose of this study was to quantify the effects of 4 days/week-20 mins/day supported aquatic jogging on the percent of adipose tissue (%) and oxygen uptake (Vo2) in female volunteers. Eleven adult female volunteers ranging (R) in age from 21 to 72 (μ=34.27, σ= 14.34) were subjects (S) in an eight week study. Each S was pre (pre)-post (pos) evaluated, after informed consent and physician's approval, on weight (Rpre=98.5 to 221 pounds (lbs.), μ=149.7, σ=33.14)--(Rpos=98.5 to 220 lbs., μ=148.1, σ=33.26), % via Jackson-Pollack (1978) (Rpre= 15.2 to 36%, μ=25.16, σ= 8.6, Rpost= 14.5 to 30.7%, μ=22.31, σ=7.78), and Vo2 via McArdle 3-minute step test (Rpre=32.56 to 48.33 ml/kg/min, μ=40.1, σ=17.45)--(Rpos=36.26 to 58.6m ml/kg/min, μ=45.18, σ20.17). Age adjusted exercise heart rate was developed for each S, and was the target heart rate for each bout. In addition, resting blood pressure and heart rate, and oral temperature were taken before each bout. Student-t results indicate a significant difference (.05 level {10df}) for % t=2.336, and Vo2 t=2.755.

45.2

OXYGEN CONSUMPTION DURING EXERCISE IN WATER. Luca Morelli*, P.G. Data, M. Tommolini*, V. Masciulli* and G. Gigante*. Univ. of Chieti, Chieti 66100, Italy

The relationship between oxygen uptake and exercise intensity is independent from life conditions, air or water. In 80 very well trained divers, immersed head out in hydrostatic balance at rest and during exercise at different level in water of 21°C, the total breathing volume, CO_2 production and oxygen consumption were measured. All divers wore neoprene wet suit (5mm) and standard fins. The divers sustained weights of 3-6-9 kg in their hands for four minutes, staying head out and breathing through a valve of low resistance. The expired air was collected in a Douglas bag and immediately analized. At rest head out in water the oxygen consumption was significantly increased (760 ml/min ± 320). During exercise in water the increase of $\dot{V}O_2$ was linear in relation to the growing load weight: 3kg, 1350 ml/min ± 280; 6 kg, 1700 ml/min ± 220; 9 kg, 2180 ml/min ± 180). In accordance to the Margaria's nomogram for indirect determination of maximal O_2 consumption (step test) we have expressed a nomogram to determinate the divers' oxygen consumption in water, in relationship with oxygen uptake, cycle/min (kick rate) and weight (3-6-9 kg).

45.3

HEART RATE DURING EXERCISE IN AIR AND UNDERWATER. Pier Giorgio Data, V. Masciulli*, M. Tommolini*, B. Loffredo*, L. Morelli* and V. Biondelli*. Univ. of Chieti, Chieti 66100, Italy

The Heart Rate (HR) constitutes an indirect index of oxygen consumption in steady state exercise during breathing. The HR was measured in 80 divers performing traditional step test in air during breathing and Breath-hold (BH). Oxygen uptake and HR were measured in divers immersed head out in water of 21°C at rest and during different levels of exercise. The HR at similar exercise intensity was measured in the same subject during Breath-hold Diving (BHD) and Scuba diving. The exercise was performed at 18, 26 and 31 ml/Kg/min during breathing in air and underwater for 4 min and during BH and BHD for 50 sec. The relationship among oxygen consumption, work rate and HR is linear in man breathing in air and immersed head out or underwater (SCUBA): the relation work rate/HR is independent on life conditions. During BH in air the HR decreases quickly when $\dot{V}O_2$ increases; during BHD the HR decreases also quickly in relation to $\dot{V}O_2$ levels but remains at minium values after 20-30 sec. It's possible that the decrease in peripheral chemoreflexes drives to hypoxia: it reflects a similar decrease in primary reflex effects on the heart and the BHD bradycardia degree does not change. The increase thoracic blood shift at high $\dot{V}O_2$ levels anticipate the minimum bradycardia values.

45.4

INFLUENCE OF A CARBOHYDRATE-ELECTROLYTE BEVERAGE ON BLOOD HOMEOSTASIS DURING FOOTBALL. D. Criswell*, S. Powers, J. Lawler, J. Tew *, S. Dodd, , Y. Iryiboz*, R. Tulley *, & K. Wheeler*. Center for Exercise Science and Departments of Exercise and Sport Sciences and Physiology, Univ. of Florida, Gainesville, FL 32611; Applied Physiology Laboratory, LSU, Baton Rouge, LA 70803.

The purpose of this study was to compare the efficacy of a 7% glucose polymer beverage containing electrolytes (GP) vs. a non-nutrient, non-electrolyte placebo drink (P) in maintaining blood homeostasis during football. Forty-four high school football players, divided into two teams and matched for size and ability, participated in a 50-play scrimmage designed to simulate game conditions. At each of six scheduled periods before and during the scrimmage, players consumed 170 ml of the assigned treatment beverage. The experimental design was double blind. Venous blood samples were drawn from 24 subjects before and after the scrimmage and analyzed for Hct, [Hb], [FFA], [lactate], [Na^+], [K^+], [Cl^-] and [Ca^{++}]. Post-exercise changes in body weight and in plasma [Na^+], [K^+], [Cl^-], [Ca^{++}], [lactate] and [FFA] did not differ ($p > 0.05$) between treatments. In contrast, the % decrease in plasma volume was significantly greater ($p < 0.05$) in the P group as compared to the GP group. These data do not support the hypothesis that carbohydrate- electrolyte drinks minimize the exercise-induced disturbances in blood electrolyte concentrations during football; however, these results do suggest that a carbohydrate-electrolyte drink may be more effective in maintaining plasma volume than water alone. Since maintenance of plasma volume is important to thermoregulation and cardiovascular dynamics during exercise, this finding warrants further study.

Supported by a grant from Ross Laboratories.

45.5

PLASMA VOLUME LOSS DURING MAXIMAL EXERCISE IN FEMALES. M.A. Kolka and L.A. Stephenson, US Army Research Institute of Environmental Medicine, Natick MA, 01760-5007.

Four adult females did maximal cycle exercise (T_a = 28°C; T_{dp} = 7°C) in the follicular (F, days 2-6) and luteal (L, days 19-22) phases of their menstrual cycles. After a 5 min warm-up, subjects exercised for 3 min at a workload which previously elicited $\dot{V}O_2$ peak. Blood samples were taken at rest, at the end of exercise, and during 30 min of recovery. Percent change in plasma volume (Δ%PV) was calculated from Hct and Hb and plasma protein concentration (PP) and plasma lactate were measured. Total circulating protein (TCP) was calculated from PP and estimated PV. Resting PV was 9% (0.26*L*) lower in L than F ($p<0.05$). TCP was lower ($p<0.05$) at rest in L (196 ± 12g) than F (214 ± 9g). Maximal exercise decreased PV 12% (0.33*L*) in L and 19% (0.56*L*) in F to 2.39 and 2.36 *L*, respectively ($p<0.05$). TCP decreased 2 g during exercise in L and 27 g in F ($p<0.05$) to 194 ± 16g and 187 ± 13g, respectively. Peak plasma lactate occurred between 2 and 5 min after exercise and averaged 11.3 (±2.2) mmol•L^{-1} in L and 10.7 (±1.7) mmol•L^{-1} in F. These data indicate 1) there appears to be an absolute limit to fluid efflux from the plasma during maximal exercise in females and 2) during maximal exercise in a temperate environment, the rate and total volume of fluid shifted from the vascular volume is different during the proliferative and secretory phases of the menstrual cycle, possibly showing a defense of the plasma protein volume during exercise in luteal-phase experiments.

45.6

ELEVATED CENTRAL VENOUS PRESSURE: A CONSEQUENCE OF EXERCISE TRAINING HYPERVOLEMIA. V.A. Convertino, G.W. Mack, and E.R. Nadel. NASA-Kennedy Space Center, FL 32899; and J.B. Pierce Fndn. Lab., New Haven, CT 06519.

Resting blood volume (BV), and mean arterial (MAP) and central venous pressures (CVP) were measured in 16 men before and after exercise training to determine if training-induced hypervolemia could be explained by a change in total vascular capacitance. Resting levels of plasma vasopressin (AVP), atrial natriuretic peptide (ANP), aldosterone (ALD) and norepinephrine (NE) were also measured. The exercise training program consisted of 10 weeks of controlled cycle exercise for 30 min/d, 4 d/wk at 75-80% of maximal oxygen uptake (VO2max). A training effect was verified by a 20% increase in VO2max, a resting bradycardia, and a 9% increase in BV. MAP was unaltered by exercise training, but resting CVP increased ($P < 0.05$) from 9.5 ± 0.5 mmHg to 11.3 ± 0.6 mmHg. The percent change in BV from before to after training was linearly related to the percent change in CVP ($r = 0.903$, $P < 0.05$). As a consequence of elevations in BV and CVP, the volume-to-pressure ratio was essentially unchanged following exercise training. Plasma AVP, ANP, ALD and NE were unaltered. Our results indicate that elevated CVP is a consequence of training-induced hypervolemia without alteration in total effective venous capacitance. This may represent a resetting of the pressure-volume stimulus-response relationship for regulation of blood volume.

45.7

INTERVAL TREADMILL TRAINING-INDUCED METABOLIC ALTERATIONS IN RESPIRATORY MUSCLES. Scott K. Powers, Stephen Grinton, John Lawler, David Criswell, William Edwards, and Stephen Dodd. Center for Exercise Science, Departments of Exercise and Sport Sciences and Physiology, University of Florida, Gainesville, FL 32611; Mayo Clinic, Jacksonville, FL and Department of Kinesiology, Louisiana State University, Baton Rouge, LA 70803

Limited data exist concerning the cellular alterations that occur in respiratory muscles following interval exercise training. Hence, we examined the metabolic adaptative strategies of both inspiratory and expiratory muscles in rats in response to 12-weeks (5 days/week) of progressive endurance training. Female Sprague-Dawley rats (age = 120 days) were randomly divided into two groups: 1) interval training (N=10; 6 x ~5-min intervals at ~80-95% VO_2 max); and 2) control (N=13). When compared to controls, interval training resulted in significantly elevated ($P<0.05$) activities of succinate dehydrogenase (SDH), 3-hydroxyacyl-Co-A dehydrogenase (HADH), and citrate synthase (CS) in the costal diaphragm, rectus abdominus, external obliques, and the plantaris muscles. In contrast, interval training did not significantly increase ($P>0.05$) the activities of SDH, CS, or HADH in the crural diaphragm, *intercostals*, or internal obliques/transversus abdominus. In general, the training-induced increases in respiratory muscle oxidative activity (i.e. SDH activity) were relatively small (range = 21-31%) when compared to the increase in oxidative capacity of the plantaris muscle (~ 61%). We conclude that increased respiratory muscle work via high intensity interval exercise training results in significant improvements in the oxidative capacities of both inspiratory and expiratory muscles.

45.8

$\dot{V}_A/\dot{Q}$ MISMATCH, BLOOD GAS AND ACID-BASE STATUS DURING AND AFTER EXERCISE IN HYPOXIA. W. Schaffartzik*, D.C. Poole, T. Derion*, K. Tsukimoto*, M. Hogan, J. Arcos*, D.E. Bebout and P.D. Wagner. Dept. of Med., U.C. San Diego, La Jolla, CA 92093

$\dot{V}_A/\dot{Q}$ mismatch increases during heavy exercise and one putative mechanism for this is the development of interstitial pulmonary edema. We hypothesized that persistence of $\dot{V}_A/\dot{Q}$ mismatch well into the recovery period would be consistent with edema; however, rapid resolution would point to mechanisms likely related to changes in ventilation and blood flow per se. 13 healthy males performed maximal cycle ergometry at P_IO_2~91 Torr. Cardiorespiratory variables and inert gas elimination measurements were made during exercise and 30 min of recovery. Two profiles were evident: 1) increase in $\dot{V}_A/\dot{Q}$ mismatch during exercise ($logSD_Q$ at rest 0.35±0.02, at exercise 0.44±0.02; $p<0.05$), returning to resting values within 2 min of recovery (n=7, G_1), 2) no change in $\dot{V}_A/\dot{Q}$ mismatch (n=6, G_2). There were no differences in anthropometric values, work rate, peak $\dot{V}O_2$ or peak ventilation between groups. However, compared with G_2, G_1 evidenced: a) lower P_aO_2 and higher P_aCO_2 in exercise and recovery, b) higher blood lactate (G_1: 13.1±2.1 mM; G_2: 10.2±0.7 mM) and lower pH_a (G_1: 7.18±0.04; G_2: 7.26±0.02; $p<0.05$), and c) higher cardiac index at maximal exercise (G_1: 12.8±0.3; G_2: 10.7±1.0 $l.min^{-1}.m^{-2}$; $p<0.05$) and through 6 min of recovery. We conclude that: 1) the time course of recovery from this mild increase in $\dot{V}_A/\dot{Q}$ inequality following exercise in hypoxia is probably not consistent with the presence of exercise-induced pulmonary edema, and 2) subjects developing increased $\dot{V}_A/\dot{Q}$ mismatch during exercise evidence greater perturbation of blood gas and acid-base status during exercise and recovery, the reasons for which are, at present, unclear.
Supported by NIH (17731), Am. Lung Assoc. of CA and DFG 452/1-2.

45.9

LIMITATIONS OF O_2 UPTAKE IN TISSUE MODELS WITH UNEQUAL DISTRIBUTION OF BLOOD FLOW. J. Piiper Department of Physiology, Max Planck Institute for Experimental Medicine, Göttingen, Germany

In many experimental studies on isolated muscles and in the whole organism, the maximum O_2 uptake has been found to decrease, along with the venous O_2 pressure, as the O_2 availability (=blood flow x arterial O_2 content) is reduced. This behavior has been attributed to diffusion limitation in O_2 uptake by exercising muscles. But in such analyses the heterogeneity of O_2 supply conditions has not been considered, although there is ample evidence for unequal distribution of blood flow in resting and exercising muscle (by microsphere embolization, inert gas washout and other methods). Calculations on tissue models with unequal and equal distribution of blood flow with respect to O_2 requirement, assuming venous blood to be in O_2 equilibrium with tissue (no diffusion limitation) showed the following features. (1) With unequal blood blow distribution, the O_2 uptake/O_2 requirement ratio started dropping below unity at a higher value of the O_2 availability/O_2 requirement ratio (critical value) than in the model reference. (2) Reduction of the O_2 availability/O_2 requirement ratio below the critical value leads to an abrupt fall of the O_2 uptake/O_2 requirement ratio at zero venous O_2 in the model with equal blood flow distribution, but to a gradual decrease of the O_2 uptake/O_2 requirement ratio with gradually decreasing venous O_2 content in the model with unequal distribution of blood flow. Thus a parallel decrease of the O_2 uptake and venous O_2 content (or O_2 partial pressure) upon decrease of O_2 availability is not necessarily due to diffusion limitation, but may also be caused by unequal distribution of blood flow.

45.10

EFFECT OF HIGH OXYHEMOGLOBIN AFFINITY ON $\dot{V}O2_{MAX}$ IN GOLDENMANTLED GROUND SQUIRRELS. William K. Milsom and Sarah F. Bradley*. Department of Zoology, University of British Columbia, Vancouver, B.C., V6T 2A9, Canada.

Hibernation and exercise are opposite extremes of metabolism and adaptations for one function may, in many cases, affect processes invloved in the other. It has recently been shown that goldenmantled ground squirrels (*Spermophilus lateralis*) have a relatively high affinity hemoglobin (FASEB J. 3:A234). Their half-saturation PO_2 (P_{50}) at 37°C and pH_i 7.49 is 18.1 ± 0.5 torr. Although this may greatly aid oxygen loading at the lungs under hypoxic conditions, which may occur in burrow environments, it should also reduce tissue diffusion rates. This may limit the rate of maximum oxygen consumption ($\dot{V}O2_{max}$) during exercise. In this study we examined this possibility by measuring oxygen consumption in animals during sleep, at rest, and during exercise to $\dot{V}O2_{max}$ on a treadmill. We found that metabolic rate fell by 45% during sleep and that both resting and sleeping metabolic rates fell significantly (~ 40%) during the winter months. The data also indicated that both $\dot{V}O2_{max}$ (35.8 ml O_2/min) and metabolic scope (7.41 x resting metabolic rate) were no different than those of rats, despite a 20 torr difference in P_{50} (~ 38 torr for rats). This suggests that the squirrels must have adaptations at the tissue level (increased capillary surface area, decreased diffusion distances, etc.) which compensate for the reduced capillary O_2 driving pressure. Supported by the NSERC of Canada.

45.11

RECOVERY FROM BURST EXERCISE IN RAINBOW TROUT WHITE MUSCLE: THE ROLE OF THE MITOCHONDRIA. Christopher D. Moyes, Patricia M. Schulte, Peter W. Hochachka. Univ. of British Columbia, Vancouver, B.C. V6T 2A9

Recovery from burst exercise in trout typically requires 12hr. Resynthesis of glycogen from lactate occurs primarily in situ: Energy for gluconeogenesis must be derived from aerobic (mitochondrial) metabolism. This study examines the regulation of white muscle mitochondrial metabolism by those extramitochondrial parameters characteristic of recovery from burst exercise (lactate, pyruvate, pH). White muscle mitochondrial pyruvate oxidation is markedly sensitive to [pyruvate] over the physiological range observed post-exercise. These kinetics are unlike those observed with carp red muscle, where the mitochondrial pathway is saturated at physiological [pyruvate] (50 uM) and regulation of pyruvate dehydrogenase (PDH) controls pyruvate metabolism. In recovery from burst exercise white muscle PDH activation state shows only modest changes in the 24 hrs post-exercise. White muscle pyruvate oxidation (100uM) is markedly inhibited by lactate (50% at 40 mM lactate). These observations are consistant with the hypothesis that white muscle pyruvate oxidation is limited by transport into the mitochondrion. These results are discussed in the context of energy demands for gluconeogenesis from lactate in white muscle post-exercise. (Supported by NSERC Canada).

45.12

INCREASE IN PLASMA POTASSIUM CONCENTRATION ($[K^+]p$) MAY NOT BE RESPONSIBLE FOR THE REDUCTION IN EXERCISE CAPACITY ASSOCIATED WITH BETA BLOCKADE (βB).
RS McKelvie*, NL Jones, GJF Heigenhauser. McMaster University. Hamilton, Ontario.

Previous studies have demonstrated that subjects taking βB have a reduced exercise capacity. Some authors have suggested this may be related to an increase in $[K^+]p$ which would alter the resting membrane potential of the muscle. The purpose of this study was to examine the effects of βB on incremental (IE) exercise capacity and $[K^+]p$ during IE. Five healthy male subjects performed IE with the power output increased every 2 min by 200 kpm/min. Arterialized venous blood was sampled during IE. The IE was performed during control (C) conditions; low dose (LD) (40 mg daily) and high dose (HD) (265±4.3 mg daily) propranolol. During IE VO_{2max} was significantly reduced with HD compared to C (C 3.7±0.34 l/min; LD 3.7±0.21 l/min; HD 3.5±0.50 l/min). $[K^+]p$ was increased with βB, with no significant difference between the LD and HD at maximum exercise (C 5.8±0.3 meq/l; LD 6.3±0.1 meq/l; HD 6.1±0.2 meq/l). Results from this study suggest that changes in $[K^+]p$ may not be responsible for the reduction in IE capacity observed with βB.

45.13

PROGRESSIVE DECREASE OF EXERCISE TOLERANCE IN CANINES WITH EVOLVING HEART FAILURE: RELATION TO CARDIAC FUNCTION. T. Kono*, H.N. Sabbah, P.D. Stein, and S. Goldstein*. Henry Ford Heart and Vascular Institute, Detroit, MI, 48202.

Exercise tolerance and LV function were evaluated in 6 dogs during the course of evolving heart failure produced by multiple sequential intracoronary embolizations with microspheres. Exercise tolerance was based on maximum treadmill exercise duration (MED) achieved using a modified Bruce protocol. The protocol was limited on the upper end to 5.0 mph and 12% grade. Each dog was exercised until it refused to exercise further. MED was evaluated at baseline (B), prior to embolization, and at 9, 13, and 20 weeks thereafter. LV function was evaluated during cardiac catheterization performed 1 week after exercise testing. Values of MED, LV ejection fraction (EF), end-diastolic volume (EDV), and end-diastolic pressure (LVEDP) are shown.

	B	9 Weeks	13 Weeks	20 Weeks
MED (min)*	31±7	23±12	20±6	16±2
EF (%)**	61±7	43±11	30±4	25±5
EDV (ml)**	59±9	59±10	89±13	105±29
LVEDP (mmHg)**	6±2	22±6	26±9	29±8

[*=P<.05;**=P<.01 based on ANOVA]

In this canine preparation, the gradual decrease in MED during the evolution of heart failure was associated with progressive LV dysfunction. The preparation may be suitable for examining the pathophysiology of exercise intolerance that accompanies heart failure.

45.14

INCREASED CAPILLARY FILTRATION INCREASES WOVEN BONE FORMATION. PJ Kelly, TH Meadows*, JT Bronk*. Mayo Foundation, Rochester, MN 55904

Fluid filtration through the capillary can be determined by steady state measurements utilizing volume of distribution techniques of plasma, red cells, and sucrose. We examined the effect of impact loading on fluid spaces of a cortical tibial defect. Bilateral cortical defects were created in the midtibial diaphysis of 34 adult dogs. The dogs were divided into 2 groups and fluid spaces were measured at three time intervals. The experimental group (n=19) had one hind leg elevated by means of a cast strap. This caused the opposite limb to become overloaded. The control group (n=15) bore weight in normal fashion. Five control dogs were sacrificed at each time period. The experimental animals were sacrificed at the same time periods as controls 7 days (n=6), 14 days (n=8), and 28 days (n=5). The values of the right and left defects of the control groups were meaned for comparison to the experimental group.

Interstitial Fluid Space (S.E. ± ml/ml)

	7 days (n=6)	14 days (n=8)	28 days (n=5)
Up	0.72 ± 0.04	0.58 ± 0.04	0.58 ± 0.06
Down	0.86 ± 0.05	0.64 ± 0.04	0.57 ± 0.04

Woven Bone Defect (%)

Up	7.76 ± 0.56	49.25 ± 2.65	54.52 ± 4.71
Down	12.58 ± 3.27	54.00 ± 2.59	75.72 ± 4.67

At 7 days and 14 days, interstitial fluid space (ISF) of the overloaded defect was significantly greater ($p<0.05$) than the elevated. At 28 days there was no significant difference between the overloaded and elevated defects likely due to the increased woven bone formation. There was no significant difference between the defects of the control group. The differences observed between the legs are due to increased impact loading. Impact loading increases capillary filtration, which may increase extracapillary perfusion of the osteoblasts. By 28 days this led to more woven bone in the cortical defect of the overloaded tibia.

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45.15

17β-ESTRADIOL, PROGESTERONE, GROWTH HORMONE AND METABOLIC RESPONSES TO PROLONGED EXERCISE AT VARIOUS PHASES OF THE MENSTRUAL CYCLE. J.A. Kanaley*, R.A. Boileau*, J.M. Bahr*, J.E. Misner* and R.A. Nelson* (SPON: F.G. Knox). Department of Kinesiology, Animal Sciences and Internal Medicine, University of Illinois, Urbana-Champaign, IL 61801.

The purpose of this study was to examine the importance of menstrual phase on the 17β-estradiol (E_2), progesterone (P), human growth hormone (GH) and metabolic responses to 90 minutes of treadmill running (60% VO_2max) in 8 eumenorrheic athletes. Subjects were tested in the early follicular (EF) (day 3-5), late follicular (LF) (day 13-15) and mid-luteal (ML) (day 20-22) phases. Blood samples were taken at rest, every 10 minutes throughout exercise and 5 and 15 minutes post-exercise. No phase-related differences in the integrated area under the curve (AUC) for E_2 and GH were observed (AUC - E_2: EF, 229.1 ± 61.8; LF, 383.2 ± 116.4; ML, 181.2 ± 84.1; GH: EF, 34.9 ± 13.4; LF, 61.9 ± 21.6; ML, 48.1 ± 12.8; $P > 0.05$). AUC for P showed significant phase-related differences (EF, 0.96 ± 0.4; LF, 2.35 ± 1.4; ML, 19.7 ± 8.5; $P < 0.01$). In addition, the pattern of P response was significantly different between phases ($P < 0.01$). Metabolism, as reflected by carbohydrate (CHO) and fat utilization, was found to be independent of phase of the menstrual cycle. It is concluded that the elevated E_2 levels in the LF phase do not influence E_2 or GH release during exercise, while menstrual phase influences the P release during exercise. It is also concluded that menstrual phase does not influence metabolism as reflected in the relative CHO and fat utilization. Supported by IAHPER.

45.16

VENTILATORY PATTERN CHANGES DURING THE MENSTRUAL CYCLE. **T. Williams, M.S.,* K. Beck, Ph.D, & B. Staats, M.D. Mayo Clinic & Foundation, Rochester, MN 55905**

In a previous study (Physiologist 30:133, 1987) we observed that progesterone (P), ventilation ($\dot{V}_E$), basal body temperature (T), and indices of ventilatory response to CO_2 increased during the luteal (L) phase of the menstrual cycle when compared to the follicular (F) phase. The maximal increases in T and P were coincident with the rise in CO_2 response but tended to lead by several days the increase in exercise $\dot{V}_E$. In this study, we analyzed the pattern of ventilation increase to determine if subtle changes in respiratory rate (RR), tidal volume (TV), timing (Ti/Ttot--inspiratory time/total breath duration), or drive (VT/Ti) were altered prior to the effect on overall T, CO_2 response, and $\dot{V}_E$. Nine untrained women (ages 26-33) performed a rebreathing CO_2 response and constant load exercise with ventilatory variables analyzed at rest, 30, 70 and 90 watts. The studies were performed on 8 occasions during one menstrual cycle: 1 F and 7 L. For each subject comparing the L days to the F day (by paired analysis), we found no differences in TV but RR was increased at 30 and 70 watts concurrent with the increase in $\dot{V}_E$. Ti/Ttot was unchanged throughout the cycle, but TV/Ti was increased at 30 and 70 watts. The temporal increase in TV/Ti matched that of $\dot{V}_E$, T, and indices of CO_2 responsiveness. In general, phasic changes in the menstrual cycle were more noticeable at 30 and 70 watts than at rest or 90 watts. We conclude that the initial rise in P in the L phase does not appear to have an effect on ventilatory pattern, drive, or timing; all changes we observed were temporally related to the menstrual-cycle-induced increases in $\dot{V}_E$ and CO_2 responsiveness. **(Funded by Minnesota Lung Association)**

45.17

INFLUENCE OF TRAINING ON THE RESTING BLOOD PRESSURE OR NORMOTENSIVE RATS CONSUMING A DIET HIGH IN FAT AND SUCROSE. H. A. Drummond*, L.A. Sebastian*, P. K. Edwards*, R. K. Coomes*, and C. M. Tipton. Dept. Exercise and Sport Sciences, The Univ. of Arizona, Tucson, AZ 85721.

Diets high in fat and carbohydrates have been associated with elevated resting systolic blood pressure (RSBP), presumably because of their effects on the sympathetic nervous system or on plasma insulin concentrations. To gain insights on the role of chronic exercise (training) on this matter, we initiated a 16 week study with adult male normotensive rats randomly assigned to control (C), exercise trained (T), or control-weight matched (C-WM). After baseline measures were secured, the rats were fed a diet of 40% fat, 45% sucrose and 15% protein (Teklad 1202). RSBP at weeks 0, 8 and 16 with $\dot{V}0_2$ max and body weight (BW=grams) at week 16 are listed below ($\bar{X}$±SE).

Group	(N)	Week 0	Week 8	Week 16	$\dot{V}0_2$max	BW
C	9	156±3	175±3	188±4	56±2	488±8
C-WM	8	155±3	165±3*	158±4*	56±4	421±7*
T	6	154±3	154±3*	148±4*	68±3*	417±8*

*ANOVA at P<.05 when compared to C.

Total Kcal consumed per gram BW over 48 hours were C = .49±.02, C-WM = .48±.02, and T = .59±.02*. Preliminary analysis suggests that the deltas between the C and C-WM groups were associated with weight differences, whereas the deltas between the C-WM and T were related to training mechanisms. Supported by NIH HL33782-04.

45.18

AUTOMATED INSTRUMENTATION FOR SIMULTANEOUS PHYSIOLOGICAL MONITORING, MECHANICAL CONTROL, AND DATA COLLECTION IN EXERCISING PRIMATES. W.R. Constable* and B. Ulrich* (SPON: S.H. Constable) USAF School of Aerospace Medicine, Brooks AFB, TX 78235 and Rothe Development Corp.

Using the programming language LabVIEW 2.0 (National Instruments, Austin, TX), and a Macintosh IIX computer system, a novel, flexible and powerful method for the complete automation of a data collection and exercise program for non-human primates has been developed. The system monitors wheel activity in the free wheel mode, while providing visual, acoustic and electromechanical cues at user specified thresholds. Exercise intensity may be precisely controlled by the system when in the motor driven mode. Work-rest cycles, if required, are user defined. Environmental and physiological temperatures are collected on single-ended analog channels while respiratory data is collected on differential-input analog channels. Heart rate is determined by counting pulses over a user defined period. Other physiological data is telemetered and interpreted by counting pulses and linearizing the frequency. After translating the signals, calculations are made where necessary. The program then proceeds to print and store the data at user defined intervals. Once the user has defined the necessary inputs, the experiment can run itself with no further hands-on involvement. The user can, however, by changing switches on the front panel, or entering new variables, change the parameters of the experiment as required at any point in the experiment. The incorporation of this novel programming approach with standard laboratory instrumentation has greatly simplified the process of development, calibration, and system maintenance while providing a powerful graphic user interface.

45.19

EFFECTS OF EXERCISE-TRAINING AND IMMERSION ON RENAL AND CARDIOVASCULAR RESPONSES TO TAIL-SHOCK STRESS IN MALE BORDERLINE HYPERTENSIVE RATS (BHR). D.E. McCoy, J.E. Steele, R.H. Cox*, R.L. Wiley*, and G.J. McGuire. Departments of Zoology and Physical Education, Health, and Sports Studies. Miami University, Oxford OH 45056.

The effects of tail-shock stress (TSS) on renal and cardiovascular function were assessed in swim-trained (T), untrained (UT), and water immersed (IM) BHR. Urine flow rate (UFR), glomerular filtration rate (GFR), renal blood flow (RBF), heart rate (HR), and blood pressure (BP) were measured in T, UT, and IM BHR before, during, and after 40min of TSS (1s shock; 0.2mA every 30s). T rats swam for 2h/day, 5day/wk for 10wks. IM rats were placed in neck-high water for 2h/day, 5day/wk for 10wks. All BHR were exposed to the restraint apparatus and TSS paradigm for 2wks prior to data collection. UFR was significantly greater ($p<.05$) during the first 20min of TSS than at rest in UT and IM BHR and remained elevated during the second 20min of TSS. T BHR showed no change in UFR during TSS. GFR, although increased during the first 20min of TSS in UT BHR, was not significantly different from rest in T, UT, and IM BHR. RBF was significantly decreased ($p<.05$) from rest during TSS in UT and IM BHR. RBF was not significantly different from rest during TSS in T BHR. HR was significantly increased ($p<.05$) during TSS in all groups. HR in T BHR was significantly lower ($p<.05$) than both UT and IM BHR at rest and during TSS. SBP and DBP were significantly increased ($p<.05$) during TSS in all groups. SBP and DBP were higher in T BHR but were not significanlty different from UT and IM BHR. These results suggest that swim-training alters renal and cardiovascular responses to tail-shock stress in BHR and that these responses in T BHR are not the result of shifts in fluid volume in response to repeated immersion in water.

45.20

THE ACCURACY OF MEASUREMENTS OF SMALL CHANGES IN SOFT TISSUE MASS USING DUAL PHOTON ABSORPTIOMETRY

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Dual-photon absorptiometry (DPA) has recently been applied to the assessment of body composition. To evaluate the accuracy of DPA in detecting small changes in the lean soft tissue mass, six healthy adult males were studied before and after the addition and removal of fluid. In each subject DPA was performed twice on 2 occasions, once prior to and following a 30 ml/kg transfusion of saline, and once prior to and following transpiration resulting in at least a 1 kg weight loss. Absolute weight and weight changes due to transfusion and transpiration were accurately reflected in the DPA total mass ($r^2=0.999$, $r^2=0.98$, respectively). Weight changes were more accurately measured by changes in DPA soft mass ($r^2=0.98$) than by changes in DPA nonfat (lean + mineral) tissue ($r^2=0.73$) and lean soft tissue ($r^2=0.73$). DPA-derived nonfat mass was highly correlated with skinfold-derived nonfat mass ($r^2=0.96$). Accuracy of total and soft tissue measurements implied correct mineral mass assessment. The poorer correlations involving the lean compartment reflected the difficulty of discriminating between lean and fat soft tissue. Although DPA is excellent for the evaluation of mineral mass and changes in the soft tissue mass, the inability of the technique to assign the increase in soft tissue into its lean and fat components limits its applicability in following body composition changes for individual subjects.

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GRAVITATIONAL BIOLOGY

46.1

EXERCISE WITHIN A VACUUM CHAMBER TO SIMULATE GRAVITY DURING SPACE FLIGHT. A.R. Hargens, R.T. Whalen*, D.E. Watenpaugh*, D.F. Schwandt*, and L.P. Krock. Life Science Div. (239-11), NASA-Ames Res. Ctr., Moffett Field, CA 94035 & Crew Tech. Div., Brooks Air Force Base School of Aerospace Medicine, TX 78235.

Presently, exercise protocols and equipment for space flight are unresolved, although recent calculations suggest that all exercise in space to date has lacked sufficient loads to maintain preflight musculoskeletal mass. With a hypothesis for using lower body negative pressure (LBNP) to create musculoskeletal and vascular loads during exercise in microgravity, we calculated and then directly measured the footward forces generated by LBNP during upright-standing and supine postures. Twelve male volunteers weighing 67.6-86.9 kg were sealed at the superior iliac crest in upright and supine LBNP chambers. Neither configuration included a saddle so that the force due to LBNP was transmitted to the feet of our subjects. Each subject was exposed to 10 mmHg increments of LBNP up to 70 mmHg (standing) or to 50-100 mmHg (supine), depending upon individual tolerance. Static reaction force was measured at each LBNP level for approximately 1-2 minutes. An additional static force approximately equivalent to one Earth body weight was generated against the feet by each 100 mmHg of LBNP either during upright standing or supine posture. Theoretically, recumbency is more analogous to actual microgravity because the footward gravitational vector is absent. These results indicate that exercise within a vacuum chamber could produce static and inertial forces similar in magnitude to those occurring on Earth. This gravity-independent technique may help maintain the musculoskeletal and cardiovascular systems of crew members during prolonged exposure to the microgravity. (Supported by NASA-Ames Research Center and Brooks Air Force School of Aerospace Medicine)

46.2

SKELETAL GROWTH AND DEVELOPMENT IN FASTING NORTHERN ELEPHANT SEALS. Patricia Patterson-Buckendahl,* C.L. Ortiz, and C.E. Cann. Department of Biology and Institute of Marine Sciences, University of California, Santa Cruz, CA 95064, and Department of Radiology, University of California, San Francisco, CA 94143.

Rapid musculoskeletal growth is a major physiological characteristic of post-natal and juvenile life of mammals. The Northern elephant seal *(Mirounga angustirostris)*, however, spends two to three months after weaning in a total fast before going to sea to feed and returns twice a year to fast on land to molt (spring) or reproduce (fall). Juveniles haulout in the fall for more obscure reasons. Peril from shark attacks and the incompatibility of fasting with normal growth have led us to investigate the possibility that important musculoskeletal development must take place on land under gravitational loading. Protein turnover in fasting elephant seals is as rapid if not greater than in normally feeding animals, suggesting that muscle development does occur (Ortiz, et al). Because muscle and bone development are interdependent, we wished to determine whether fasting elephant seals form new bone, and if so, whether it differs from that formed at sea. Two CT scans of a live weanling pup showed that the forelimb bones increased 10% in length and 10-25% in volume during the intervening three weeks. Histomorphometric analysis of ulnae from pups and juveniles which died of natural causes while on land showed that 20 to 45% of the bone surface was actively involved in remodeling, confirming the capability for skeletal growth during the fast. Examination of bone sections from juveniles by back-scattered electron microscopy shows that porosity, mineral density, and mineral composition vary in a cyclic manner consistent with changes in nutritional status and/or gravitational loading. (Supported in part by NIH-MBRS RR-08132)

46.3

RESPONSE OF HINDLIMB MUSCLES OF THE RHESUS MONKEY TO A 14-DAY SPACE FLIGHT (COSMOS 2044) AS DETERMINED BY MUSCLE BIOPSIES S. Bodine-Fowler, R. R. Roy, J. Kim*, W. Rudolph*, N. Haque* and V.R. Edgerton Div. Orthopaedics & Rehabilitation, UCSD, San Diego, CA 92161, and Dept. Kinesiology and Brain Research Institute, UCLA, Los Angeles, CA 90024

Space flight has been shown to cause considerable atrophy in hindlimb muscles of the rat (Martin, T.P. et al., *JAP*: 65:2318, 1988; Miu, B. et al., *FASEE J.* 4: 65, 1990). The purpose of this study was to investigate the effect of a 14-day space flight (Cosmos 2044) on the morphological and metabolic properties of hindlimb muscles in a non-human primate, *Muccaca Mulatta*. Muscle biopsies were taken from the soleus (Sol), medial gastrocnemius (MG) and tibialis anterior (TA) muscles of two Rhesus monkeys 45 days prior to the flight and 1 day after the flight. During the 60-day period between the pre and postflight biopsies, each monkey gained ~300 g of body weight. Muscle biopsies, weighing ~8-14 mg, were taken from two independent sites in each muscle of the using a 3 mm Bergstrom biopsy needle. In the Sol of both flight monkeys, the mean cross-sectional area of fibers taken from postflight biopsies was significantly larger than fibers from preflight biopsies. This growth in fiber size paralleled the growth observed in control monkeys of the same age and size. The mean SDH activity of the muscle fibers from pre and postflight biopsies were not significantly different in the Sol of both flight monkeys. Muscle fibers in the postflight biopsies of the MG and TA were significantly larger in one flight monkey and unchanged in the other flight monkey. The lack of growth in the fibers of the MG and TA of the one monkey suggests that space flight may have caused some atrophy in these muscles, since the fibers in the MG and TA of control monkeys increased in size. The apparent differences in the response of the Sol, MG and TA in rats vs. Rhesus monkeys to space flight may be related to the manner in which the animals are restrained and/or the possibility that the monkeys are doing some exercise with their unrestrained foot. Supported by NASA grant # NCC 2-535.

46.4

OXIDATIVE CAPACITY AND SOMA SIZE OF LUMBAR MOTONEURONS AFTER SPACE FLIGHT AND HINDLIMB SUSPENSION. B. Jiang*, R. R. Roy and V. R. Edgerton. Brain Research Institute, UCLA, LA, CA 90024-1568.

Space flight or hindlimb suspension (HS) results in a decreased mass and in alterations of the metabolic and contractile protein profiles of skeletal muscles towards that resembling "faster" muscles. Given the potential influence of motoneurons (MN) on muscle properties, MNs of the lumbosacral segment of the spinal cord were studied in 3 groups of rats (n = 5/group): 14-day space flight (Cosmos 2044, Fl), synchronous control (Con) and 14-day HS. Succinate dehydrogenase (SDH) activity and cross-sectional area (CSA) of the soma of MNs were measured using a modification of the procedures described by Chalmers et al. (J Histochem Cytochem 37:1107, 1989). SDH reaction product formation was linear with incubation times of 2-12min. Thus, optimal SDH activity (optical density, OD) was measured at 8min. Soma size was determined for MNs in which there was a visible nucleus.

Group	n	SDH($OD \cdot min^{-1} \times 10^{-2}$)	n	CSA(μm^2)
Con	323	4.54 ± 0.46	293	417 ± 91
Fl	360	4.81 ± 0.41	319	351 ± 82
HS	389	4.02 ± 0.45	351	410 ± 90

There were no significant differences in MN mean SDH (±SEM) activity among the 3 groups. The mean CSA (±SEM) in Fl rats was 16% smaller ($P>0.05$) than Con and there was a shift toward smaller somas in Fl compared to Con rats. In Con rats, the smaller MNs showed a wide range of SDH activities, whereas the larger MNs consistently had relatively low SDH activities. These interrelationships between size and SDH activity were maintained in Fl and HS groups. These data indicate that the oxidative potential of lumbar MNs was unaffected by "unloading", whereas soma size seemed to be mildly affected by space flight. These results are in marked contrast to the dramatic decreases in mass and/or oxidative potential of some muscle fibers innervated by these lumbar MNs. These data suggest that MN size and metabolic integrity are not as markedly affected by "unloading" as the muscle fibers they innervate. Supported by NASA Grant # NCC 2-535.

47.1

EFFECTS OF ENDOTHELIUM REMOVAL ON CEREBRAL ARTERY AUTOREGULATION AND RESPONSES TO HYPOXIA AND HYPERCAPNIA. Nan A. Norins and Jane A. Madden, The Medical College of Wisconsin and Zablocki V.A. Medical Center, Milwaukee, WI 53295.

We examined the effect of endothelium removal on autoregulation and on the response to hypoxia and hypercapnia in feline middle cerebral arteries. Approximately 8 mm long cerebral artery segments were mounted on glass cannulas (with all side branches tied off) in a chamber containing warmed, gassed (PO_2= 140 torr, PCO_2 = 37 torr, pH 7.4) physiological saline solution (PSS). Internal pressure was adjusted by raising or lowering a reservoir filled with the same PSS and connected to the inflow cannula. The vessels were observed with a video system and their diameters measured. Following a 90 minute equilibration at 100 mm Hg, the vessels were tested for a functional endothelium by measuring the dilatory the response acetylcholine (ACH; 10^{-6}M) after constriction with norepinephrine (NE; 10^{-6}M). Vessel diameters were measured as pressure was raised in 20 mm Hg steps from 60 to 140 mm Hg. As expected, vessel diameters either did not change or decreased slightly throughout the *pressure range*, indicating autoregulatory ability. The arteries were then exposed to low O_2(< 50 torr) or high CO_2 (65 torr) and the diameters remeasured over the pressure range. The vessels were returned to control conditions and the endothelium mechanically removed. Contractions to NE were of the same magnitude as before endothelium removal and exposure to ACH did not produce any dilation. The pressure/diameter curves repeated under control conditions were not different from those obtained in endothelium intact vessels. Curiously, arteries without endothelium appeared to be more responsive to hypoxia and hypercapnia than vessels with endothelium, and the autoregulatory response appeared to be preserved under these conditions. These data indicate endothelium removal does not compromise autoregulatory ability in cerebral arteries. However, the dilatory responses to hypoxia and hypercapnia after endothelium removal suggests that a mechanism other than the release of prostacyclin may play a role.

47.2

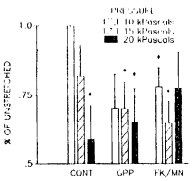
ISOLATED VASCULAR RINGS CANNOT PREDICT STENOTIC RESPONSES **William P. Santamore, Kun S. Li, Francis D. Ferdinand, Thomas N. Tulenko Philadelphia Heart Institute, Presbyterian Medical Center, Philadelphia, PA 19104**

Isolated ring preparations examine isometric or isotonic vascular contractions. However, in a stenosis, the contraction is neither isometric nor isotonic. Thus, we hypothesized that vascular ring preparations might not be able to predict stenotic hemodynamic responses. Canine carotid arteries were isolated and perfused with a physiological salt solution under constant pressure (100 mmHg) and with a fixed distal resistance. After creating an intraluminal stenosis, proximal pressure, distal pressure, flow, and arterial dimensions were continuously recorded as norepinephrine (NE) was added to the perfusate. The proximal diameter was considered to represent solely the effects of vasoconstriction, while the stenotic diameter was also affected by stenotic pressures. The stenotic diameter shortened significantly more than the proximal diameter (1.2 ± 2 vs. 0.5 ± 0.1 mm, $P<0.01$) and the half maximum effective doses (ED_{50}) were significantly interrelated for distal pressure and stenotic diameter data and unrelated for proximal diameter data. In another set of experiments, we added nitroglycerin (NTG) either before or after NE (10^{-9}M-10^{-6}M). Adding NTG (10^{-7}M) before NE shifted the ED_{50} from 7.77 X 10^{-8} to 1.50 X 10^{-6}. Adding 10^{-7}M NTG did not reestablish flow: 3.16x10^{-6}M NTG was required to reestablish flow (23.2 ± 2.7 ml/min.). This vasodilation response did not occur in isolated arterial rings (NE + NTG = 38.7 ± 8.1gm/cm^2, NTG + NE = 45 ± 2.1gm/cm^2, $P<0.05$). Thus, with prior administration of NTG, higher concentrations of NE were needed to decrease flow. More importantly, without prior vasodilation after vasospasm, the same concentration of NTG did not reestablish flow. Thus, quantitatively and qualitatively significant different responses were obtained in stenotic arteries versus arterial rings. These differences may be secondary to the intraluminal pressure changes.

47.3

STRETCH-DEPENDENT INHIBITION OF ADENYLATE CYCLASE ACTIVITY IN PORCINE CORONARY VASCULAR SMOOTH MUSCLE CELLS. Ira Mills and Henry Gewirtz. Rhode Island Hospital, Brown University, Providence, RI 02903

We tested the hypothesis that adenylate cyclase (AC) in coronary vascular smooth muscle cells (VSMC) is sensitive to the degree of pulsatile stretch and thus could be involved in myogenic responses of the coronary circulation. VSMC were plated on collagen coated flexible-bottomed wells (3×10^5 cells/well) and allowed to seed for 48 hours. VSMC were then subjected to vacuum-operated cyclic deformation (0.5s strain, 0.5s relaxation at 60 cycles/min X 30 min) at pressures of 10, 15 and 20 kPascals. Unstretched VSMC were used as controls. VSMC were homogenized and membrane preparations (27,000 x g; n=5) were prepared. Membranes were assayed for AC activity under basal (CONT), slightly stimulatory (0.1 uM Gpp(NH)p)(GPP), or maximally stimulatory (100 uM forskolin with 5 mM $MnCl_2$)(FK/MN) conditions as shown below (% of unstretched $\pm$ SEM;*,P<0.05 vs. unstretched controls). Unstretched AC activities (pmoles of cyclic AMP/min/mg) were as follows: CONT, 4.0±1.2; GPP, 16.7±4.3;MN/FK 286±43. Basal AC activity was inhibited in a stretch-dependent manner. Stimulated AC in the presence of GPP or FK/MN was less dependent on the level of pressure studied but were significantly reduced versus unstretched controls at 2 of the 3 pressures examined. These data provide evidence supportive of a role of AC in myogenic responses of the coronary circulation.



47.4

CORONARY VASODILATION DECREASES MYOCARDIAL FUNCTION. W. Velez, H.J. Mass, E.A. Pou, O.I. Santiago and K.W. Scheel. Department of Physiology, Ponce School of Medicine, Ponce, Puerto Rico 00732 and Department of Physiology, Texas College of Osteopathic Medicine, Ft Worth, TX 76107

The purpose of this study was to determine the relationship between increases in coronary flow (CBF) and myocardial segment function. Using an isolated, empty beating heart, we measured segment function with ultrasonic crystals. Injections of adenosine or chromonar increased CBF in the circumflex artery. As CBF was increased to 25% above control levels, percent segment shortening (%SL) increased 22%, end-diastolic length (EDL) increased 12% and velocity of shortening (dL/dt) increased 25%. However, CBF of levels greater than 75% of control resulted in decreases in %SL and dL/dt of 18 and 12%, respectively. EDL, however, increased 11%. To determine the influence of workload, we examined this relationship in open-chest preparations. Increases of 22% and 21% in %SL and dL/dt were seen with a 25% increase in CBF. However, CBF above 110% of control led to 18 and 15% decreases in %SL and dL/dt. This data suggests the presence of an optimal range between CBF and regional segment function, and appears independent of workload. **Supported by NIH HL35030, RR08239 and the Puerto Rico Heart Association.**

47.5

MYOCARDIAL FUNCTION EXHIBITS AUTOREGULATION. H.J. Mass*, S.E. Williams, O.I. Santiago*, and K.W. Scheel, Department of Physiology, Texas College of Osteopathic Medicine, Ft Worth, TX 76107

We studied the relationship between myocardial segment function and coronary flow in an isolated, blood perfused beating heart preparation. We measured myocardial segment function (percent segment shortening, %SL, and velocity of shortening, dL/dt) in the circumflex perfusion region with ultrasonic crystals. Coronary flow was measured with an electromagnetic flow probe. As perfusion pressure was varied in 10 mmHg increments between 20 and 150 mmHg we found that in the pressure region between 80 and 110 mmHg, flow remained relatively constant. %SL and dL/dt also remained relatively constant between these pressures. It would therefore appear that function as well as flow behaves in an autoregulatory manner. **Supported by NIH HL35030, a grant from the Texas Heart Association and Puerto Rico Heart Association.**
*Department of Physiology, Ponce School of Medicine, Ponce, Puerto Rico.

47.6

CORONARY PULSE FLOW AS AN INDEX OF REGIONAL SEGMENT FUNCTION. O.I. Santiago, H.J. Mass, S.E. Williams, E.A. Pou, W. Velez and K.W. Scheel. Department of Physiology, Ponce School of Medicine, Ponce, Puerto Rico 00731 and Department of Physiology, Texas College of Osteopathic Medicine, Ft Worth, TX 76107

We examined the relationship between coronary pulse flow and regional segment function in the open chest and isolated heart preparations. Coronary pulse flow was defined as the peak diastolic flow minus the peak systolic flow. We measured regional segment function (percent segment shortening, %SL, and velocity of shortening, dL/dt) with ultrasonic crystals. In the open chest preparation, we produced changes in segment function by aortic constriction and small increases in circumflex coronary flow through local injection of adenosine. In the isolated heart preparation, we varied perfusion pressure from 20 to 150 mmHg. There was a direct correlation, $r^2 = .95$, between pulse flow and %SL for each experimental preparation. This data suggests that pulse flow can be used as an index of myocardial function under the above conditions. Supported by NIH RR08239, HL35030 and the Puerto Rico Heart Association.

47.7

EFFECTS OF ISOFLURANE ON REACTIVE HYPEREMIA AND CORONARY RESERVE AFTER HYPOPERFUSION IN ISOLATED HEARTS. M Boban,* DF Stowe, JP Kampine, ZJ Bosnjak. Anesthesiology and Physiology, Medical College of Wisconsin, Milwaukee, WI 53226

We examined the effects of 1.25, 2.5% and no isoflurane (ISO) on coronary flow (CF) in 6 groups (n=10 each) of isolated guinea pig hearts. Three groups were subjected to 0% and three groups to 25% of control perfusion pressure (55 torr) for 30 min. ISO was given only for 10 min before, during and 10 min after hypoperfusion (HP). Coronary reserve was tested with adenosine prior (A1) to ISO and after (A2) 40 min of reperfusion (RP). Data were analyzed by ANOVA. Results in the table are mean ± SEM.

		CF (ml/g/min)					
%PP	ISO%	CONTROL	A1	10'ISO	1'RP	40'RP	A2
0	0	5.9±0.3	10.3±0.4	5.9±0.3	8.3±0.6	4.0±0.3 †	5.3±0.6
	1.25	6.2±0.4	11.1±0.6	7.0±0.4	10.6±0.7 *	4.5±0.3 †	7.4±0.8 *
	2.5	5.7±0.2	10.8±0.6	7.6±0.4 *	9.7±0.3 *	4.0±0.3 †	6.1±0.8
25	0	6.2±0.4	11.3±0.4	6.2±0.4	8.8±0.6	5.1±0.5	9.2±0.6
	1.25	5.5±0.3	10.4±0.6	6.2±0.3	8.1±0.5	4.7±0.3	8.0±0.6
	2.5	5.7±0.3	9.9±0.6	7.6±0.6 *	9.2±0.5	4.7±0.4	8.3±0.6

† vs CONTROL
* vs 0%ISO
p≤0.05

ISO increased CF prior to HP (10' ISO). During the first min of RP (1'RP) ISO enhanced the reactive hyperemic response only in the 0% HP group. After 40' min of RP CF returned to control after 25% but not after 0% HP. Maximal CF (A2) after 40' min RP was greater in the 25% HP groups. CF was enhanced by ISO in the 0% but not in the 25% HP groups. The results suggest that maximal coronary reserve can be improved with ISO; this is more evident after total global ischemia. (Supported by NIH grant HL 34708)

47.8

ROLE OF NITRIC OXIDE ('N=O) IN CORONARY REACTIVE HYPEREMIA (RH) AND THE ACTIVE HYPEREMIC RESPONSE TO PACING (AH). Masayuki Ueeda*, Luis H. Arroyo* and R. A. Olsson. Univ. of South Florida, Department Internal Medicine, Tampa, Fl. 33612

The role of EDRFs such as 'N=O in physiological responses is incompletely understood. This study tests the hypothesis that 'N=O mediates RH and AH, using a guinea pig heart Langendorff preparation perfused at 55 mm Hg and paced at 250/min. Perfusion with buffer containing 50 μM N^{ω}-nitro-L-arginine (NNLA) inhibited 'N=O production, as evidenced by a 40% reduction in basal coronary flow (CF) and a 30% reduction in the CF response to 100 nM bradykinin, 0.1 ml/min for 10 sec. NNLA did not reduce the peak RH response to a 30 sec coronary occlusion but shortened the duration of RH. NNLA did not alter the CF response to pacing at 500/min for 1 min. These results suggest that 'N=O participates in RH but, perhaps not AH.

47.9

RATE & FORCE DEPENDENT CHANGES IN THE THERMAL IMAGES OF WORKING MYOCARDIA. Christopher J. Wingard and C. J. Swanson, Wayne State University, Detroit, MI. 48202.

We have previously shown (FASEB Journal 4(3), A433,1990), that the application of new, chiral-nematic, thermotropic liquid crystals of the cyano-biphenyl series have sufficient time and spacial resolution to accurately map the dynamic thermal changes (<0.1°C) associated with the superficial coronary vasculature. Employing an improved imaging system/SIT camera, and post-acquisition software (Image, NIH; Enhance, MicroFrontier Corp.), we report here on the complex changes occurring in the working, supported rabbit myocardial thermograms as a function of induced changes in steady-state rate and force development effected by epinephrine infusion. Besides the ability to record and digitize dimensional information and changes in the surface vasculature, the current recording system and protocol developed, allows for quantitative estimation of the thermal distribution of the left-ventricular (LV) surface. As the work function is increased, we see a global rise in mean LV surface termperature and beat-to-beat intensity (=temperature) change in the imaged coronary vasculature. The correlation of the thermographic information with other cardiac parameters (ie. coronary flow, A-V temperature difference, stroke work, etc.) can be used to estimate changes in heat production and distributional losses and gains. The described method has potential utility in cardiac energy balance/efficiency studies as well as vessel imaging.

47.10

THE ELECTRO-MECHANICAL EFFECTS OF HYPOXIA ON HUMAN CORONARY ARTERIES. K. Rückborn[1], G. Siegel[2], F. Schnalke[2], J. Müller[3] and H. Warnecke[3] (SPON: D.R. Harder). [1]Institute of Physiology, The University of Rostock, Gertrudenstraße 9, DDR-2500 Rostock, Germany; [2]Institute of Physiology, Biophysical Research Group, The Free University of Berlin, D-1000 Berlin 33, Germany; [3]German Heart Institute Berlin, D-1000 Berlin 65, Germany

In isolated segments of the canine common carotid artery we found that with a diminution of the O_2 partial pressure in the blood substitute solution, from 535 mm Hg to 35 mm Hg, the cell membrane of the vascular smooth muscle cells becomes hyperpolarized and the muscle relaxes [Z. Kardiol. 78, Suppl. 6, 124-131 (1989)]. Further reduction of the oxygen tension attenuates these effects, and even depolarization and contraction occur.

We obtained quite similar results from human coronary arteries which were taken from heart transplant patients. During oxygen deficiency, control preparations showed a maximal hyperpolarization of ΔV = 10.9 mV and a maximal relaxation of ΔT = 0.506 g. Arteriosclerotic arteries, however, became hyperpolarized by merely ΔV = 7.9 mV and relaxed by ΔT = 0.247 g. The isometric pretension was 2 g in both experimental series. The hypoxic hyperpolarization and dilation can be amplified by the prostacyclin analogue iloprost (10^{-7} mol/l) both in normal and in arteriosclerotic blood vessels. The depolarization and constriction within the range 40 mm Hg > P_{O_2} > 0 mm Hg is completely suppressed by iloprost: hyperpolarization and vasorelaxation occur. Comparing normal vessels to arteriosclerotic ones, the latter are less hyperpolarized and relaxed with iloprost. Two series of experiments, one with an application of indomethacin (10^{-5} mol/l) and another one with deendothelialized blood vessels, confirm the hypothesis that the endothelium of arteriosclerotic coronary arteries may produce less prostacyclin and EDHF.

RED BLOOD CELLS

48.1

VOLUME-SENSITIVE Na/H EXCHANGE IN AN ELASMOBRANCH RED CELL: CAN IT FUNCTION IN VOLUME REGULATION? John A. Payne and David H. Evans. Univ. of Florida, Gainesville, FL 32611

We have examined the response of nurse shark (Ginglymostoma cirratum) red cells to hypertonic shrinkage and have characterized a volume-sensitive Na/H exchange system. When hypertonically (isotonic (960 mOsm) + 300 mOsm tetramethylammonium-Cl) shrunken in the presence of ouabain (100 μM), these cells show large increases in net Na and Cl influx with no alteration of K content. However, volume recovery (21% in 3 h) is severely limited by the high osmolarity of the medium. Net Na, Cl, and water influxes following shrinkage could be inhibited entirely by 1 mM amiloride when $[Na]_o$ was 80 mM. Concurrent with net Na and Cl uptake during volume increase was an amiloride-sensitive, Na_o-dependent proton efflux. These data support the presence of a volume-sensitive Na/H exchange system in these cells. Interestingly, since shrunken cells do not attain even near-normal volume and net Na influx becomes inactivated before reaching apparent thermodynamic equilibrium, the Na/H exchanger appears not to be regulated primarily by cell volume, but by some other cell parameter, most likely cell pH. Although sensitive to cell volume, Na/H exchange has essentially become ineffective in volume regulation under the high osmolarity conditions of marine elasmobranchs. The retention of an osmotically inactive solute such as urea has obviated the need for volume regulatory ion transport mechanisms under hypertonic conditions. (Support by NSF 88-01572 & Sigma Xi).

48.2

D-GLUCOSE PERMEABILITY IN RIVER LAMPREY (LAMPETRA FLUVIATILIS) AND CARP (CYPRINUS CARPIO) ERYTHROCYTES. Kirsti Tiihonen* and Mikko Nikinmaa. Department of Zoology, University of Helsinki SF-00100 Helsinki, Finland.

The characteristics of 3-O-methyl-D-glucose (3-OMG), a non-metabolized D-glucose analog, transport in lamprey and carp erythrocytes were studied with tracer methods. In lamprey erythrocytes the half-time for the equilibration of 3-OMG at 20°C was approx. 8 min. Phloretin, an inhibitor of carrier-mediated glucose transport, at 1 mM concentration increased the half-time to 38 min. To further characterize the 3-OMG transport system of lamprey erythrocytes at increasing concentrations of unlabelled 3-OMG we measured the initial rate of influx. 3-OMG was taken up by lamprey erythrocytes both by facilitated and by simple diffusion. The presence of carrier-mediated transport was indicated by saturation kinetics and inhibition by phloretin. The Km and Vmax of the saturable component of 3-OMG transport were 1.6 mM and 12.4 mmol/l cells/h respectively. In contrast, the erythrocytes of carp were almost impermeable to 3-OMG, with a half-time for equilibration of 14.2 h. Since the transport showed no sign of saturation kinetics, it appears to proceed by simple diffusion only. These results suggest that, as for most other teleost fish so far studied, the low glucose permeability is insufficient to maintain normal energy metabolism of carp erythrocytes. In contrast, the facilitated glucose transport in agnathans seems to be quite effective.

48.3

Na/H EXCHANGE AS A CAUSE OF FAILURE OF ION BALANCE AT LOW TEMPERATURE IN GUINEA PIG RED CELLS. Zhihong Zhao* and John S. Willis, Department of Physiology and Biophysics, University of Illinois, Urbana, Il 61801

Most mammalian cells fail to maintain ion gradients at temperatures below 20°C, because of the failure of the Na pump and/or insufficient decrease of passive ion permeabilities (e.g. for Na). It has also been shown, in guinea pig red blood cell (RBC), that a component of Na influx sensitive to amiloride is larger at 20°C than at 37°C. This study has dealt with the questions of whether this amiloride-sensitive component of Na influx is the well-studied Na/H exchange mechanism, and, if so, why it is more active at 20°C than at 37°C. We have found that the amiloride-sensitive Na influx is stimulated by intracellular acidification, osmotic shrinkage and phorbol esters at 37°C. These are all features expected of the Na/H exchange mechanism. By measuring the effects of intracellular H^+ and osmotic shrinkage on amiloride-sensitive Na efflux in a reversed Na gradient, we have also demonstrated the presence of a H^+ modifier site at 37°C. At 20°C, in non-acidified cells, amiloride-sensitive Na influx is not in exchange for either Na^+ or H^+ as measured by Na efflux or by H loss from the cells. The sensitivity of amiloride-sensitive Na influx to cytoplasmic H^+ is greater at 20°C than at 37°C, but the maximal amiloride-sensitive Na influx stimulated by intracellular H^+ is greater at 37°C than at 20°C. We interpret these results to mean that amiloride-sensitive Na influx in guinea pig RBC is through the Na/H exchange mechanism, that the greater sensitivity of Na influx to cytoplasmic H^+ at 20°C is mainly due to the shift in the sensitivity of the modifier site; and that at 20°C, Na influx is uncoupled from H loss. (NIH GM 11494).

48.4

ERYTHROCYTE VOLUME CHANGES IN YOUNG HYPERTENSIVE RATS. James M. Norton. Univ. New England, Biddeford, ME 04005.

In order to link abnormal red cell indices with the pathogenesis of hypertension, erythrocyte indices and volume distribution curves were obtained for spontaneously hypertensive rats (SHR) and for normotensive control rats (WKY) over the age range of 3-24 wk. At each age, red cell count (RCC), hematocrit (HCT) and mean cell volume (MCV) were determined for heparinized blood samples. MCV was calculated both from RCC and HCT values and by microcomputer analysis of erythrocyte volume distribution curves generated by an electronic cell counter linked to a cell size distribution analyzer. RCC and HCT were found to be significantly higher for SHR than for WKY, and MCV significantly lower, at nearly all ages tested. Both SHR and WKY showed an initial increase in primary population MCV from 3-7 wk, followed by a gradual decline in MCV to the adult level seen at 24 wk. The rate of increase in mean cell volume is greater in the SHR than in the WKY over the 3-7 wk time period, which corresponds to the early developmental phase of the hypertension seen in SHR.

(supported by the American Heart Association Maine Affiliate, Inc.)

48.5

UREA AND WATER PERMEABILITIES OF THREE TYPES OF ERYTHROCYTES. C. Levinson*, W.R. Galey and J. Brahm*[1]. Department of Physiology, University of New Mexico, Albuquerque, NM 87131.

There are known to be special pathways across the erythrocyte (RBC) membrane for both water and urea, as their permeabilities are greater than those of a simple lipid bilayer. It has been postulated that urea, a small hydrophilic solute, travels through the same channel as water (Solomon, 1983). We have examined urea permeability, osmotic water permeability (Pf) and diffusive water permeability (Pd) in dog, normal human and McLeod RBC. McLeod cells are human RBC with distinct antigenic and morphologic abnormalities. Urea permeability is 50% less in McLeod cells and 60% less in dog RBC compared to normal human RBC. Osmotic water permeability is 42% greater in McLeod cells and 45% greater in dog RBC compared to normal human cells. Diffusive water permeability is 43% greater in McLeod cells and 42% greater in dog RBC than in normal human RBC. Three major conclusions are drawn from these studies. First, the observation that urea permeability does not parallel water permeability suggests that water and urea do not move through a common pathway. Second, the greater Pf/Pd ratio seen in dog RBC indicates these cells have wider or longer water channels than human RBC. Third, the similar Pf/Pd ratio coupled with the increased water permeability of McLeod cells suggest these cells have more water channels of the same size as those found in normal human RBC. This work was supported by NATO 0334/87 and the New Mexico affiliate of the American Heart Association.

Reference:

Solomon, A.K. et al. 1983. Ann. N.Y. Acad. Sci. 414:97-124.

[1]Affiliation: Panum Institute, Univ. of Copenhagen, DK 2200 Denmark

48.6

A PREDOMINANT ROLE OF LIVER IN ACYL-PLATELET-ACTIVATING FACTOR (PAF) FORMATION FROM [^{3}H]LYSO-PAF IN PICHINDE VIRUS-INFECTED GUINEA PIGS. C. Qian*, C.T. Liu, and C.J. Peters*. U.S. Army Med. Res. Inst. of Infect. Dis., Ft. Detrick, MD 21701-5011

The cellular metabolic cycle of PAF involves biosynthesis and conversion of PAF to acyl-PAF via lyso-PAF. In the present study, the fate of administered [^{3}H]lyso-PAF was compared between uninfected control and Pichinde virus-infected strain 13 guinea pigs (PVIGP) on postinoculation days 7, 10, and 14 (n=4/group x4). Under anesthesia, animals were bled 5, 30, and 60 min after an IV injection of 1.9 nmol (7.5 μCi) [^{3}H]lyso-PAF/kg. Terminal samples of heart, lung, kidney, and liver were excised. In blood samples of both control and PVIGP, [^{3}H]lyso-PAF was the major component, with trace amounts of acyl-PAF, PAF, and neutral lipids. The heart tissue from both control and infected animals showed the lowest value of radioactivity. When comparison was made with controls, PVIGP showed an increased circulatory disappearance of injected [^{3}H]lyso-PAF; and high acylation of [^{3}H]lyso-PAF in lung, heart, and liver were observed. The liver showed the most extensive changes, including increased incorporation, acylation, and neutral lipid formation after Pichinde viral infection. Results support our previous observations that an increased production of acyl-PAF from [^{3}H]PAF or [^{3}H]lyso-PAF occurred in isolated neutrophils from PVIGP (FASEB J 4:A461; 1990). In summary, an augmented acylation of exogenous [^{3}H]lyso-PAF was demonstrated in the lung, heart, and, mostly liver of PVIGP as compared with controls.

BODY FLUID REGULATION

49.1

EFFECT OF VOLUME EXPANSION ON PLASMA ENDOTHELIN LEVELS IN SHR AND WKY RATS. Ali A. Khraibi, Denise M. Heublein, Franklyn G. Knox, and John C. Burnett, Jr., Mayo Clinic, Rochester, MN 55905

Preliminary reports suggest that circulating levels of endothelin may be increased in hypertension. The objectives of this study were to determine plasma endothelin levels in a genetic model of hypertension during control conditions and in response to acute saline volume expansion. The Okamoto spontaneously hypertensive rat (SHR) and control Wistar-Kyoto (WKY) rats were used in this study. One group of each strain served as control and another group of each strain was volume expanded (5% b.w. saline over a period of 30 min). Endothelin-3 was measured in plasma using a double-antibody radioimmunoassay kit (Peninsula Labs). In the control groups of SHR and WKY rats, plasma endothelin levels were 9.39±1.76 pg/ml (n=7) and 9.10±1.93 pg/ml (n=6) respectively (NS). In the volume expanded group of SHRs, plasma endothelin was 6.40±1.73 pg/ml (n=6; NS as compared to control SHR), whereas it was 4.20±0.68 pg/ml in the volume expanded group of WKY rats (n=8; $p<0.05$ as compared to control WKY rats). These data show that basal levels of plasma endothelin are similar in the SHR and WKY rats, and that these levels decrease significantly in response to acute saline volume expansion in the WKY rat, but not in the SHR.

49.2

HYPERKALEMIA AFTER HYPEROSMOLAR EXPANSION WITH SOLUTES DISTRIBUTED IN BODY WATER: SOLUTE SPECIES DIFFERENCES. Antonios H. Tzamaloukas, Jack E. Jackson*, Doris Miyashiro*, Debra Long*, Tim Chapman* and Thomas W. Chick*. VA Med. Center and Univ. of New Mexico, Albuquerque, NM 87108

Hyperosmolar expansion reportedly produces hyperkalemia if the infused solute has extracellular but not body water distribution. We studied whether the species of solute with body water distribution affects internal potassium balance by comparing 2 groups of anesthetized, ventilated, acutely anuric (ureteral ligation) dogs infused in 2 steps with isonatremic NaCl plus either 1.1 m ethanol (group A, n=6) or 1 m urea (group B, n=6). Estimated extracellular expansion was 15% for the 1st, and 30% for the 2nd expansion. Results ΔK mmol/l, ΔOs mOsm/kg:

	ΔK: 1st Exp.	2nd Exp.	ΔOs: 1st Exp.	2nd Exp.
Group A	-0.44±0.34	-0.42±0.39	+55±5	+80± 8
Group B	+0.26±0.39	+2.05±1.03	+44±5	+90±12

Acid-base parameters were comparable between groups A and B. Hemolysis was ruled out by low serum hemoglobin levels. Transient hyponatremia followed infusion of hyperosmolar urea (ΔNa -5.3±3.0 after the first, -4.7±1.3 mmol/l after the 2nd expansion), but not infusion of hyperosmolar ethanol. In anuria, expansion with hyperosmolar solutions of certain solutes distributed in body water leads to hyperkalemia. Transient osmotic gradients producing transient osmotic fluid shifts of intracellular fluid extracellularly is one of the possible mechanisms for this hyperkalemia (Supported by a AHA Grant-in-Aid).

49.3

BRADYKININ-INDUCED DIPSOGENESIS IN CAPTOPRIL-TREATED RATS. Melvin J. Fregly and Neil E. Rowland. Univ. of Florida, Gainesville, FL 32610.

The dipsogenic responsiveness to acute administration of the peptide, bradykinin (B), was studied in 2 groups each of 6 male Sprague-Dawley rats. One group of rats was administered captopril (C) (35 mg/kg, i.p.) 15 min prior to the study. The second group received saline. Fifteen min later, both groups received 100 ug B/kg, i.p. The rats were placed alone into metabolic cages without food and given a preweighed bottle of tap water. Water intakes and urine outputs were then measured hourly for 3 hr. Two additional experiments were carried out at weekly intervals. One used a higher dose of B (200 ug/kg, i.p.) while the third used saline. Both doses of B initiated a robust drinking response and urine output in C-treated rats which were significantly ($P<0.05$) greater than those of controls. To assess whether B might induce drinking by way of angiotensin II (AII) receptors, the AII receptor blocker, Sar^1Ile^8 AII (Sar 300 and 600 ug/kg, s.c.) was administered to both B-(200 ug/kg, s.c.) and B + C-treated (35 mg/kg, i.p.) groups of rats in a two-way ANOVA statistical design. B again stimulated drinking in C-treated rats, but the drinking was not blocked significantly by administration of Sar. Blockade of the AI converting enzyme increases the half-life of B to unmask its dipsogenic properties. The results suggest further that B does not appear to induce drinking via interaction with receptors for AII. (Supported by Grant N00014-88-J-1221 with the U.S. Navy).

49.4

ANGIOTENSIN-RELATED THIRST AND SODIUM APPETITE: DIFFERENCES BETWEEN RATS, MICE, AND HAMSTERS. N.E. Rowland, J. Kerr*, and M.J. Fregly. Univ. of Florida, Gainesville, FL 32611-2065.

It is well known that rats and many other mammalian and non-mammalian species drink water in response to either exogenous administration or endogenous production of angiotensin (ANG) II. Examples of this include central and peripheral injections of ANGII, treatments with serotonin, isoproterenol, ANG converting enzyme inhibitors, thirst after cold exposure, or by colloid-induced hypovolemia. Many of these treatments can also induce a salt appetite in rats. In contrast, both ingestion of water and salt appetite of mice and hamsters are either refractory or unresponsive to many, but importantly not to all of the above treatments despite increased ANGII production. It is not clear why the behavioral response profiles differ for this seemingly basic function. (Supported by NSF and Grant N00014-88-J-1221 with the U.S. Navy).

49.5

DIFFERENCES AMONG RAT STRAINS IN DRINKING AND SODIUM PREFERENCE: DEVELOPMENTAL FACTORS AND POSSIBLE MECHANISMS. C. Poortman*, G. Smith*, L.J. Yu*, M. Garcea*, M.J. Fregly and N.E. Rowland. Univ. of Florida, Gainesville, FL 32611-2065.

We and others have reported that rats of the Fischer 344 (F344) strain lack the preference for dilute NaCl solutions shown by more commonly used strains such as Sprague-Dawley (SD). In the first new study, we examined development of acceptance for salt in preweaning F344 and SD rats using an intra-oral infusion method. Both strains showed similar preferences for hypertonic NaCl solutions up to weaning, but unlike SD, F344 rejected NaCl immediately after weaning. In a second study, we found that F344 rats drank less water than SD after either peripheral or cerebroventricular injection of ANGIII, but were equally responsive to ANGI and ANGII. It is possible that either faster metabolism of ANGIII and/or reduced receptor activation by ANGIII underlie the reduced water and salt intakes in F344 rats. Additionally, we report that F344 rats drink many times during meals of chow pellets. This is similar to the pattern seen in salivaless rats although we do not have direct evidence for reduced prandial salivary flow in F344 rats. (Supported by the Am. Heart Assn. FL affiliate, and the NSF).

49.6

COMPARISON OF SWINE AND DOGS AS MODELS FOR THE STUDY OF NEUROENDOCRINE RESPONSES TO FLUID DEPRIVATION

C.E. Wade, Letterman Army Inst. Res., San Franscio, CA 91429

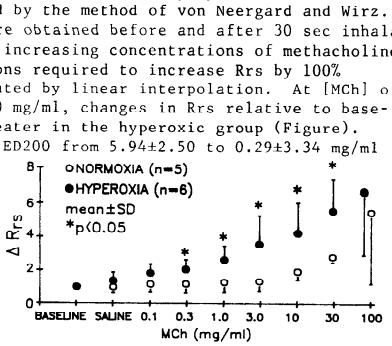
Neuroendocrine responses to 24 hr of fluid deprivation were evaluated in pigs and dogs of similar weights (23.0±0.8 vs. 23.1±1.7 kg). Fluid deprivation decreased ($P<0.05$) body weight by 1.0±0.3 kg in the swine and 0.9±0.1 kg in dogs, while plasma osmolality was increased by 13±4 and 14±3 mOsm/kg, respectively. Hematocrit was unchanged in both groups, while plasma protein increased from 6.0±0.1 to 6.3±0.1 g/dl in pigs and in dogs from 6.2±0.2 to 6.7±0.2 g/dl. Initial plasma vasopressin levels were higher in pigs, 6.6±0.8 vs 3.0±1.2 pg/ml, but the response to fluid restriction was similar. Control plasma cortisol, ACTH and PRA levels also were higher in pigs prior to fluid deprivation compared to dogs. In both groups no changes in ACTH or aldosterone were noted. PRA was raised to 6.5±2.2 ngAI/ml/hr in pigs compared to 1.4±0.2 ngAI/ml/hr in dogs. In dogs, cortisol levels were increased from 1.5±0.2 to 2.7±0.4 μg/ml, but in pigs the change was not significant. While there were some species differences in initial values, possibly due to handling procedures, swine and dogs appear to be equally good models for the study of neuroendocrine responses to fluid deprivation.

MECHANICS OF BREATHING

50.1

HYPEROXIA INCREASES AIRWAY REACTIVITY IN IMMATURE RATS M. Hershenson,* D. Ray,* A. Garland,* L. Alger,* C. Hernandez,* R. Bullock,* J. Solway. Univ. of Chicago, Chicago, IL 60637

To test whether chronic hyperoxia increases airway reactivity in developing animals, 21 day old rats were exposed to normoxia or hyperoxia (>95% O2) for 8 days. Rats were then anesthetized (pentobarbital), beta-blocked (propranolol), tracheotomized, ventilated (120/min; 8ml/kg) and placed in a body plethysmograph. Total respiratory system resistance (Rrs) was calculated by the method of von Neergard and Wirz. Rrs measurements were obtained before and after 30 sec inhalations of saline and increasing concentrations of methacholine (MCh). Concentrations required to increase Rrs by 100% (ED200) were calculated by linear interpolation. At [MCh] of 0.3, 1, 3, 10 and 30 mg/ml, changes in Rrs relative to baseline (ΔRrs) were greater in the hyperoxic group (Figure). Hyperoxia decreased ED200 from 5.94±2.50 to 0.29±3.34 mg/ml ($p<0.01$). We conclude that chronic hyperoxia increases airway cholinergic reactivity in immature rats. Supported by HL 41009, HL 02005, HL 02376 and the American Lung Association.



50.2

HYPERPNEA-INDUCED BRONCHOCONSTRICTION (HIB) IN IMMATURE GUINEA PIGS TM Murphy, DW Ray, LE Alger*, IJ Phillips*, L Roy*, AR Leff and J Solway. Univ. of Chicago, Depts. of Peds. and Med., Chicago, IL 60637

Adult guinea pigs demonstrate dry gas HIB mediated by tachykinin release from airway sensory nerves. To assess this response in newborn animals, we compared the fractional increases in respiratory system resistance (FIRrs) caused by 5 min dry gas hyperpnea (2, 3.2, 4.4, and 6.5 times baseline eucapnic minute ventilation [MV]) in 5-day old guinea pig pups with those found in adults after similarly scaled hyperpnea challenges. Rrs peaked 4-5 min after the cessation of hyperpnea in both groups, but FIRrs was greater ($p<.04$) and more variable ($p<.05$) in adults than in pups (8.0±1.8 vs 3.8±0.5 [SE] at the greatest stimulus). In addition, adults doubled their baseline Rrs after a smaller hyperpnea stimulus compared with pups (4.8±0.7 vs 5.2±0.4 times baseline MV; $p<.04$). The reduced hyperpnea responses seen in pups were not due to inadequacy of the contractile apparatus or of tachykinin release/receptor activation, as FIRrs responses to iv methacholine (10^{-10}-10^{-7} mol/kg) and to iv capsaicin (0.01-1.0 ug/kg) were similar in pups and adults (methacholine ED200 -7.6±0.3 vs -8.0±0.1 log mol/kg, p=NS; capsaicin ED200 -0.7±0.4 vs -0.4±0.1 log ug/kg, p=NS). Thus, the reduced dry gas hyperpnea responses seen in pups must stem from differences in physical effects of respiratory heat/water loss with maturation, or from differences in transduction of those physical effects to sensory nerve stimulation. Supported by HL41009, HL02205, HL02376, HL35718, HL32495, the Chicago Lung Association, and the Louis Block Fund.

50.3

AIRWAY DYNAMICS AND DEEP INHALATION-INDUCED BRONCHOSPASM IN ASTHMATICS. V. Brusasco, R. Pellegrino*, B. Violante*, E. Crimi*. Università di Genova, 16132 Genova, and Ospedale A. Carle, 12100 Cuneo. Italy.

In few asthmatics, deep inhalation (DI) induces a bronchoconstriction which seems to be due to a myogenic effect rather than to the mechanical interdependence between airway and lung parenchyma (Marthan & Woolcook, ARRD 140:1354, 1989). In 4 asthmatics with decreasing FEV_1 during successive forced expiratory maneuvers we determined the ratio of maximum expiratory flow at 40% of FVC from maximal and partial flow-volume curves (M/P_{40}) and the time course of changes in specific airway conductance after a single DI ($sGaw_{DI}/sGaw$). FEV_1 decreased progressively during 6 forced expiratory maneuvers over 10 min from 2.77±0.22SE L to 1.98±0.20 L ($P < 0.02$), while M/P_{40} was not significantly changed from 1.57±0.25 to 1.68±0.30. $sGaw_{DI}/sGaw$ 3 s after DI was 1.06±0.08, not different ($P > 0.2$) from 1.23±0.12 in 4 healthy controls.30 s after DI, $sGaw_{DI}/sGaw$ was 0.73±0.06, different ($P < 0.005$) from 1.03±0.03 in controls. The DI-induced decrease of FEV_1 was significantly blunted by nifedipine. We conclude that in asthmatics DI may trigger a myogenic bronchoconstriction preceded by a transient bronchodilation likely due to the interdependence between airway and parenchyma.

50.4

HYPERINFLATION AFTER HISTAMINE CONSTRICTION DECREASES LUNG RESISTANCE (R_L) BUT ALSO DECREASES AIRWAY SIZE. W. Mitzner, R. Brown, C.Herold, C. Hirshman, E.Zerhouni. The Johns Hopkins Medical Inst. Baltimore, MD.

Asthmatic subjects and hyperreactive dogs have been reported to increase airway resistance following hyperinflation, whereas normals show a decrease. We studied the response of airways in vivo to hyperinflation following histamine constriction, by direct visualization using high resolution computerized tomography (HRCT). Five anesthetized mongrel dogs were ventilated at constant tidal volume. Diameters of airways ranging in size from 1 - 10 mm were measured in a lung region adjacent to the base of the heart. Within this region, ten 1 mm thick serial HRCT slices were made in each dog. The same airways could be identified in the same or adjacent slices by means of several landmarks in the parenchyma. All measurements were made at FRC in the following 3 sequential states: 1) control; 2) 1 min after aerosol histamine challenge sufficient to cause a 3 fold increase in lung resistance; and 3) 1 min following a standardized hyperinflation equal to three tidal volumes. On separate occasions conventional R_L was measured with an identical protocol. The table shows mean changes in R_L and airway areas averaged over all sizes in each dog, presented as percent of control.

	Control	Histamine	Hyperinflation	
HRCT airway area	100	42	32	*p < .05
RL	100	365	290	*p < .05

These results indicate that the commonly observed decrease in lung resistance following hyperinflation in constricted lungs may have been erroneously interpreted as indicating airway dilation.

50.5

EFFECT OF TEMPERATURE ON THE CLOSING AND REOPENING (C-O) OF LUNG UNITS IN CONTROL AND CHLORPHENTERMINE (CP) TREATED RATS. T.A. Jones*, G.A. Krause*, E.L. Petsonk*, M.J. Reasor*, and D.G. Frazer. Depts. of Physiol., Pharmacol. and Pol. Sci., WV Univ., and DRDS, NIOSH, Morgantown, WV 26505.

The normalized pressure-volume (P-V) hysteresis ($K=H/H_{max}$) of excised rat lungs cycled between pressures of +3 and 30 cm H_2O is greatly increased at 45°C relative to 24°C, while lungs from rats treated with the lipidotic drug CP exhibited only a small increase in K (Jones et al, Physiologist 31(4):A222, 1988.). By superimposing sinusoidal volume oscillations on quasistatic P-V curves, it is possible to predict C-O of lung units (Frazer et al., Respir. Physiol. 61:277-288, 1985). In this study, sinusoidal volume oscillations were superimposed on P-V curves performed between +3 and 30 cm H_2O at 24°C and 45°C on lungs from control and CP-treated rats. Control rats exhibited a large increase in C-O at 45°C, but only small increases were seen in CP treated rats. This study suggests that the increase in K in response to increased temperature is likely due to increased C-O of lung units possibly resulting from reduced surface activity of alveolar surfactant. Reduced temperature effects on CP-treated rat lungs may be due to the preservation of surface activity at 45°C which results in the reduction of C-O of lung units.

50.6

HYPOXIA AND HYPERVOLEMIA INDUCED AIRWAY CHANGES DEMONSTRATED BY HIGH RESOLUTION COMPUTED TOMOGRAPHY (HRCT). R.C. Wetzel, C.J. Herold*, E.A. Zerhouni*, and J.L. Robotham. Depts. of Anesthesiology/Critical Care Medicine and Radiology, The Johns Hopkins University, Baltimore, MD 21205

HRCT allows differentiation of pulmonary structures with diameters approaching 300 microns. To determine airway responses to ventilation with hypoxic gas mixtures and acute volume loading, the lungs of six anesthetized and ventilated (V_T=15 ml/kg, f=10 bpm) pigs were imaged by HRCT (Siemens DRH, Somatom Plus). Scans were obtained at an end-expiratory pressure of 5 cmH_2O, with 1 sec scan times and 1-2 mm thick slices. Bronchial diameters in three size ranges were measured during room air or after 10 min hypoxic (PiO_2=30 torr) ventilation and normo and hypervolemia. pHs and pCO_2s did not vary.

	Bronchial Diameter (mm)		
Range:	1-2.5 mm	2.6-4.9 mm	5-8 mm
Normoxia:	1.7±0.2	3.6±0.2	6.1±0.2
Hypoxia:	2.3±0.1*	4.6±0.2*	6.7±0.3*
Normovolemia:	2.1±0.2	4.3±0.2	7.1±0.4
Hypervolemia:	1.6±0.5*	3.8±0.3*	6.0±0.4*

Conclusion: HRCT non-invasively demonstrated (* $p<.01$) airway dilation during hypoxia (28±5%) and decreased diameter during acute normoxic hypervolemia (- 18±2%).

50.7

UPWARD MOVEMENT OF PLEURAL LIQUID ALONG LOBAR MARGINS DUE TO CARDIOGENIC MOTION. P. M. Wang* and S. J. Lai-Fook. University of Kentucky, Lexington, KY 40506.

Anesthetized paralyzed rabbits (3-4 kg) were mechanically ventilated with 100% O_2 in the supine position. A rib capsule was placed in the 6-8 th rib of the right chest near the dorsum. A transparent parietal pleural window was made between the 4th and 5th rib overlying a lobar margin near the sternum. The vertical distance between the capsule and window was 3-4 cm. During apnea, airway pressure was adjusted to 2-10 cmH_2O to position the window over the lobar margin, and fluorescent dye (0.01% sodium fluorescein) was injected (0.1 ml/min for 3-5 min) through the rib capsule into the pleural space. The dye was detected at the window via fluorescent videomicroscopy and the video signals recorded. Concentration (light) versus time was measured off-line from the video images using a video photoanalyzer and stored on a computer. Transit time of dye movement was calculated from the difference between the concentration-weighted mean time of the concentration-time curve and the mean injection time. In 3 rabbits, transit time averaged 4.2 ± 1.7(SD) min. Transit time measured after apnea with mechanical ventilation was < 1 min. Transport of pleural liquid that occurred upwards along lobar margins would compensate for gravity-induced pleural liquid drainage to dependent chest regions. (Supported by HL 36597).

50.8

CHANGES IN LENGTH OF EXPIRATORY MUSCLES DURING EUPNEA IN PRONE ANESTHETIZED DOGS. Gaspar A. Farkas & Mark A. Schroeder. Mayo Clinic & Foundation, Rochester, MN 55905

Changes in posture from supine to prone are associated with increases in the phasic activation of rib cage and abdominal expiratory muscles. To assess the mechanical role of their recruitment, we measured changes in length of the triangularis sterni (TS) and the transversus abdominis (TA) muscles using sonomicrometry in 9 pentobarbital sodium anesthetized dogs. Animals were studied during spontaneous breathing, either in the supine or in the prone (spinal suspension) posture. Peak inspiratory (L_{insp}) and end-expiratory (L_{exp}) muscle length were evaluated and related to the resting muscle length (L_R) determined at the relaxed position of the respiratory system (hyperventilation-induced apnea). Results are shown below and are given as $\%L_R$ (x̄ ± SE).

	TRIANGULARIS STERNI		TRANSVERSUS ABDOMINIS	
	L_{insp}	L_{exp}	L_{insp}	L_{exp}
SUPINE	108.7 ± 2.9*	94.4 ± 2.3*	102.2 ± 0.8*	99.1 ± 0.7
PRONE	112.5 ± 5.9*	96.6 ± 2.5	101.0 ± 0.6	93.4 ± 1.9* †

* $p < 0.05$ from L_R; † $p < 0.05$ from supine

These results demonstrate that (1) in the supine position, only the TS shortens to a length below L_R; (2) in the prone position, increased activation of the TS is not associated with increased shortening; and (3) in the prone position, only the TA shortens to a length below L_R. We conclude that active expiration shifts from being primarily a rib cage event in supine animals to being an abdominal event in prone dogs.

50.9

EXPIRATORY MUSCLE ACTIVATION AND MECHANICAL ROLE IN SUPINE ANESTHETIZED DOGS: EFFECT OF FORELIMB POSITION. M.A. Schroeder & G.A. Farkas. Mayo Clinic, Rochester, MN 55905

In supine anesthetized dogs, spontaneous breathing is associated with phasic expiratory muscle activation. A major function of their recruitment appears to be one of regulating lung volume. Arm elevation leads to an increase in lung volume, the effects of which are not known. Eight spontaneously breathing anesthetized dogs were studied supine, either with the forelimbs unrestrained (control) or extended cephalad. Extending the forelimbs elicited an increased phasic expiratory activation of the triangularis sterni and transversus abdominis in five dogs. Expiratory contribution was assessed by quantifying the difference in lung volume measured at end-expiration and at neutral FRC (hyperventilation-induced apnea). When the amount of EMG activity was expressed as a percent of that recorded during breathing against 25 cm H_2O PEEP (max activation) and expiratory contribution as a percent of tidal volume (V_t), results were as follows ($\bar{x} \pm$ SE).

	CONTROL	EXTENDED	P VALUE
Triang. Sterni	46.5 ± 27.8 %max	64.2 ± 35.4 %max	NS
Trans. Abdominis	12.8 ± 5.6 %max	32.8 ± 13.1 %max	0.05
Exp. Contribution	19.9 ± 3.4 %V_t	25.2 ± 4.4 %V_t	0.05

These results demonstrate that (1) in the supine position, a substantial portion of V_t can be attributed to active expiratory muscle contraction, (2) the position of the forelimbs enhances both the activation and the role of the expiratory muscles.

50.10

PROPORTIONALITY BETWEEN CHEST WALL RESISTANCE AND ELASTANCE. G.M. Barnas, D. Stamenovic and J.J. Fredberg. University of Maryland, Baltimore, MD 21201, Boston Univ., The Biomechanics Institute, Boston, MA 02215, Harvard Univ., Boston, MA 02115.

Fredberg and Stamenovic (J. Appl. Physiol. 67: 2408-2419, 1989) demonstrated that resistance (R) and elastance (E) of lung tissue during external forcing under a wide range of conditions were related by wR = nE, where w = 2π times forcing frequency and n (hysteresivity) was remarkably constant. From data gathered in awake, relaxed humans, we calculated hysteresivities of the chest wall (n_w) and its major compartments, the rib cage (n_{rc}), diaphragm-abdomen (n_{d-a}) and the belly wall (n_{bw}) in the normal ranges of breathing frequency (f) and tidal volume (V_T). n_w remained in a relatively narrow range (0.27 to 0.37) and neither n_w nor the comparmental n's changed much with f or V_T. Compared to n_w, n_{rc} and n_{bw} tended to be slightly low, while n_{d-a} tended to be slightly higher than n_w. We conclude that: 1) elastic and dissipative processes within the chest wall appear to be coupled; 2) n's of the various chest wall compartments are well matched; and 3) R of the relaxed chest wall can be estimated from E. (Supported by an ALA grant, HL33009 and HL44128).

50.11

INTERDEPENDENCE BETWEEN LUNGS WITH DIFFERENT ELASTIC PROPERTIES: STATICS. R.W. Schriner,* S.S. Margulies, M.A. Schroeder,* R.D. Hubmayr. Mayo Foundation, Rochester, MN 55905

Motivated by the introduction of single lung transplantation into clinical practice, we compared the elastic properties of lungs and chest wall in 6 dogs before and after inducing unilateral emphysema with papain. *In situ* relaxation volumes of emphysematous (FRC_E) and non-emphysematous (FRC_{NE}) lungs were measured in the supine posture with a N_2 equilibration technique through a divided airway. Total lung capacity (TLC_E, TLC_{NE}) was defined as the gas volume at an airway pressure of 30 cm H_2O. FRC_E and TLC_E increased to 214 ± 68% and 186 ± 39% of baseline. FRC_{NE} fell to 81 ± 28% ($p \leq 0.05$) while TLC_{NE} remained unchanged at 97 ± 21%. Unilateral emphysema did not alter the esophageal pressure/volume curve of NE, but tended to shift the chest wall curve to a higher neutral volume (increase of 12 ± 14% baseline TLC, $p \leq 0.1$). Stepwise deflations of the respiratory system from TLC resulted in similar patterns of emptying ($\blacktriangle V_E/\blacktriangle V_{NE}$) as deflations of the isolated lungs. This finding suggests that in the intact dog, both lungs are exposed to the same mean pleural pressure. We conclude that (1) the static volume distribution between E and NE is determined only by differences in lung recoil and compliance,(2) unilateral hyperinflation does not cause the dropout of lung units in NE since TLC_{NE} remained constant, and (3) the increased neutral volume of the chest wall represents a chronic adaptation to hyperinflation which minimizes the expected decrease in lung recoil pressure at the new system FRC. **Supported by HL38107.**

50.12

DIAPHRAGM MECHANICS IN UNILATERAL CANINE EMPHYSEMA. R.D. Hubmayr, G.A. Farkas, R.W. Schriner,* S.S. Margulies, M.A. Schroeder.* Mayo Foundation, Rochester, MN 55905

Motivated by the introduction of single lung transplantation into clinical practice, we studied the effects of unilateral hyperinflation on diaphragm mechanics in 5 dogs with papain-induced emphysema. Emphysematous (E) and non-emphysematous (NE) lungs were separated with a divided airway and their FRCs determined in the supine posture with a N_2 equilibration technique. FRC_E was 2.7±1.2 times greater than FRC_{NE}. The lengths (L) of mid costal muscle bundles of the emphysema lung apposed hemidiaphragm (Di_E) and its counterpart (Di_{NE}) were measured with sonomicrometry. L and airway occlusion pressures ($\blacktriangle Pao_E$, $\blacktriangle Pao_{NE}$) at FRC were measured during bilateral phrenic stimulations between 1 and 50 Hz without allowing a redistribution of volume between the lungs. In every animal and at all stimulation frequencies, $\blacktriangle Pao_{NE}$ exceeded $\blacktriangle Pao_E$, the mean difference ranged from 1.2±0.6 cm H_2O during a twitch to 6.0±2.9 cm H_2O during a 50 Hz tetanus. We measured active and passive length/tension characteristics of Di_E and Di_{NE} *in vitro* but found no systematic differences between them. When measured at optimal L (L_o), the maximal tensions of Di_E and Di_{NE} were 2.18±0.41 and 2.19±0.53 kg/cm^2, respectively. During stimulation of the phrenic nerves there was no difference in the active L expressed as $\%L_o$, suggesting that Di_E and Di_{NE} produced a similar force. We conclude that unilateral hyperinflation affects diaphragm geometry and, thereby, influences its efficiency as a regional pressure generator. Unless counteracted by non-uniform diaphragm activation or by the actions of other respiratory muscles, the differences in mechanical efficiency between Di_E and Di_{NE} may affect the interpulmonary distribution of ventilation. **Supported by HL38107.**

50.13

PERFORMANCE OF THE DIAPHRAGM IN CATS WITH INTERNAL LOADING BY ACUTE PLEURAL EFFUSION. WS Krell, P Lynne-Davies, Wayne State University and VAMC Allen Park, Detroit MI 48201.

We have previously reported that internal elastic loads associated with pleural effusions produce an increase in the effective and passive elastance of the respiratory system. These changes appear to be vagally modulated. In an attempt to partition this response, in our present studies we measured airway opening pressure (Pao) and transdiaphragmatic pressure (Pdi) under control conditions, during the first breath following exposure to an external load, and in the maximal response observed during breaths 3-5. The measurements were made before and after internal loading, and after vagotomy. We observed: (a) Pao showed no change in the first breath; (b) Pao max was unchanged following internal loading but decreased slightly (p=.05) after vagotomy; (c) Pdi increased in tidal breathing with loading (p=.005) and still further after vagotomy (p=.0006); (d) Pdi max remained constant in all experimental conditions. We conclude there is no evidence for vagal modulation of the diaphragmatic response to this type of load nor does the muscle fatigue under loads sufficient to depress tidal volume by 1/3. It remains uncertain whether the reduction in Pao max and increase in Pdi after vagotomy reflect fatigue in other respiratory muscles and/or loss of vagal control.

Supported by NIH-NHLBI #001954 and a Research Gratn from the American Lung Association.

50.14

A FORMULA TO DETERMINE CROSS-SECTIONAL AREA OF THE CHEST. K. Chihara,* A. Zapletal,* M. Ward* and P.T. Macklem. Meakins-Christie Laboratories, Montreal Chest Hospital, McGill University, Montreal, Quebec, Canada.

We assumed the cross-sectional area of the rib cage (Arc) was determined by the maximum anteroposterior (AP) and lateral (lat) diameters of the rib cage, and developed a formula to determine Arc by measuring these diameters. Cross-sectional configuration of upper and lower rib cage (CSC) at TLC and FRC were obtained in 11 sitting normal subjects by molding two tubular air tight bean bags, connected by a hinge, circumferentially around the rib cage and subjecting them to a negative pressure causing each bag to become rigid. CSC was obtained by tracing the inside shape of the bags. We assumed CSC as a composite of 2 bilateral semicircles attached to the lateral walls of a rectangle. The diameter of the semicircle is then given by AP. Thus, the formula is: $Arc.f=(lat-AP)*AP+\pi*(AP/2)^2$. The validity of this formula and two other formulae in which CSC were assumed to be a rectangle (Arc.r) or a ellipse (Arc.e) were tested by comparing with the planimetrically determined values of CSC (Arc.p). Arc.f agreed with Arc.p for both upper and lower rib cage better than the other formulae: Arc.f=0.992*Arc.p, Arc.r=1.197*Arc.p, Arc.e=0.936*Arc.p (for upper rib cage). Arc.f=1.01*Arc.p, Arc.r=1.238*Arc.p, Arc.e=0.971*Arc.p (for lower rib cage. We concluded that Arc is given by measuring only AP and lat using Arc.f. (Supported by the EL/JTC Memorial Research Fund).

50.15

AIRFLOW ASSOCIATED WITH STRIDE IN THE HORSE. C.W. Frevert*, C.S. Nations*, H.J. Seeherman, S.H. Loring, and R.B. Banzett, Respiratory Biology Program, Harvard School of Public Health, Boston, Ma.

Galloping horses frequently synchronize respiration and stride in a 1:1 ratio. This coordination has led some authors to hypothesize that the respiratory system is mechanically coupled to locomotion (1). One consequence of such coupling is that breathing might be driven largely by locomotion; the work of breathing would then be essentially transferred from the respiratory muscles to locomotor muscles. To test this hypothesis, we measured airflow at the nares, pleural pressure (P_{pl}), abdominal pressure (P_{ab}), transdiaphragmatic pressure (P_{di}), and stride-related horizontal and vertical accelerations at the withers in horses on a treadmill. During the gallop, breaths were usually coordinated 1:1 with stride, but some horses breathed at ratios other than 1:1. In these latter horses, we averaged the flow signal over many strides; the flows associated with breathing were minimized and the flows associated with stride remained. The volume change associated with stride was no more than 10-20% of tidal volume (V_T). The relationships of P_{pl}, P_{ab}, and P_{di} to breathing and stride show that the diaphragm contracts during inspiration and provides most of V_T. We conclude that in the galloping horse, only a small part of V_T is the result of stride related mechanical forces and that diaphragmatic contraction plays a key role in inspiration. (Supported by NIH# HL19170, HL02374, and Massachusetts Thoroughbred Breeders Association) 1) Bramble, D.M. Amer. Zool. 29:171-186, 1989.

50.16

AIRWAYS MECHANICS DURING LARGE AMPLITUDE LOW FREQUENCY OSCILLATION. **J. Sato, B.L.K. Davey and J.H.T. Bates. Meakins-Christie Laboratories, McGill University, Montreal, Quebec, H2X 2P2, Canada.**

In four normal, anesthetized, paralyzed and tracheostomized dogs we measured tracheal pressure, airway flow and alveolar pressure (using a closed-chest alveolar capsule technique). Following 30-second periods of apnea, the dogs were sinusoidally oscillated with different tidal volumes (15, 25 and 35 ml/Kg) and frequencies (0.25, 0.5 and 0.83 Hz) using four gas mixtures (air, 80% helium + 20% oxygen, 80% neon + 20% oxygen, and 50% sulphur hexafluoride + 30% nitrogen + 20% oxygen). The pressure drop across the airways (Paw) was obtained by subtracting alveolar pressure from tracheal pressure. The amplitude of the swings in Paw showed a transient decrease which persisted for about 10 seconds following the onset of oscillation. The Paw-flow diagram also had a figure-of-eight shape. We suggest that these data demonstrate the existence of a significant lung volume history effect on airway calibre. We have developed an airways model whose resistance is determined by flow, lung volume, gas density, gas velocity, and the viscoelastic properties of the airway wall. The model is able to account for the main features of our data. (Supported by MRC Canada, the Canadian Lung Association and the EL/JTC Memorial Research Fund).

50.17

LENGTH-SPECIFIC EFFECTS OF AMINOPHYLLINE ON *IN VITRO* FORCE GENERATING CAPACITY OF CANINE DIAPHRAGM. H.-Y. Tao and G.A. Farkas. Mayo Clinic & Foundation, Rochester, MN 55905

At short muscle lengths, decreases in force are caused, in part, by a decreased Ca^{2+} activating system. It has been suggested that theophylline enhances Ca^{2+} influx during skeletal muscle activation. The effects of aminophylline on acute shortened diaphragm are not known and formed the basis of this study. Diaphragmatic (costal diaphragm) bundles (n=28) were excised from 8 anesthetized dogs. Bundles were maintained in an oxygenated Krebs solution at 37°C. Optimal length (L_o) was determined in normal Krebs (NK) as representing that length at which peak force was generated. The bathing solution as then replaced with either NK or NK + aminophylline (150 mg/L). Following a 20-minute equilibration period, diaphragm bundles were randomly studied at L_o or at 70% L_o. Twitch and force frequency characteristics were determined. Our results indicate that at L_o, aminophylline had no effect on the *in vitro* twitch or force frequency characteristics of costal diaphragm. At 70% L_o, however, although the twitch characteristics were similar, we observed that the force generated at submaximal stimulation frequencies and the maximal tetanic tension (P_o), corrected for cross-sectional areas, was significantly increased in the aminophylline treated bundles. At 70% L_o, P_o ($\bar{x}$±SE) was 0.87±0.08 kg/cm^2 in NK vs 1.24±0.18 in NK + aminophylline ($p<0.05$). We conclude that aminophylline at a concentration of 150 mg/L has no potentiating effect at L_o, but enhances muscle force at suboptimal lengths.

50.18

LUNG VOLUMES AND ESOPHAGEAL PRESSURES DURING SHORT PERIODS OF MICROGRAVITY AND HYPERGRAVITY. G. K. Prisk, A.R. Elliott, H.J.B. Guy* and J.B. West. Department of Medicine, S-031, University of California San Diego, CA 92093.

We measured respired volume and esophageal pressure (P_{es}) in three normal, seated subjects (2 males, aged 34 and 50, and 1 female aged 40) exposed to short periods of microgravity (0-G) and approximately twice normal gravity (2-G) in a NASA KC-135 microgravity research aircraft. The subjects breathed tidally through a ultra-sonic flowmeter and made occasional excursions to residual volume at the different G levels. Volume was corrected for changes in cabin pressure and temperature. P_{es} was measured via an esophageal balloon coupled to a Validyne MP-45 differential pressure transducer.

Functional residual capacity (FRC) decreased by 280 ± 40 (SE) ml between 2-G and 0-G, and by 210 ± 40 ml between 1-G and 0-G. There was a concomitant rise in P_{es} of 2.1 ± 0.3 cmH_2O between 2-G and 0-G. P_{es} at 1-G was intermediate to, although not significantly different from, the values at 2-G and 0-G. There were no changes in either tidal volume or the swing in P_{es} during tidal breathing, indicating that the work of breathing probably remained unchanged.

The rise in P_{es} at 0-G accounts for nearly 40% of the previously reported 5.4 cmH_2O increase in central venous pressure between 2-G and 0-G (Norsk et al., J. Appl. Physiol., 63(6), 2433-2437, 1987). We conclude that in order to adequately assess the central cardiovascular effects of microgravity, and in particular the changes in cardiac transmural pressures, it is necessary to take into account the rise in intrapleural pressure associated with the reduction of lung volume. (Supported by NASA, NAG9-271 and NAS9-16037).

50.19

ANALYSIS OF NONLINEAR MECHANICAL PROPERTIES OF THE RESPIRATORY SYSTEM. D.N. Campbell, G.M. Barnas, G. Ho, M. Ashby, C.F. Mackenzie, A.J. Smalley and J. E. Mendham. Univ. of Maryland, Baltimore, MD 21201

We tested whether measurements of respiratory system resistance (R) and elastance (E), which have been shown to be non-linear, were affected by linearity of analysis technique or type of forcing waveform. We measured pressure and flow at the mouth of 5 awake, relaxed subjects during forcing (0.2 to 0.6 Hz, 250 to 750 ml) with 3 different flow waveforms: 1) sinusoidal, SINE; 2) quasi-sinusoidal, QUASI (sinusoidal inspiration, passive expiration); and 3) STEP (step inspiration, passive expiration). R and E were calculated using linear, Fast Fourier Transform (FFT) and a non-linear analysis (NLA). During QUASI and STEP with NLA, E was about 3 to 8% higher, and R at 0.2 Hz 15 to 25% higher, than with FFT. Waveform did not affect R, but E was 3 to 10% higher during QUASI and STEP than during SINE. We conclude that the non-linearity of respiratory system mechanical properties leads to small, consistent differences in E when different waveforms are used for forcing; however, R and E can be measured with reasonable accuracy with linear analysis and during several types of forcing. (Supported by an ALA grant, HL33009 and HL44128).

50.20

REDISTRIBUTION AND CONTINUITY OF PLEURAL LIQUID. S.H. Loring and J.P. Butler. Respiratory Biology Program, Harvard School of Public Health, Boston, MA 02115.

If the intrinsic shape of the lung differs from that of its container, at static equilibrium there will be areas of contact between lung and chest wall, with intervening collections of pleural liquid. Does lung motion in breathing redistribute the liquid to promote a continuous and uniformly thick layer? Mass conservation is inconsistent with the uniform motion of a compliant boundary over a region of varying thickness. A small volume flux through a thin region cannot match the larger volume flux through an adjacent thick region. Thus, the thin region will thicken and the thick region will thin. This redistributes liquid, leading to more uniform thickness and preventing regions of contact.

To test the theory, we placed a membrane on a thin layer of viscous liquid in a tray with an uneven bottom. Statically, the membrane was flat, and thus the liquid was of uneven thickness, thinnest over the humps in the tray. When the membrane was dragged to and fro, the liquid layer became more uniform in thickness as the membrane conformed to the topography of the tray. With *motion, pressures increased* over the hills, and decreased over the valleys. Membrane shape exhibited irreversible behavior, reflecting interaction between compliant boundaries and fluid mechanical forces. We conclude that regions of contact between lung and chest wall cannot exist in vivo. Supported by HL33009.

50.21

A NONLINEAR VISCOELASTIC MODEL OF LUNG TISSUE MECHANICS. B. Suki and J.H.T. Bates. Meakins-Christie Laboratories, McGill University, Montreal, Quebec, Canada.

The volume dependence of lung tissue resistance (R_{ti}) and elastance (E_{ti}) has generally been attributed to the phenomenon of plastoelasticity. In this paper we propose an alternative representation by developing a model in the framework of nonlinear viscoelasticity which is capable of adequately accounting for most of the known nonlinear and frequency-dependent features of lung tissue mechanics. The derivation of the model is based on several observed and hypothetic characteristics of lung tissue. These include 1) the reduction of R_{ti} and E_{ti} with increasing tidal volume (V_T) is determined by the fundamental component of the volume spectrum; 2) the nature of the V_T-dependence of R_{ti} and E_{ti} is independent of frequency; and 3) the harmonic production in the lung is also frequency-independent. The parameters in the model were identified and the model was then used to simulate real measuring situations by driving the model with different classes of input signals. R_{ti} and E_{ti} were estimated from the simulated input-output relationships by using four evaluation techniques commonly applied in respiratory mechanics. This analysis shows that in the worst case combination of input signal and evaluation technique the V_T-dependence of R_{ti} and E_{ti} can be misestimated by as large as 300 and 75%, respectively. (Supported by the EL/JTC Memorial Research Fund).

COMPARATIVE ASPECTS OF EPITHELIAL TRANSPORT

51.1

INHIBITION OF CHLORIDE PUMP ACTIVITY THROUGH SULFHYDRYL BINDING IN APLYSIA GUT. G.A. Gerencser. Department of Physiology, University of Florida, Gainesville, FL 32610.

N-ethylmalemide (NEM) inhibits net Cl^- absorption across the Aplysia foregut. Additionally, both a Cl^--stimulated ATPase activity and an ATP-dependent Cl^- transport process were found in Aplysia foregut absorptive cell basolateral membranes (BLM). In an attempt to further characterize this Cl^- pump, BLM vesicles from Aplysia foregut absorptive cells were prepared utilizing differential centrifugation and sucrose density gradient techniques. Sulfhydryl ligand participation in ATP-dependent Cl^- transport was confirmed in three ways. First, dithiothreitol partially restored a p-chloromercurobenzoate sulfonate (PCMBS)-inhibited ATP-dependent Cl^- transport. Second, dithiothreitol restored intravesicular negativity inhibited by PCMBS. Third, dithiothreitol had no effect on either ATP-dependent Cl^- transport or ATP-dependent intravesicular negativity inhibited by NEM. These results are consistent with the hypothesis that surface sulfhydryl groups participate in the functioning of the active electrogenic Cl^- transport mechanism in Aplysia gut.

Supported by a grant from the Eppley Foundation for Research, Inc.

51.2

INHIBITION OF Cl SECRETION IN NECTURUS GASTRIC MUCOSA AND RABBIT COLON BY AN EXTRACT OF ACORUS CALAMUS. J.R. Demarest, D.W. Martin and M.L. Siems*. Dept. Zool., U. of Arkansas, Fayetteville, AR 72701

Extract of sweet flag, Acorus calamus, has been reported to possess antiulcer and antidiarrheal activities. In both gastric mucosa and colon, fluid secretion is coupled to electrogenic Cl^- secretion. The short circuit currents, I_{sc}, of these epithelia are equal to the sum of amiloride sensitive Na^+ absorption by surface cells and Cl^- secretion from multicellular glands. The effects of Acorus extract were investigated in vitro with cimetidine (10^{-4} M) treated Necturus gastric mucosa and cAMP (10^{-3} M) stimulated rabbit colon. Necturus gastric mucosa exhibited dose dependent, reversable decreases in I_{sc} and transepithelial conductance, G_t, with apical exposure to increasing concentrations of aqueous extract of Acorus roots. Effects on I_{sc} and G_t were significant with 5% extract ($p<.05$). Decrements in I_{sc} (19±1 $\mu A/cm^2$, gastric mucosa; 20±10 $\mu A/cm^2$, colon) caused by 20% extract were unaffected by 10^{-4} M apical amiloride, when I_{sc} equals net Cl^- secretion in both epithelia. These data suggest that inhibition of Cl^- secretion may be responsible for the effects of Acorus extract on gastrointestinal epithelia. (Supported by NIH DK38664)

51.3

CYCLIC ADENOSINE MONOPHOSPHATE STIMULATES TRANSEPITHELIAL ION TRANSPORT IN THE ISOLATED CLAM MANTLE. R.L. Hudson. Physiology and Biophysics, University of Illinois at Chicago, Chicago, Il. 60680.

The isolated mantle of the freshwater lamellibranch mollusc, Unio, has been used to investigate the mechanisms of ion transport utilized in shell formation (L.B. Kirschner, Science 131:735,1960). This shell-secreting tissue is composed of two parallel epithelial sheets separated by a hemolymph-containing sinus. The shell-facing surface of the mantle is composed of a single layer of cells that function to isolate a site of calcification from the rest of the body fluids. The shell-facing epithelium is dissected from the mantle and mounted in a Ussing-chamber for studies of transepithelial ion transport using electrophysiological and isotopic flux techniques. Previous studies (R.L.Hudson,FASEB J. 4:A446,1990) have shown that this tissue generates a spontaneous transepithelial electrical potential difference that is dependent upon permeant weak acids, the most significant is the CO_2/HCO_3^- /carbonic anhydrase system. In the absence of CO_2/HCO_3^- or in the presence of CO_2/HCO_3^- plus acetazolamide this potential is abolished. Under voltage-clamp conditions, the short-circuit current (blood to shell) is not directly dependent upon Ca^{2+}, Na^+, K^+, or Cl^- fluxes (determined by ion-substitution and isotopic tracer experiments). This current is dramatically increased by the addition of the membrane-permeant cAMP analogs (8-bromo-, dibutyryl-, 8-(4-chlorophenylthiol)-cAMP) from the resting current (<10 $\mu Amps/cm^2$) to high values (100 - 200 $\mu Amps/cm^2$). This current is stable for several hours, is not due to Ca^{2+}, Na^+, K^+, or Cl^- fluxes, and is dependent upon a functioning CO_2/HCO_3^- /carbonic anhydrase system. It is inhibited by acetazolamide, DIDS, SITS, Co^{2+}, and Ni^{2+} (all from blood-side). These results support the hypothesis that this calcifying tissue preforms it's physiological role by regulating acid/base traffic into and out of the mineralizing compartment with calcium following passively. (Supported by NIH-AR39700)

51.4

MECHANISM OF STAPHYLOCOCCAL ENTEROTOXIN B ALTERED INTESTINAL FLUID AND ELECTROLYTE TRANSPORT. Yuan-Heng Tai. Walter Reed Army Institute of Research, Washington, DC 20307-5100.

Staphylococcal enterotoxin B (SEB) is a highly toxic and readily available bacterial enterotoxin responsible for the most prevalent type of foodborne debilitating enteric intoxication in humans. The mechanism of action of SEB on intestinal fluid and electrolyte transport was studied in the rat ileum using in vivo single perfusion and in vitro Ussing chamber-voltage clamp techniques. In the in vivo experiments, ^{14}C-PEG (av. M.W. 3350) was used as the non-absorbable marker for water transport. SEB at 5μg/ml in the perfusate was able to decrease the rate of absorption of fluid, sodium, and chloride within 30 min. of exposure. The secretory effect of SEB was also reversible, i.e., the transport rates returned towards normal in approximately an hour after SEB was removed from the perfusate. The SEB-induced decrease in fluid and electrolyte absorption could be prevented by adding the cyclooxygenase inhibitor, indomethacin (10^{-5}M) to the perfusate. The in vitro study was carried out by measuring the electrical parameters and Na and Cl fluxes across a tissue mounted as a flat sheet in Ussing chambers under short-circuit conditions. 5μg/ml of SEB in the mucosal bathing solution stimulated the short-circuit current and electrogenic Cl secretion. The results suggest that the secretory effect of SEB may be mediated by intracellular prostaglandins.

51.5

ELECTROPHYSIOGICAL CHARACTERISTICS OF THE YOLK SAC MEMBRANE OF THE CHICK EMBRYO. Makoto Takada and Nancy B. Clark, Univ. of Connecticut, Storrs, CT 06269.

The yolk sac provides calcium to the developing chick embryo during early embryogenesis and stores excess calcium during the latter half of incubation. ^{45}Ca is transported from yolk to blood, and this transport is enhanced by 1,25-dihydroxyvitamin D_3 ($1,25\text{-}(OH)_2D_3$). We have studied the electrical characteristics of this membrane at different developmental stages in Ussing chambers in order to elucidate the mechanism(s) of calcium transport. The potential difference (PD) and short circuit current (SCC) across the yolk sac membrane increases with embryonic age (9 day <12 day<15 day). The PD and SCC are directly proportional to the sodium concentration of the bathing medium. Sodium is transported from the yolk side (brush border side) to the blood side (basolateral side) of the membrane. Kinetic analysis (Eadie-Hofstee Plot) indicates two kinds of sodium channels exist in the membrane. In chick embryos pretreated with $1,25(OH)_2D_3$ (48 and 24 hr before test), PD and SCC are not significantly different from alcohol-injected controls. If amiloride (10^{-5}M) is applied to either the BBM or BLM, there is no change in PD or SCC. Similarly, application of ouabain (10^{-4}M) to the BBM has no effect in either controls or $1,25(OH)_2D_3$-treated embryos. However, application of ouabain to the BLM of controls causes over 50% reduction in SCC, while that of $1,25(OH)_2D_3$-treated animals is 88% of normal. $1,25(OH)_2D_3$ may be blocking the effect of ouabain on the sodium pump or stimulating the biosynthesis of a ouabain-insensitive sodium pump. The PD and SCC are not affected by changes in the calcium concentration of the bathing medium. The transport of calcium in either direction across the yolk sac membrane is not affected by application of lanthanum (1mM), dinitrophenol (160μM) or cytochalasin B (2μg/ml), despite a significant decrease in SCC caused by these inhibitors. At the present time we have evidence of active sodium transport but no evidence of active calcium transport by the yolk sac membrane. Supported by Grant 88-12131 from the National Science Foundation.

51.6

EFFECT OF HEAT STRESS ON TRANSEPITHELIAL TRANSPORT BY FLOUNDER RENAL TUBULE PRIMARY CULTURES (PC). J. Larry Renfro, Raghuveerender Upender*, Mary Brown*, and Lawrence E. Hightower*. Univ. Connecticut, Storrs, CT 06269.

To determine the limits of thermal tolerance, electrical potential difference (PD), resistance (R), short circuit current (SCC) and phlorizin-sensitive SCC (Na-dependent glucose transport) of flounder proximal tubule PCs were measured at 22°C immediately following 1 h exposure to temperatures ranging from 22°C to 37°C. At temperatures below about 28°C electrical properties were unaltered, but at higher temperatures damage was apparent. SDS-PAGE analysis of protein patterns showed that heat stress proteins were maximally induced in tissues exposed to 27°C for 6 h. Exposure to 32°C for 1.5 h caused a significant decline in PD (-0.51 ± 0.03 to -0.30 ± 0.08 mV), SCC (16 ± 1.5 to 9 ± 2.3 uA/cm^2) and phlorizin-sensitive SCC (7 ± 0.7 to 3 ± 0.8 uA/cm^2); however, in tissues exposed to 27°C for 6 h prior to 32°C-exposure, electrical characteristics were unchanged compared to tissues held continuously at 22°C. Sulfate secretion was also inhibited by 32°C unless "protected" by prior exposure to 27°C for 6 h. Supported by NIEHS ES03848.

61.1

METABOLIC COST OF AROUSAL IN BRAZILIAN HUMMINGBIRDS. J.E.P.W.Bicudo, J.F.Steffensen*, M.Berger*, C.Bech* and A.S.Abe*, Museu de Biologia Prof. Melo Leitao, Santa Teresa, ES, Brazil and Universidade de Sao Paulo, SP, Brazil.

Hummingbirds are among the smallest homeotherms having very high mass specific standard oxygen uptake. They do not feed at night and must rely upon stored energy reserves to maintain themselves during periods of inactivity. The ability of some homeotherms to become torpid, or to reduce their oxygen consumption ($\dot{V}O2$) and allow body temperature (Tb) to approximate ambient temperature (Ta), represents one mechanism to reduce high costs of temperature regulation during inactive periods at lower Ta. Laboratory studies of hummingbirds suggest that they enter torpor only when energy reserves reach a critical, lower threshold. The length of a torpor bout is regulated by when this nocturnal threshold is reached. $\dot{V}O2$ and Tb during entering, progression and arousal from torpor were measured in various brazilian hummingbird species of different body masses, ranging from around 2 g to 10 g. In all the species studied, $\dot{V}O2$ dropped together with Tb during torpor. When Tb approached nocturnal Ta, $\dot{V}O2$ was kept fairly constant over a period of several hours until the birds started to arouse. Arousal was always characterized, in all the species considered, by a progressive increase in $\dot{V}O2$, with a peak value approximately 30-40% higher than resting values, followed by a sudden drop of $\dot{V}O2$ to more stable values (resting), when normal Tb (37 °C) was finally reached. The mass specific $\dot{V}O2$ values (peak values) for small hummingbirds were significantly higher than those encountered for larger hummingbirds. It is concluded, therefore, that the energetic cost of arousal to attain resting Tb in small hummingbirds, probably because of surface-to-volume considerations, is significantly higher when compared with that of larger ones. Supported by the Hasselblad Foundation, Sweden, and Brazilian National Science Foundation, CNPq.

61.2

METABOLIC ACCLIMATION IN THE AXOLOTL, AMBYSTOMA MEXICANUM. Karen A. Talentino and Denise Caruso. Simmons College, Dept. of Biology, Boston, Ma. 02115.

The neotenic salamander Ambystoma mexicanum was studied to confirm earlier results that revealed its capacity for metabolic acclimation - the ability of some ectotherms to adjust their metabolic physiology in response to extended exposure to a particular environmental temperature. Animals were obtained from the Indiana University Axolotl Colony. Metabolic rates were determined using closed system respirometry; dissolved oxygen analysis was accomplished using a Cameron Dual-Channel Oxygen meter. Following determination of Standard Metabolic Rates, animals were maintained at either 15°C (cold acclimation) or 25°C (warm acclimation) for an acclimation period of 3 weeks. Metabolic rates were determined at 15°, 20° and 25°C at the end of the acclimation period. Our results confirm that there are significant differences in metabolic rates of the two groups at 15° and 20 C, thus indicating that some degree of metabolic acclimation can occur in axolotls. Biochemical correlates of this acclimation, including ganglioside and other glycolipid, liver protein and LDH isozyme analysis, are also being investigated. Since this species is not exposed to significant temperature fluctuations in its natural habitat, the capacity for acclimation presumably reflects retention of physiological capabilities from ancestral forms exposed to greater environmental variability.

61.3

PHYSICAL FACTORS DETERMINING BODY TEMPERATURE IN MOIST-SKINNED ANIMALS: THE EFFECTS OF ENVIRONMENTAL RELATIVE HUMIDITY AND TEMPERATURE ON BODY TEMPERATURE IN THE BULLFROG. Roy S. Meyers, Heidi Roy* and Scott Sergenton*. Skidmore College, Saratoga Springs, N.Y. 12866

Although strong evidence exists for behavioral thermoregulation in some Anuran amphibians, the effects of the major baseline passive physical factors (environmental temperature [Te], relative humidity [RH]) that determine body temperature have not been systematically investigated in most species. To this end, the effect on resulting deep body temperature (Tb, measured by telemetry) of systematically varying relative humidity (RH = 40-100%) at each of three different environmental air temperatures (5,15,25°C) was studied in the semi-aquatic bullfrog *Rana Catesbeiana* (17 animals) confined so that behavioral thermoregulation was precluded. At 25°C, Te-Tb was found to depend inversely and linearly on RH (Te-Tb= -0.153*RH+12.75, R=.89) rather steeply ($\Delta Tb/\Delta RH$= -0.153). At RH < 84%, animals were always colder than their environment due to obligatory evaporative water loss (EWL) while above this RH animals were warmer due to an inability to dissipate metabolic heat by EWL. Body temperature dependency was less severe at 15°C ($\Delta Tb/\Delta RH$= -0.031) and virtually non-existent at 5°C ($\Delta Tb/\Delta RH$ <.001) in part due to less EWL at lower air temperatures. For a bullfrog in an environment at 25°C and RH=40 the implications are substantial; an 8.5° depression in Tb constitutes a thermal disadvantage in any "attempt" to achieve its preferred Tb of 26-28°C. Preliminary data on a more terrestrial anuran (*Bufo marinus*) at 25°C suggest a similar but less steep dependency on RH, possibly indicating the evolution of a lower evaporative skin conductance.

61.4

COMPARISON OF OXYGEN CONSUMPTION RATES OF TWO SCORPIONFISH LIVING AT DIFFERENT DEPTHS AND OXYGEN CONCENTRATIONS. T.-H. Yang and George N. Somero. Scripps Institution of Oceanography, UCSD, La Jolla, CA 92093

Scorpaena guttata and Sebastolobus alascanus (Scorpaenidae) are demersal fishes, commonly found off the California coast: S. guttata lives in shallow water (<100 m depth; temperature 10-20°C) and is not exposed to low [O_2], while S. alascanus lives in upper continental slope (300-1200 m; temperature 3-7°C) and is found in oxygen minimum layer ([O_2] 0.2-0.5 ml O_2/liter). This study was initiated to examine the adaptation of S. alascanus to low [O_2] and more episodic food supply. Fishes in this study were acclimated to 9.0°C (±0.5°C) for at least one month before initial oxygen consumption rate (QO_2) measurements were obtained. The QO_2's for fish fed ad libitum of both species were indistinguishable. Long term (3-4 months) fasting significantly reduced QO_2; S. guttata QO_2 averaged 1.7 times that of S. alascanus. The response to low oxygen concentrations was also different between these two species. Deeper living S. alascanus regulated QO_2 to the lowest concentration tested (0.3 ml O_2/liter). S. guttata could not regulate its QO_2 below 1 ml O_2/liter. Ventilation frequencies (V_f) of S. alascanus increased with decreasing [O_2], effectively compensating for very low [O_2]. V_f of S. guttata also increased as [O_2] decreased to 1 ml O_2/liter, and then decreased. These respiratory responses to low [O_2] indicate that S. alascanus is a very good oxygen regulator. The lower QO_2 of fasting S. alascanus implies this species is adapted to lower density and more episodic food supply of continental slope.

61.5

EXPERIMENTAL EVOLUTIONARY ADAPTATION TO TEMPERATURE. Albert F. Bennett and Richard E. Lenski. Ecology and Evolutionary Biology, University of California, Irvine CA 92717

A model bacterial system (Escherichia coli) was used to determine the rate and extent of adaptation, measured directly as fitness improvement, to 3 experimental temperature regimes (32C, 42C, and daily alteration between them) in comparison to both ancestral and control (37C) lines. 6 replicates of each experimental line were cloned from a single cell from a line raised at 37C for 2000 generations; hence all adaptation was derived from de novo mutations. Significant fitness improvement at 42C occurred by 200 generations (less than one month). After 2000 generations, all 3 experimental lines had significantly improved fitness in comparison with the ancestral line (32C = +10%, 42C = +26%, 32/42C = +10%) ($p<0.001$) and the 37C controls ($p<0.05$). Adaptation to a particular temperature did not necessarily result in a correlated loss of fitness at other temperatures: the 42C line, for instance, did not lose fitness in comparison to the ancestral line when assayed at 37, 32, or 27C. These experiments have shown that this is a feasible model with which to investigate the mechanisms, correlations, and repeatability of environmental adaptation of biological systems.
(Supported by NSF Grants DCB 8812028 to AFB and BSR 8858820 to REL and a UCI Faculty Research Fellowship.)

61.6

THE DYNAMICS OF RECOVERY IN THE FROG RANA SYLVATICA FOLLOWING EXTENSIVE FREEZING. Jack R. Layne, Jr. and Melissa C. First . Nazareth Coll., Rochester, NY 14610

Freezing arrests physiological functions in wood frogs (R. sylvatica) even though they recover from freezing bouts that last as long as a few weeks. We monitored recovery in regard to restoration of blood flow, breathing, heartbeat, and muscle contraction. Frogs were frozen at - 2 to - 3 C for 24 hours and thawed rapidly at high temperature (23 to 25 C) or slowly at low temperature (6 to 8 C). Fast thawing restored bodily functions faster but the recovery rate was less for this group than the slow thaw group (78% vs 92%). All frogs had heartbeats 0.5 to 1 hour after the onset of thawing, and heart rates increased as their body temperatures equilibrated with the thawing environment. Indeed, stable heart rates (18.5 beats/min) were seen 3 to 4 hours after the onset of slow thawing. Regular breathing returned later with the first evidence of this parameter not until 3 to 4 hours after thawing. Contrastingly, twitch and tetanic contraction strength of gastronemius muscles that had been frozen and thawed in vivo showed no significant ($P > 0.05$) differences among control, 1, 2, and 24 hour thaw groups. Our data indicate that recovery is not uniform and tissues like skeletal muscle are little impaired by the present freezing episodes. At the systemic level, the cardiovascular system rebounds fastest from freezing which reflects the importance of timely reperfusion for recovery of the whole organism.

61.7

ABSENCE OF FEVER IN PLANARIAN: Turbellaria, *Phogocata gracilis*. M. Cabanac and B. Drolet*, Laval University, Québec, Canada, G1K 7P4.

Fever, a defense response, has been obtained in all classes of vertebrates, in all classes of arthropods, and the class Hirudinea of annelids. Molluscs failed to respond by a behavioral fever to the injection of various pyrogenic substances. It was therefore of interest to assay fever in Platyhelmintes. Groups of 5 to 10 planarian (Turbellaria: *Phogocata gracilis)* were placed in a water gradient of temperature extending from 0 to 40°C over 0.8 m. In control sessions, the planarians avoided water at less than 9°C and more than 23°C. In the 4h following *intracœlomic* injection of *E. coli* endotoxin (2.5, 5, and 10 $ng.mg^{-1}$), human interleukin-2 (0.5, and 2 $mU.mg^{-1}$), interferon a (0.02, 0.2, and 1 $U.mg^{-1}$), and vehicle the thermopreferendum was not different from control. The pyrogenic drugs were toxic at higher concentrations, therefore active. The diffusion of injected substances to the whole body was verified with a dye. These negative results are not in favor of fever in Plathyhelmintes. The absence of fever in both Plathyhelmintes and Molluscs, while Arthropods and Annelids can have fever, might be explained by a common phylogenetic origin of the former. (Supported by N.S.E.R.C., Canada)

61.8

LOW TEMPERATURE ACCLIMATION EFFECTS ON LIPID AND FATTY ACID METABOLISM IN TWO TELEOSTS. Thomas D. Singer and James S. Ballantyne. Univ. of Guelph, Dept. of Zoology, Guelph, Ont., CANADA, N1G 2W1

Poikilotherms acclimated to low temperatures show positive metabolic compensation in enzymes associated with oxidative metabolism whereas enzymes of nitrogen metabolism are noncompensatory and glycolytic enzymes show variable effects in some tissues. Compensatory effects in lipid catabolizing enzymes have not been previously studied. Two species of teleosts lake char, *Salvelinus namaycush*, which remain active over winter, and yellow bullhead, *Ictaluras natalis*, which are "dormant" over winter, were acclimated to 2°C and 10°C. Activities of enzymes involved in lipid catabolism were determined in white and red muscle, heart, kidney and liver at both temperatures. Levels of individual non-esterified fatty acids (NEFA) were measured in plasma as were individual fatty acids of total lipids in red muscle and liver in all fish. Lake char showed positive compensation for 3-Hydroxyacyl CoA dehydrogenase (HOAD), an enzyme involved in ß-oxidation of fatty acids, in all tissues. Yellow bullhead showed noncompensatory activity for HOAD in all tissues. Total plasma NEFA levels were significantly higher in lake char than yellow bullhead. Similarly, levels of total lipids were significantly higher in red muscle and liver of lake char than in yellow bullhead. Lake char exhibited a doubling in the levels of total lipid in liver tissue acclimated to 2°C compared to 10°C, however, no change was detected in the red muscle. These results indicate that the positive compensation of lipid catabolism may be an important adaptational strategy of fish that remain active at low temperatures. This contrasts with the strategy employed by fish that are "dormant" at low temperatures. This research was funded by an Natural Sciences and Engineering Research Council of Canada operating grant to JSB.

61.9

TRIACYLGLYCEROL LIPASE (TAGL) OF ANTARCTIC FISH TISSUES PREFERENTIALLY MOBILIZES UNSATURATED FATS. J. R. Hazel and B. D. Sidell, Arizona State University, Tempe, AZ 85287 and University of Maine at Orono, Orono, ME 04469

Energy metabolism in aerobic tissues of Antarctic fishes is supported primarily by the oxidation of fatty acids that are abundant in these species. Trematomus newnesi is a relatively active, pelagic member of this group in which these features are particularly pronounced. To characterize lipolytic activity in T. newnesi, we have: 1) determined total TAGL activity in oxidative muscle, liver, heart, and adipose tissue; and 2), determined substrate specificity of TAGL in adipose tissue. Total lipase activity ranged from undetectable in heart to 32 pmoles (oleate released from ^{14}C-triolein)/min/gm wet weight in liver. By competing various unlabeled, homogeneously acylated triacylglycerols (TAG) against ^{14}C-triolein, the preferred order of substrate utilization was determined to be polyunsaturates > monoenes > saturates. Not only were saturated TAGs poorly hydrolyzed, they actually facilitated hydrolysis of triolein. Among the saturates, trimyristin (14:0) was a particularly unsuitable substrate. Notably, 14:0 accounts for a disproportionate fraction of the acyl chains stored in adipose tissue of T. newnesi. Our data suggest that the pattern of fatty acids present in adipose tissue may reflect preferenda of lipolytic rather than lipogenic enzymes.
(Supported by NSF grants DPP 88-19469 and DCB 8901469)

61.10

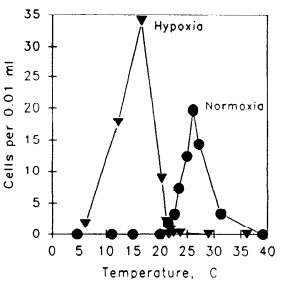
RELATION OF CUTANEOUS EVAPORATION TO SKIN BLOOD FLOW AND TEMPERATURE IN PIGEONS. A. M. Gabaldón*, R. A. Furilla*, and M. H. Bernstein. NM State Univ., Las Cruces, NM 88003

Cutaneous evaporation (CE) contributes greatly to heat loss in some heat-stressed birds. To evaluate factors governing CE, we measured dermal temperature (T_d) and relative blood flow (RBF), along with CE, in dorsal skin of awake pigeons (Columba livia, mass 0.65 kg) exposed to dry air at temperatures (T_a) from 32 to 50°C. Over this range of T_a, steady-state cloacal temperature increased from 41 to 44°C, and T_d increased from 39 to 43°C, augmenting the vapor pressure (PH_2O) at the skin's boundary layer. CE increased with T_d from 2 to 14 mg/(cm^2 kg h). When T_a exceeded T_d, so that heat could not be lost convectively from skin, RBF decreased. Under these conditions, the primary driving force for CE appears to be the PH_2O gradient between the skin and air, as determined by T_d, rather than the rate of water delivery to the skin via the blood. The rise in T_d when it is exceeded by T_a suggests that heat transfer from air to skin may exert a substantial influence on T_d and therefore on CE. The reduced skin blood flow may reflect circulatory shifts from the skin to other heat loss regions, such as the respiratory tract, where warm arterial blood can be evaporatively cooled by panting or gular flutter.
(Supported by NSF grant BSR-8806604.)

61.11

BEHAVIORAL HYPOTHERMIA IN A HYPOXIC PROTOZOAN, PARAMECIUM CAUDATUM. Gary M. Malvin and Stephen C. Wood. Lovelace Medical Foundation, Albuquerque, NM 87108.

Regulation of body temperature often depends on behavioral mechanisms. Most animals show a preferred temperature (T_p) in a temperature gradient. Hypoxia reduces T_p of vertebrates. This is adaptive because it lowers the demand for O_2 when it is scarce. Unicellular animals also have preferred temperatures based on membrane potentials. However, a behavioral response to hypoxia has not been previously documented in those organisms. We tested the hypothesis that Paramecium caudatum will select a lower temperature under hypoxic conditions. Paramecia (≈ 100) were placed in an aqueous thermal gradient ranging from 2 to 40°C. The gradient was enclosed so that the PO_2 surrounding the gradient was controlled. T_p of the paramecia was determined by measuring both the temperature and paramecium density at 12 locations along the gradient. As shown in the figure, during normoxia, T_p was 26°C. However, 3 hours after the gradient PO_2 was lowered to < 1 torr, T_p fell to 16°C. A return to normoxic conditions caused T_p to return to 26°C. These results indicate that, like vertebrates, the unicellular paramecium lowers its temperature under hypoxic conditions. This organism may be useful in understanding the interactions between respiration and temperature regulation at the cellular level. Supported by NIH grant HL38942 and the Flinn Foundation, Phoenix, AZ.



61.12

PHYSIOLOGICAL SIGNIFICANCE OF HYPOTHERMIA IN HYPOXIC BUFO MARINUS. Stephen C. Wood, Lovelace Medical Foundation, Albuquerque, NM 87108

Previous studies have documented behavioral hypothermia in hypoxic vertebrates. A theoretical advantage of this response in ectothermic species, is a reduction of oxygen demand (Q_{10} effect). Whether or not this metabolic savings occurs would depend on activity levels and ventilatory responses to hypoxia. Other potential advantages of hypothermia are increased arterial saturation (left-shifted dissociation curve from temperature and pH effects) and decreased ventilatory response. Previous work showed that normoxic toads in a gradient select a mean temperature of 25° C and hypoxic toads (10% inspired O_2) select 15° C. The present study examined these potential effects of hypothermia in Bufo marinus (n = 7 to 18) at 25 and 15° C under both normoxia (21 - 35% inspired O_2) and hypoxia (10% inspired O_2). Toads were exposed to graded hypoxia over a 6 day period to determine the metabolic response. At 25°, oxygen uptake (VO_2) increased significantly from 21 to 10% inspired O_2. Video recording revealed this to result from both increased activity and ventilation. At 15° C, there was no increase in VO_2 from 21 to 10% O_2. Measurements of ventilation frequency revealed a significant ventilatory response to hypoxia at 25 but not at 15° C. Thus, cooling to 15° C during hypoxia resulted in a significant reduction of oxygen demand due to Q_{10} effect plus reduced activity and ventilatory work. Arterial blood gas analyses showed that hypoxia at 25° C caused a significant drop in saturation and PO_2 and rise in pH (hyperventilation). Cooling to 15° C during hypoxia caused a significant rise in arterial saturation but no change in PO_2. Hypoxia at 15° C did not affect arterial pH (no hyperventilation). In conclusion, hypoxia is a significant stress to Bufo marinus at their normal selected temperature and a trivial stress after they cool to 15° C. Supported by the Flinn Foundation, Phoenix, AZ.

61.13

INTERACTIONS AMONG TEMPERATURE, GROWTH RATE AND MUSCLE METABOLIC ORGANIZATION IN COD (*Gadus morhua*). Dany Pelletier*, Helga Guderley and Jean-Denis Dutil* Université Laval, Québec, P.Q. and Institute Maurice Lamontagne, Fisheries and Oceans, Rimouski, P.Q. Canada.

In fish, the sensitivity of muscle enzyme levels to starvation and temperature is well known. Recent data suggest that muscle enzyme levels are also positively correlated with growth rates. We have examined the effect of temperature and growth rates on muscle enzyme levels in juvenile cod (35 - 55 cm). Individually tagged cod were maintained at 4, 10 and 15°C for 8 weeks and were fed at 0.175 to 0.9% of their wet body mass per day at 4°C, 0.4 to 2.8% at 10°C, and 0.7 to 3.5% at 15°C. These rations yielded growth rates ranging from slight degrowth to 1.2% per day. Since temperature and growth rate could have differing effects on aerobic and anaerobic energy metabolism, we examined important enzymes in both processes. Both aerobic and anaerobic enzyme activities in white muscle are positively correlated with growth rate and the correlation is strongest for the glycolytic enzymes. We propose that muscle enzyme levels can be used as indicators of growth rates of cod under culture conditions.

61.14

RESPIRATORY, METABOLIC AND THERMAL PHYSIOLOGY OF LEATHERBACK TURTLES AT REST AND EXERCISE ON THE BEACH IN COSTA RICA. Frank V. Paladino, Michael P. O'Connor*, and James R. Spotila*. Department of Biological Sciences, Purdue University, Fort Wayne, IN 46805 USA and Drexel University Philadelphia, PA 19104.

Body mass (M ±5kg), respiratory frequency (*f*, breaths/min), tidal volume (*T. V.* ± .001 *l*) ventilation (V_e ± 1 ml/min/kg), oxygen consumption (V_{O2} ± .001 Watts/kg), carbon dioxide production (V_{CO2} ± 1 ml/kg), body and ambient temperatures (T_b and T_a ± .1 °C) were measured for at least 5 different female leatherback turtles, *Dermochelys coriacea*, on the beach in Costa Rica while resting restrained in a net and while actively covering the nest. M ranged from 250 - 430 kg (X = 370), at rest; *f* ranged from 1.02 - 3.3 (X = 1.98); *T.V.* ranged from 4.2 - 6.5 (X = 5.14); V_e ranged from 16.1 - 33.8 (X = 27.5); V_{O2} ranged from .186 - .544 (X = .387); T_a ranged from 21 - 23.8 (X = 21.9); and T_b ranged from 30.2 - 32.4 (X = 31.3). While actively covering the nest and throwing sand; *f* ranged from 4.17 - 6.4 (X = 4.8); *T.V.* ranged from 6.4 to 10.3 (X = 7.5); V_e ranged from 65.1 - 160.9 (X = 99.2); V_{O2} ranged from .878 - 1.818 (X = 1.510). These metabolic, thermal and respiratory data were used to calculate the operative temperatures of the turtles on the beach and were used to develop a heat energy exchange model while active and at rest on the beach. Metabolic, respiratory, and thermoregulatory mechanisms of leatherbacks have important implications for considerations of size and function in animal biology and diving physiology.

61.15

DEPENDENCY OF SURFACE TEMPERATURE REGULATION ON BODY SIZE IN MAMMALS. P.K. Phillips*, J.J. Klir*, J.E. Heath, D.A. De Lamo*, and A.F. Sanborn. University of Illinois, Urbana Illinois 61801.

The ability to regulate surface temperature permits mammals to regulate heat flow to the environment. Surface temperature is regulated by controlling insulation and blood flow. The hypothesis that regulation of surface temperature increases in effectiveness with body size was tested in a series of animals ranging from 80g Mongolian gerbil to 3000kg African elephant. The animals were studied at several ambient temperatures. The study deals largely with herbivores, however some small carnivores were included for comparison. Infrared thermography was used to measure surface temperature and to identify thermal windows specialized for heat loss. An index comparing the control of surface temperature to metabolic rate was used to relate thermoregulatory control to body size. The larger the body size the greater the significance of control of surface temperature to thermoregulation in general.

Most of the animals used in this study were made available through the generosity of Brookfield Zoo, Brookfield, IL and Wildlife Prairie Park, Peoria, IL.

61.16

MOLT ENERGETICS OF THE NORTHERN ELEPHANT SEAL. G.A.J. Worthy*, P.A. Morris*, D.P. Costa, and B.J. Le Boeuf*. Department of Marine Biology, Texas A&M University at Galveston, Galveston, TX 77553-1675 and Biology Department, University of California, Santa Cruz, CA 95064

The northern elephant seal (Mirounga angustirostris) is a large, sexually dimorphic phocid seal that annually undergos a molt during which all of the hairs are shed along with large sheets of cornified epidermis, through which the club hairs penetrate. This "catastrophic" molt takes place on land and lasts an average of 32.0 ± 6.6 days, during which time the animals are fasting. Adult females lose 24.5 ± 5.9% of their starting mass, with approximately 14% of this associated with the shedding of the pelage and epidermis. Molting, female northern elephant seals exhibited an average daily metabolic rate, measured using tritium turnover, of 2.0 ± 0.6 times their predicted basal metabolic rate. This energy demand was met by losing 3.0 kg/d of total body mass. Body composition on arrival (26.4 ± 4.2% fat) did not differ significantly from that at departure (27.4 ± 3.1% fat). Fat catabolism accounted for 41% of mass lost and 93.6% of derived energy. These energy expenditures suggest that the molt period is a time of relatively low energy expenditure and that females can not only survive the fast but produce an entire new pelage using existing reserves. Funded by the Office of Naval Research through grant N00014-87-0178.

61.17

COMPARATIVE EVAPORATIVE COOLING IN GRASSHOPPERS AND BEETLES. Henry D. Prange and Jignesh Modi*. Medical Sciences Program and Dept. of Biology, Indiana Univ. Bloomington, IN 47405

The maximum environmental and internal temperature tolerance and rates of evaporative water loss of a temperate woodland-dwelling beetle, *Calasoma scrutator*, and a open-land-dwelling grasshopper from the southwest United States, *Schistocerca nitens*, were studied. Both species were able to maintain their internal temperatures below ambient by evaporative cooling when faced with high environmental temperatures. The beetles' upper lethal environmental temperature was 46 °C. Their upper lethal internal temperature was 44 °C. The maximum depression of internal temperature they could maintain was 2 °C. The grasshoppers could withstand environmental temperatures in excess of 52 °C; their upper lethal internal temperature was also higher, 48 °C. Grasshoppers could maintain as much as an 8 °C depression of internal temperature below that of the environment. In spite of the beetles' lower temperature tolerance their maximum rates of evaporative water loss were approximately twice that of the grasshoppers and their increase evaporation had a much lower temperature of onset. These differences in physiological capability are appropriate considering the probable differences in heat stress imposed by the respective environments of these insects.

COMPARATIVE PHYSIOLOGY: MAXIMAL EXERCISE

62.1

FUEL SELECTION IN RUFOUS HUMMINGBIRDS: ECOLOGICAL IMPLICATIONS OF METABOLIC BIOCHEMISTRY. R.K. Suarez*, J.R.B. Lighton*, C.D. Moyes*, G.S. Brown*, C.L. Gass*, and P.W. Hochachka. Dept. of Biological Sciences, SFU, Canada, Dept. of Biology, UCLA, U.S.A., and Dept. of Zoology, UBC, Canada.

Hummingbirds in hovering flight display the highest mass-specific rates of aerobic metabolism (VO_2/Mb) known amongst vertebrates. Their high metabolic rates and nectarivorous diets led us to wonder what metabolic fuels are oxidized under various conditions. Respirometric techniques were used to measure VO_2 and VCO_2 at rest and in flight. Respiratory quotients ($RQ = VCO_2/VO_2$) indicate that fatty acid oxidation serves as the primary energy source in fasted resting birds, while subsequent foraging flight results in a rapid shift towards the use of carbohydrate as the metabolic fuel. Maximal activities of hexokinase and carnitine palmitoyl transferase in the flight muscles indicate that glucose or long chain fatty acids can be oxidized at rates sufficient to account for VO_2/Mb during flight. We suggest that hummingbirds derive maximal net energy gains by adopting foraging strategies which result in oxidation of carbohydrate in preference to fat. Supported by Natural Sciences and Engineering Research Council of Canada Operating Grants to R.K. Suarez and P.W. Hochachka.

62.2

ENERGY METABOLISM DURING RECOVERY FROM EXHAUSTIVE EXERCISE IN RAINBOW TROUT WHITE MUSCLE. P.M. Schulte and P.W. Hochachka. University of British Columbia, Vancouver, B.C. V6T 2A9

The difficulty of obtaining muscle samples from fish without any struggling makes detailed analysis of the behaviour of the labile high energy phosphates complex. We have used a new sampling procedure to reduce this problem. Cannulated trout (Dorsal aorta) were killed by the infusion of Somnotol (2mL, 65mg/mL) and a muscle sample freeze clamped. We observed no overshoot in ATP concentration during recovery from exhaustive exercise. Resting [ATP], 7.52±0.49 umoles/g wet wt (±SEM) was higher than previously observed and not significantly different from reported overshoots. We ascribe this discrepancy to more accurate sampling of the resting fish. Phosphocreatine concentration [PCr] is fully recovered by 2h post exercise while [ATP] is still less than 50% of resting levels. [ATP] does not completely recover for 24h. However, at 2h post exercise energy charge is not significantly different from the resting value. These results clearly demonstrate a lack of functional coupling between ATP concentration and [PCr]. Caution must be exercised in relating [ATP] to the energy status of the cell, particularly in tissues with high levels of purine nucleotide cycling. This work was supported by NSERC, Canada.

62.3

CARDIAC DYNAMICS AND BIOCHEMISTRY IN EXERCISE-TRAINED RAINBOW TROUT. A.P. Farrell, J.A. Johansen* and R.K. Suarez. Simon Fraser University, Burnaby, B.C., Canada, V5A 1S6.

Exercise-training improves maximum swimming performance in a variety of fishes. Therefore we examined whether or not maximum cardiac performance is improved in order to support the increased O_2 demand of the trained fish. Following a 28-day training regime, maximal cardiac performance was evaluated with an *in situ* perfused heart. Trained fish displayed significantly higher values for maximum cardiac output, maximum stroke volume and maximum myocardial power output, and the heart was more sensitive to venous filling pressure. Heart rate and the sensitivity to adrenaline were not significantly different. Maximal activities of several key enzymes were measured in both cardiac and skeletal muscle. Hydroxyacyl CoA and glutamate dehydrogenase activities increased in all tissues. Carnitine palmitoyltransferase and citrate synthase increased in the endocardium. We conclude that, concommitant with increased swimming performance, exercise-training in rainbow trout significantly improves the heart's ability to pump blood and there are associated increases in enzyme activity. Supported by NSERC Canada.

62.4

MUSCLE PERFORMANCE DURING SWIMMING IN SCALLOPS. R.L. Marsh and S.K. Guzik*. Department of Biology, Northeastern University, Boston, MA 02115.

We estimated muscle performance during swimming at 10 °C in two independent ways. Muscle length changes during swimming were measured using sonomicrometer transducers connected on opposite sides of the shell. Simultaneous measurements of pressure in the mantle cavity were made with a Millar pressure transducer. Muscle strain is 20-35 % during swimming and pressures reach peak values of 2.7-3.5 kPa. Using volume changes estimated from the length measurements, we calculated an average power during a full cycle of 14 W/kg of muscle and a peak instantaneous power of 64 W/kg. We also used the measured length cycles to run simulated swimming bouts. In these *in vitro* measurements, portions of the striated adductor muscle were connected to a computer controlled ergometer lever. This system provides direct measures of muscle performance under conditions similar to those *in vivo*. Peak instantaneous power during these simulations was 70-80 W/kg and power averaged over a complete cycle was 14-15 W/kg. The excellent agreement between the *in vivo* and *in vitro* measures suggests that *in vitro* simulations of locomotor movements will provide a valuable tool in the study of the limits of muscle performance. Supported by NIH AR39318 and RR07143.

62.5

DO INSECTS HAVE A MAXIMAL OXYGEN CONSUMPTION?
R.J. Full and C. Min*. Univ. of Calif., Berkeley, CA 94720

Maximal O_2 consumption (V_{O2max}) is defined as that rate of O_2 consumprtion which does not continue to increase with an increase in work output. In most animals, activity beyond their V_{O2max} leads to anaerobic metabolism and the build-up of an end-product. Flight activity in insects has been considered to be entirely aerobic. We attempted to determine whether the cockroach, *Blaberus discoidalis*, had a V_{O2max} by exercising it on a treadmill enclosed in a respirometer at speeds ranging from 0.1 to 1.0 km/h. Cockroaches running at 0.8 km/h attained a V_{O2max} 23-fold higher than their resting V_{O2}. Exercise at 1.0 km/h did not result in a further increase in V_{O2} and the insects fatigued rapidly. To investigate the pathways fueling cockroach running beyond V_{O2max}, cockroach leg and thoracic muscle tissue was tested from animals following 10 min periods of rest, and running at 0.5 and 1.0 km/h. Levels of lactate, arginine phosphate (AP), adenosine triphosphate (ATP) and α-glycerophosphate were measured immediately after exercise. No significant changes were found in concentrations of metabolites between resting and exercising insects. Increases in lactate and α-glycerophosphate and decreases in ATP and AP would be expected in a loosely coupled system if non-aerobic metabolism sustained running at speeds higher than V_{O2max}. Supported by NSF Grant DCP 89-04586.

COMPARATIVE PHYSIOLOGY: FIELD PHYSIOLOGY

63.1

CIRCULATORY RESPONSES IN GREY SEALS DIVING AT SEA: PROFOUND BRADYCARDIA DURING CONTINUOUS DIVING.
M.A.Fedak & D.Thompson. Sea Mammal Research Unit, N.E.R.C., Cambridge, CB3 0ET, UK.

Heart rate (HR), swimming speed and dive depth were monitored in free-ranging grey seals as they swam in the open sea off western Scotland. The animals were caught in nets and fitted with VHF (173MHz) and acoustic (80KHz) transmitters glued to their fur. HR information was obtained from surface mounted electrodes and broadcast as an FM tone. Depth and velocity data were transmitted as pulse trains from another transmitter on an adjacent frequency. Surface periods were brief (15-90s) even after long dives, with rapid rhythmic HR (107-120bpm). Most dives were short and showed moderate bradycardia, with arhythmic HR of 30-60 bpm. While ascending, HR increased rapidly to breathing levels in anticipation of surfacing. While foraging, extended sequences of long dives occurred during which HR fell to very low levels. Average rates reached 6.4 bpm with intervals between beats of up to 30s. There was no correlation between HR and swimming speed. The lowest rates observed were as low as those seen in forced submersions in the laboratory and lower than reported in free diving Weddell seals. However, in grey seals, dives with low HR were not followed by extended recovery periods, suggesting that these dives did not involve a large anaerobic component and may instead involve some degree of reduced metabolism.

63.2

ADAPTATIONS TO PROLONGED FASTING IN FREE-LIVING WEANED GREY SEAL PUPS.
John J. Reilly* (Spon. M.A. Fedak) Sea Mammal Research Unit, N.E.R.C., Madingley Rd, Cambridge CB3 0ET, UK.

The water and energy metabolism of 12 free-living weaned grey seal (*Halichoerus grypus*) pups was studied using labelled water methods. Changes in urine output and serum composition were also measured. The duration of the post weaning fast ranged from 10 to greater than 28 days. Mean daily energy expenditure was 12.0MJ(SE 1.0), equivalent to 2.7 times the basal metabolic rate predicted from Kleiber's allometric equation. On average, lipid catabolism provided 94% of the energy used. Water turnover rates were lower than predicted. Daily rates of urinary water and solute output were also low and these declined significantly as the fast progressed. There was no evidence that the prolonged fast leads to dehydration. The principal adaptations to prolonged fasting in grey seal pups are lowering of field metabolic and water turnover rate, and reliance on stored lipid as fuel.

63.3

THE ENERGETICS AND WATER TURNOVER OF HARBOR SEALS.
John J. Reilly* and Michael A. Fedak. Sea Mammal Research Unit, Madingley Rd, Cambridge, CB3 0ET, UK

Male harbor seals (*Phoca vitulina*), during their summer breeding season in northern Scotland, spend a significant fraction of each day in the water displaying and interacting with other seals. They also make longer trips to sea to feed. The water and energy metabolism of three free-living adult males was investigated using labelled water methods. In spite of feeding, all three animals were in negative energy balance during the study. Using doubly-labelled water, the energy expenditure of one individual was estimated to be 52.5MJ/d, equivalent to six times the basal metabolic rate predicted from Kleiber's allometric equation. The rates of water turnover and energy expenditure observed were considerably higher than those reported from studies of phocids which fast during mating, and are consistent with behavioural differences between mating harbor seal males and those of other phocid species. Studies of free-ranging, foraging, phocid seals present great practical problems: these are currently the only published data on the energetics of any phocid seal at sea.

63.4

ENERGY BALANCE AND WEIGHT CONTROL OF THE BROAD-TAILED HUMMINGBIRD: IS HYPOTHERMIA NECESSARY?
William A. Calder, Univ. of Arizona, Tucson, AZ 85721

Rapid metabolic turnover in small homeotherms complicates seasonal choices between benefits of stored reserves and transportation costs. A male hummingbird, defending a territory and mating, ingested only 11% of crop capacity per meal and expended it before feeding again. In 15 h, body mass increased only 1%. Confined to a lab, mass at dusk predicted duration of torpor. Free in nature, intake at dusk of 34% of body mass (0.38 g sucrose in 0.65 g water) met estimated energy cost of normothermy all night. At dawn, fasted mass was 2.96 ± 0.03 g (sd), without day-to-day carryover until breeding activity ceased. Then fasted mass crept up 27 mg daily. Confined to the lab for 1-2 da, mass also increases. The correlation of stable mass with vigorous flight activity suggests that "weight control" is achieved as a balance between intake and expenditure without a need for "set-points". Trends in daytime capture masses of broadtails wintering in Jalisco indicate storage adequate for nocturnal normothermy.

63.5

DEPTH, SWIMMING SPEED, AND BODY TEMPERATURE OF THE BLUE MARLIN, MAKAIRA NIGRICANS, OBSERVED BY ACOUSTIC TELEMETRY.
Barbara A. Block, Francis G. Carey* and David T. Booth. The University of Chicago, Chicago, Il. 60637 and Woods Hole Oceanographic Institution, Woods Hole, Mass. 02543.

Multiplex acoustic transmitters were used to monitor the depth, swimming speed, body temperature and water temperature preference of six blue marlin, Makaira nigricans, in the Hawaiian islands. The blue marlin ranged in size between 70 kg and 220 Kg and were tracked for durations of 1 to 5 days. The 400 hours of depth data indicate that blue marlin remain in the top 200 meters of the water column. Vertical excursions are characterized by rapid short duration dives to various depths. Several marlin spent longer periods of time at depths between 50 and 130 meters. Speed was telemetered by a speedometer attached directly to three blue marlin providing continuous monitoring of swimming speed during vertical and horizontal movements. Fastest sustained cruising speeds occurred during the 8 to 12 h period after tagging and ranged between 75 to 150 cm/sec. Short maximum bursts of speeds up to 220 cm/sec were frequently recorded and were usually associated with rapid changes in depth. The slowest movements (less than 20 cm/sec) were associated with the fish being close to the surface. Blue marlin prefer to remain in the warm mixed layer (25-27°C). The coldest water temperature (17°C) was associated with the deepest dive recorded (209 m). Muscle temperature remains similar to water temperature, however a 2° C increase in muscle temperature was observed in one individual immediately after the struggle associated with capture, tag and release. All of the blue marlin tracked moved away from the area of tagging and four maintained consistent courses which resulted in marlin moving distances of up to 270 Km away from the island of Hawaii. Supported By The Billfish Foundation and NSF DCB8958225.

63.6

BLOOD CHEMISTRY OF TWO SPECIES OF FLOUNDER ALONG THE NORTHEAST COAST OF THE U. S.: SEASONAL AND GEOGRAPHICAL VARIATIONS.
M. A. Dawson, C. A. Kuropat*, R. Mercaldo-Allen*, and D. Kapareiko*. National Marine Fisheries Service, Milford, CT 06460.

Measurements of blood chemistry are useful indicators of condition in fish, the main limitation being the lack of background information available for most species. Such information for a particular species obtained under a variety of natural conditions will make this type of measurement valuable in assessing condition in the field. The present study describes the blood chemistry of the yellowtail flounder, Limanda ferruginia, and winter flounder, Pseudopleuronectes americanus, throughout the year at several stations along the Atlantic coast of the U. S. Georges Bank was used as a reference area; blood chemistry of fish collected in this area was compared to that of fish collected at inshore areas, some of which are known to have considerable anthropogenic pollution. The parameters measured were hematocrit, hemoglobin, plasma osmolality, sodium, potassium, and calcium. Station-related differences were noted in all six parameters; the most common in both species was a change in the plasma calcium level. A lower sodium level at the inshore stations was more prevalent in yellowtail than in winter flounder. Seasonal variations were found in hematocrit, hemoglobin, plasma sodium, and calcium.

63.7

OXYGEN STORES AND AEROBIC METABOLISM IN LEATHERBACK SEA TURTLES.
M.E. Lutcavage*, P.G. Bushnell*, and D.R. Jones. Univ. of British Columbia, Vancouver, Canada V6T2A9

The leatherback sea turtle, Dermochelys coriacea, is a large, deep diving species that has an O_2 carrying capacity twice that of smaller, shallow-diving sea turtles. In order to complete our understanding of total O_2 stores available while diving, we measured lung and blood volumes of nesting leatherbacks. Blood volume (7.7%) was slightly higher, yet lung volume was considerably smaller (64 ml/kg BTPS) than in other sea turtles, so that total body oxygen stores were evenly divided between lung (12 ml/kg) and blood and tissues (15 ml/kg). If the total O_2 store is available in the dive despite probable lung collapse at around 120 m then, based on our own and other values for leatherback $\dot{V}O_2$'s, aerobic dive limits would range from 5 to 106 min. Since observed dive times average about 10 min, we would predict that $\dot{V}O_2$ during active dives is about 1.32 ml/min/kg if leatherbacks use only 50% of the total oxygen stored.

Supported by NSERCC.

63.8

PHYSIOLOGICAL AND TOXICOLOGICAL EFFECTS OF WATER CHEMISTRY CHANGES IN THE GILL MICRO-ENVIRONMENT OF FRESHWATER ORGANISMS.

Richard C. Playle, Dept. of Biology, University of Waterloo, Waterloo, Ontario, Canada. N2L 3G1

Soft water of low buffer capacity was drawn from the branchial surface of fathead minnows, using opercular catheters. Water passing over the gills was more basic than inspired water if the inspired water was pH 4-6. Expired water was more acidic than inspired water if the inspired water was pH 6-10. These pH changes are explained by base (mostly ammonia) and CO_2 released at the gills, which alkalinize and acidify water, respectively. These results indicate that any gill contaminant whose toxicity varies with pH may be more or less toxic at the gills than predicted from bulk water chemistry alone. For example, copper shifts from 100% Cu^{2+} at pH 5 to about 60% $CuOH^{+}$ at pH 9. However, because of pH changes near the gills, there is about 95% Cu^{2+} in the gill micro-environment at both inspired pH 5 and 9, which may explain the similar behaviour of Cu at these inspired pHs. Alteration of water chemistry near the gills appears to be a general phenomenon of freshwater organisms, eg. minnows, trout, mayfly nymphs. Gas transfers at the gills are important to consider when dealing with physiology and toxicology of organisms in poorly buffered water.

63.9

DESERT-DWELLING WOLVES MUST DRINK: WATER BALANCE AND METABOLISM IN *Canis lupus pallipes*.
D. Afik and B. Pinshow. Blaustein Inst. Desert Res. and Biology Dept. Ben-Gurion Univ., Sede Boqer Campus, 84993 Israel.

The wolf subspecies *C. l. pallipes* [adult body mass (m_b) 18-22 kg] thrives in very arid areas in Israel. Other desert-dwelling canids of similar size reduce their internal heat load through low metabolic rate, but must drink water to survive. To ascertain whether desert wolves are similarly constrained, we measured in 3 hand-reared females 1) rates of metabolism (MR) and evaporative water loss (EWL) under controlled conditions at ambient temperatures from 0 to 40°C; and 2) water turnover rates (WTR) while they were kept in a 0.16 ha outdoor enclosure with shade and water available. All test temperatures were in the wolves' thermal neutral zone. Mean standard MR (SMR) was 1.20 W/kg in winter, and 1.59 W/kg in summer; winter and summer SMRs were, respectively, 33.6% and 12.15% lower than predicted allometrically. EWL was significantly higher in summer than in winter. Total body water averaged 68% of m_b in both seasons, but mean WTR was significantly higher in summer (1704 ml/day) than in winter (483 ml/day). After 21 hours of water deprivation in late summer, wolves lost 11.8% of their initial m_b, but made up only 44% of their water deficit in their first post-dehydration drink. Morphological examination of kidneys from 2 males indicated no extraordinary renal concentrating ability. The data suggest that wolves must have free water available to meet the physiological challenge of the hot desert climate. Supported by The J.N.F. Ecology Fund.

63.10

CLIMATE CHANGE: MECHANISTIC MODELS AND EXPERIMENTS TO ASSESS GROWTH AND REPRODUCTION POTENTIAL IN CARNIVOROUS LIZARDS.
W. P. Porter, B. W. Grant and A. E. Dunham. Dept. of Zoology, Univ. of Wisconsin, Madison, WI 53706 and Dept. of Biology, Univ. of Penn., Philadelphia, PA 19104.

A stochastic microclimate model and a heat and mass balance model were used to calculate the potential for growth and reproduction of the canyon lizard (*Sceloporus merriami*). Geological data and spatial and temporal climatic data from 18 sites in Texas were used to simulate microclimatic conditions for the entire state over a 10 year period. Calculations of egg production potential indicate pronounced year to year variability due to effects of changing climate. The model predicts that relatively small variations in projected climatic conditions over the next 25 years will result in substantial effects on lizard growth and egg production. Empirical reproductive data for selected sites in Texas were used for 'ground truth' determinations.

63.11

WATER AND ENERGY LIMITATIONS TO FLIGHT DURATION IN SMALL, MIGRATING BIRDS. N. Carmi-Winkler, B. Pinshow and W. P. Porter. Blaustein Inst. Desert Res. and Biology Dept. Ben-Gurion Univ. Sede Boqer Campus, 84993 Israel; and Dept. of Zool. Univ. of WI, Madison, WI 53706.

We examined physiological limitations to flight duration in migrating birds by developing a model that predicts rates of energy use and water loss. Model predictions were based upon flight path meteorological data, and preflight body mass (m_b) and fat and water contents. The model predicted that: 1) The smaller the bird, the greater the limitation to flight duration posed by dehydration rather than energy reserve depletion. 2) Due to dehydration, small birds ($m_b \approx 10$ g) that cross the Sahara, for example, cannot make a 30 h non-stop flight, but could cover the same distance by resting between bouts of flight. 3) Small, lean (initial fat content $< 30\% m_b$) birds that do not feed on the wing must stop *en route*, at least once, to feed. Available data from birds trapped at stopover sites in the Sahara support these predictions. Sensitivity analysis of the the model indicated that ambient air temperature (T_a) and humidity, and expired air temperature (T_{ex}) are very important variables influencing the bird's water budget, and therefore flight duration. This suggests the importance of (1) efficient cooling in the nasal passages of flying birds, and (2) the choice of flight altitude (which affects both T_a and T_{ex}). Supported by the J.N.F. Ecology Fund.

63.12

ENERGETIC COSTS OF LOW-LEVEL JET AIRCRAFT OVERFLIGHT IN CARIBOU. J.A. Kitchens and R.G. White. Institute of Arctic Biology, University of Alaska Fairbanks, Fairbanks, AK 99775

Energetic costs can be deduced by determining costs of observed behavioral responses, particularly when heart rate is used as an indirect measure of energy expenditure (Fancy and White, Rangifer, 1985). This project will involve simultaneous recording of heart rate and behavioral responses during low-level jet overflights. Individual caribou calibrated for both heart rate and energy expenditure will be fitted with a sound monitor system. A dose response curve relating energy expenditure to sound exposure will be developed for application to field studies and computer simulation modeling. Response to sound occurs over short time periods necessitating instantenous measurement of heart rate and oxygen consumption. The latter requires use of an enhancement for distortion correction in the calorimetry system (Kokjer et al., J. Wildl. Manage, 1990). Initial results suggest that accurate estimates of the energy cost of the alert response and short-term activity events must be determined using this application. Research is supported by the U.S.A.F. through a cooperative agreement with the U.S.F.W.S. and the Institute of Arctic Biology.

63.13

SEASONAL CHANGES IN THE DIVING PATTERN AND ENERGETICS OF THE AUSTRALIAN SEA LION. D.P. Costa*, L. Rea, M. Kretzmann, and P.H. Thorson. Institute of Marine Sciences, University of California, Santa Cruz, CA. 95064.

We examined changes in enegy consumption and dive pattern of female Australian sea lions during winter and summer breeding seasons. At-sea metabolic rates were measured using the oxygen-18 doubly-labeled water method and at-sea behavior with time depth recorders. A total of 16 dive records from 14 individuals, indicate that Australian sea lions are shallow divers reaching an average maximum depth of 92 m with a mean depth of 67 m. Dives lasted an average of 3.3 min, the longest averaged 5.74 min. While at-sea 50-60% of the time was spent underwater, with little rest or surface swimming. There were subtledifferences between summer and winter diving pattern. Winter dives were exclusively flat bottomed, whereas summer dives were predominately flat bottomed with bouts assumed to be midwater feeding. Rates of oxygen consumption based on DLW suggest that these animals are diving longer than their available oxygen stores should allow (estimated oxygen stores allow 1.8 min dives). Shallow bottom feeding Australian sea lions expend more energy foraging than do deeper mid-water feeding California sea lions. Australian sea lions expend 7.3 times their predicted basal metabolic rate whereas California sea lions expend only 4.8 times their predicted basal rate. Similarly, smaller Antarctic fur seals feeding shallow on krill expend 7 times the predicted basal rate. This is consistent with data on penguins, which suggests that deep diving is energetically less costly than shallow diving.

63.14

FIELD DETERMINATION OF WATER KINETICS IN CARIBOU. K.L. Gerhart, R.G. White, and R.D. Cameron. Institute of Arctic Biology, University of Alaska Fairbanks, Fairbanks, AK 99775

We are developing in vivo techniques for the estimation of body water pool size and turnover in free-ranging caribou (Rangifer tarandus granti) using radioactive tracers, new recapture technologies, and computer simulated modeling. Initially, tame rumenfistulated reindeer were injected with ^{14}C urea and tritiated water. Rumen and blood were sampled every 3 min for 30 min and thereafter at 12 h intervals for 5 d post-injection. The distribution and kinetics of both tracers within th body water pools were described best by, 2-compartment models. However, terminal rate constants could not be determined for either tracer using only the first 30 min of data. In field trails, caribou were darted from a helicopter, injected and sampled for 30 min, and released; they were recaptured 2-3 d later using a remotely triggered capture collar (Wildlink, Inc.) for a final blood sample. Advantages and limitations of the technique will be discussed. This research is supported by the U.S. Fish and Wildlife Service, Alaska Department of Fish and Game, Institute of arctic Biology, and a National Science Foundation Research Fellowship.

63.15

THE EFFECTS OF NEST DENSITY (LOCATION) ON THE RESPIRATORY ENVIRONMENT OF BANK SWALLOW BURROWS. David D. Nusbaumer and Delbert L. Kilgore, Jr. Univ. Montana, Missoula, MT. 59801

Diffusion is an important mechanism for the exchange of gases between animals in burrows and the external environment. Colonial, burrowing birds construct nests close to neighboring burrows. The proximity of burrows could influence the diffusion of gases between nests and the free atmosphere, resulting in elevated concentrations of CO_2 in burrows located in regions of high nest density. Gas samples were collected from nest chambers of 40 bank swallow burrows (8 surrounded by 0, 1, 2, 3, or 4 neighboring burrows) and analyzed for CO_2 concentration. Other variables that may influence the respiratory environment within a burrow were also evaluated (i.e., nest depth, biomass of occupants, and wind speed and direction). A multiple linear regression model was used to analyze preliminary data. The overall coefficient of multiple determination was 0.43. Biomass has a significant positive effect on CO_2 level in burrows ($p < 0.05$), while nest density does not ($p = 0.0955$). (Supported by NSF Grant DCB8811413)

63.16

EXISIENCE OF A CRITICAL BODY WEIGHT FOR INITIATION OF REPRODUCTION IN MUSKOXEN. R.G. White and W.E. Hauer*. Institute of Arctic Biology, University of Alaska Fairbanks, AK 99775

Muskoxen (*Ovibos moschatus*) display plasticity in age of first reproduction and incidence of breeding pauses. The effect seems related to population size and range carrying capacity, i.e., it is nutritionally based. Experiments with a captive herd of muskoxen showed that plane of nutrition in late August through late October (fall) is critical to lactating females as they make their entire annual weight gain at this time (White et al. 1989, Can. J. Zool. 57:1125-1133). We hypothesize that muskox must obtain a critical body weight in order to reach puberty and to conceive annually. Muskoxen were given access to either high (H) or low (L) quality forage in fall and winter and to high quality in summer. Females on the L treatment failed to conceive if body weight was less than 185 kg during the rut (fall). Likewise, young females did not conceive if less than 185 kg during the rut. Female offspring, given the L treatment after 1 y of age, took 1 to 3 years longer than those given the H treatment to reach pubertal body weight.

A further hypothesis, that the nursing behavior of muskox calves could inhibit estrous independent of maternal body weight was rejected.

This research was supported by the Earthwatch program of the Center for Field Research.

64.1

REGIONAL BLOOD FLOW DISTRIBUTION IN CONSCIOUS RESTING RATS DETERMINED BY MICROSPHERE DISTRIBUTION. I. Kuwahira*, N.C. Gonzalez, N. Heisler and J. Piiper. Dept. Physiol., Max Planck Institute for Experimental Medicine, Göttingen, D-3400, F.R.G.

Considerable discrepancies exist among reported values of organ blood flow (BF) in conscious resting rats, which may be attributable to differences in animal handling procedures. In order to keep disturbances at a minimum we designed a box to keep conscious untrained rats at a true resting state for several hours. Blood pressure, heart rate(HR), and organ BFs were determined by application of the microsphere distribution and reference sampling technique in 11 male Sprague-Dawley rats. After acclimation 15μm Sn-113 labelled microspheres were infused into the ascending aorta, and the reference blood sample was withdrawn from the middle caudal artery, and organ BFs were computed according to standard procedures. Compared to previously reported values, the rats accommodated to the box with negligible physical activity showed lower HR, and BFs to brain, diaphragm and hindlimb muscles lower by more than 40%, 10% and 60%, respectively, whereas splanchnic BF to stomach, intestines, spleen, pancreas and liver was higher by more than 60%. In the 7 hindlimb muscles, the BF to the soleus muscle (which is considered as the most active for postural maintenance) was relatively high as compared to the others. The results indicate that minor physical activity, restraining stress and poor acclimation to a new environment may induce a marked redistribution of resting BFs.

64.2

CALCITONIN GENE RELATED PEPTIDE PRODUCES MARKED VASODILATION IN THE CANINE FORELIMB PERFUSED AT NATURAL FLOW. David E. Dobbins and Joe M. Dabney, Department of Physiology, USUHS, Bethesda, MD 20814-4799.

Calcitonin gene related peptide (CGRP) is a 37 amino acid peptide which is found in high concentrations in the perivascular nerves innervating the resistance vessels of the peripheral circulation. In the current study we have infused CGRP at three infusion rates (.01, .1 and 1.0 μg/min into the brachial artery for thirty minutes at each infusion rate) in the isolated, innervated canine forelimb perfused at natural flow. We measured large artery and vein pressures, small artery and vein pressures and blood flows in both the skin and skeletal muscle circulations for the calculation of total and segmental (large artery, small vessel and large vein) vascular resistances. Infusion of the lowest dosage of CGRP produced slight vasodilation in some animals but did not significantly alter the mean resistances of all the animals as a group. The middle dosage resulted in a 55% decrease in total forelimb resistance which was equally distributed between the skin and skeletal muscle circulations and a small but significant decrease in systemic arterial pressure. The highest dosage of CGRP resulted in a 65% decrease in total forelimb resistance which was also equally distributed between the skin and muscle circulations and a 34% decrease in systemic arterial pressure. The decreases in forelimb resistances were manifested in both large artery and small vessel resistances. The potent vasodilatory effects of CGRP and its concentration in perivascular nerves innervating the resistance vessels of the circulation suggests a potential role for CGRP in control of circulatory function under normal and/or pathophysiological conditions. Supported by USUHS grant # RO76DD.

64.3

VASODILATOR ACTION OF A PARATHYROID HORMONE-RELATED PROTEIN (PTHrP). M.F. Crass, III and P.J. Scarpace. Dept. of Physiol., TTUHSC, Lubbock, TX and GRECC, DVA Med. Ctr., Gainesville, FL 32608

PTHrP, or hypercalcemia of malignancy factor, has been identified in a variety of normal tissues and possesses an aminoterminal region sequence homology with parathyroid hormone (PTH). Others have reported that both polypeptides exert similar effects on classical PTH target tissues with mediation involving cAMP accumulation. To assess possible effects of PTHrP on vascular function, a synthetic amino-terminal fragment, PTHrP-(1-34), was studied in isolated perfused rat aorta (IPRA) and in cultured rat aorta vascular smooth muscle cells (VSMC). Results with PTHrP-(1-34) were compared to those with PTH-(1-34), a known vasodilator purportedly acting via a cAMP-dependent signal transduction mechanism. The PTHrP peptide fragment showed a greater potency and efficacy with respect to PTH-(1-34) in eliciting concentration-related (10^{-10} to 10^{-8} M) vasodilations in the IPRA. Both peptides produced comparable stimulations of cAMP accumulation in VSMC. These preliminary results confirm the vasorelaxant properties of PTHrP and provide evidence for cAMP mediation. Recent demonstrations of expression of PTHrP in a variety of normal nonmalignant tissues, in concert with demonstrated vasoactive properties, suggest that parathyroid hormone-related proteins could act in an autocrine or paracrine fashion to regulate local blood flow in certain tissues. (supported in part by HL 29108 and DVAMC)

64.4

RESPONSE TIME OF INNERVATED SKELETAL MUSCLE TO HYPOXEMIC PERFUSION DURING SYSTEMIC NORMOXIA IN DOGS. Scott E. Curtis* and Stephen M. Cain. Univ. of Alabama at Birmingham, Birmingham, AL 35294

When whole body O_2 supply is decreased, skeletal muscle responds by increasing O_2 extraction but vasodilation is delayed. The nature and time course of responses in skeletal muscle in the absence of systemic hypoxia have not been explored. Six adult dogs of mixed breed were anesthetized, paralyzed, and ventilated with room air. The musculature of the left hindlimb was vascularly isolated so that it received blood flow from a pump-membrane oxygenator system that originated in the right femoral artery. When limb O_2 uptake and perfusion pressure were stable while perfused with normoxic blood (PaO_2~100 torr) at constant flow (~60 ml·kg^{-1}·min^{-1}), perfusion was suddenly changed to a second pump-membrane system at the same flow rate but with a PaO_2 of 25 torr for 30 min. Within 3 min of local hypoxemic perfusion, vascular resistance fell from 1.24 ± 0.09 PRU to 0.69 ± 0.08 PRU ($p<0.05$). Muscle O_2 uptake fell from its normoxic level of 4.72 ml·kg^{-1}·min^{-1} to its nadir, 3.02 ± 0.45 ml·kg^{-1}·min^{-1} ($p<0.05$), within 2 min with hypoxemic perfusion. O_2 extraction ratio increased from 38 ± 3% to 69 ± 4% ($p<0.05$) within 3 min of hypoxia. Contrary to results when systemic hypoxia is present vascular resistance and O_2 extraction changed together within minutes of hypoxic onset. The extent to which increased vasoconstrictor tone associated with systemic hypoxia modulates these responses is still unclear. (Supported by NIH Grant #HL 26927)

64.5

URIC ACID: A PHYSIOLOGIC INHIBITOR OF XANTHINE OXIDASE. D. A. Parks, S. Tan, R. A. Evans and J. K. Wheat. Depts. of Anesthesiology, Physiology and Perinatal Medicine. Univ. of Alabama at Birmingham, Birmingham, Al 35233.

Reactive oxygen metabolites play a major role in the pathogenesis of the structural and functional alterations associated with ischemia-reperfusion. Xanthine oxidase (XO) plays a key role in the generation of these cytotoxic oxygen species. Human plasma is endowed with a host of antioxidant defenses including uric acid (UA), a major product of nucleotide metabolism. We have previously demonstrated that ischemic liver releases XO into the plasma. It was the purpose of the present study to determine if UA, in addition to serving as an antioxidant, could alter production of oxidants by XO. Uric acid was quantified in neutralized acid extracts of plasma from healthy volunteers using a 5 μ C-18 column, mobile phase of 99.8% 30 mM KH_2PO_4 and 0.2% methanol at 1.5 ml/min. The activity of XO was determined by monitoring formation of UA at 292 nm in the presence of xanthine. Our estimates of UA in the plasma, about 290 μM, are within published values. Activity of XO was decreased 83, 93, 98 and 100% by 150, 200, 250, and 300 μM UA, respectively. Both K_m and V_{max} were altered by the addition of UA, consistent with uncompetitive inhibition. Although UA is not a very potent inhibitor ($Ki=10^{-4}$M), compared to allopurinol ($Ki=10^{-7}$M), physiologic levels of UA result in complete inhibition of XO activity. These results suggest that although XO may be released into the circulation following ischemia, the high concentrations of UA present in plasma may reduce the toxicity associated with production of oxidants by XO.

64.6

AN INEXPENSIVE LABORATORY MODEL FOR NEONATAL CYANOSIS Linda J. Veit* and Leslie J.Kohman, SUNY Health Science Center, Syracuse, New York 13210.

Cyanotic congenital heart disease (CHD) can be mimicked in large animals by surgical creation of right to left shunts. A small animal model would be more economical; however size precludes surgical manipulation. We have created neonatal cyanosis in the rabbit by rearing in a controlled hypoxic environment. Rabbits are ideal because they may nurse only once per day (the doe will stop lactating if placed in the hypoxic chamber with the neonates). A nearly airtight plexiglass chamber is constructed with dimensions of a standard rabbit cage. Nitrogen and compressed air are mixed and passed into the chamber at a low rate (≈1L/min). Continuous monitoring with an O_2 sensor (Sensormedics) allows stabilization of oxygen content within 0.5%. Carbon dioxide is absorbed by soda lime and water by anhydrous calcium sulfate. The litter is placed in the chamber soon after birth and returned to the doe for 1hr daily to nurse while the cage is cleaned. Satisfactory growth and development, despite obvious cyanosis, have been observed up to 6 weeks in a 10% O_2 environment. Preliminary data verified that the right ventricle: left ventricle weight weight ratio increased from 0.5 in normal hearts to 0.8 in cyanotic 3 week hearts. The pulmonary: systemic arterial pressure ratio increased by approximately 50 %. These changes are typical of CHD and therefore illustrate the suitability of this model for investigating various stresses in cyanotic neonates.

64.7

EFFECTS OF THIORPHAN AND ATRIAL NATRIURETIC PEPTIDE (ANP) ON RENAL FUNCTION DURING HEMORRHAGIC HYPOTENSION (HH). C Yuan, MB Pamnani, J Schooley, and J Moore. Nephrology Serv., WRAMC, Washington DC, and Dept. Physiol., USUHS, Bethesda, MD

The role of ANP during HH is not clear, nor is the effect of exogenous ANP on survival and renal function during HH. We now report the effects of iv infused ANP (A) with and without thiorphan (T), a neutral endoprotease inhibitor, on renal function during HH. Thiorphan has been shown to potentiate the effects of exogenously administered A, increasing UV, $U_{Na}V$, and cGMP excretion in the rat. Alone, it increases UV and $U_{Na}V$. Using a Wiggers-Lamson method, male Wistar rats underwent 3 hours of HH with MAP = 50 mmHg. Animals received A (0.5 μg/kg/min), or T (0.5 mg/kg/ min), or A and T (0.5 μg/kg/min and 0.5 mg/kg/min) during the first hour of hemorrhage. Controls (C) received vehicle only. The C group had a 63% mortality (n=8) at 3 hours, while animals receiving A and T (A/T) had a 30% mortality (n=10). Rats receiving A or T had a 70%, (n=10) and 75% (n=8) mortality respectively. There was a significant ($P < .05$) increase in UV in the A/T rats during the second and third hours of hemorrhage when compared with C, but there was no difference between the T and A groups relative to C. There was no difference in inulin clearance or in $U_{Na}V$ between the groups. The A/T group had a significant increase ($P < .05$) in cGMP excretion during the first hour of hemorrhage relative to C while there was no significant difference between the A and T groups and C. The combination of A and T may prolong survival during HH, and appears to increase UV, possibly through enhancement of ANP as is suggested by the increase in cGMP excretion. T and A alone do not seem to have a significant effect.

64.8

CALCIUM MOBILIZATION IN HEPATOCYTES DURING HEMORRHAGIC SHOCK. S.R.Maitra*,P.R.Kennedy*,S.Dulchavsky*,E.Geller*. (Spon:W.Michael Foster).Div.of Trauma, Dept.of Surgery,School of Medicine, SUNY @ Stony Brook, Stony Brook, New York 11794-8191.

The effects of hemorrhagic shock (HS) on hepatocyte intracellular free Ca^{2+} concentration (Ca_i) and hormone induced mobilization of calcium into cytosol were studied. Rats were anesthetized with pentobarbital sodium and both femoral arteries and one femoral vein were cannulated. Rats in one group were subjected to HS(n=5) by rapid phlebotomy to a mean arterial pressure of 40mm/Hg and maintained in shock for 30 minutes. The rats in the control group (n=5) were observed for 30 minutes. The livers from rats in both groups were perfused in situ and hepatocytes were prepared using collagenase digestion methods. Ca_i was measured using the Ca^{2+} selective indicator Fura-2, under basal and epinephrine stimulated conditions. Changes in the Ca_i were calculated directly from the dual excitation fluorescence data using Spex cation measurement system. Apparent basal Ca_i in control rat hepatocytes was 112±13nM(mean±SE); it increased to 194% above basal level after stimulation of cells with 10^{-5}M epinephrine. In contrast, 10^{-5}M epinephrine only caused an increase in Ca_i of 25% above basal level in HS rat hepatocytes. These results show that HS attenuates hormone mediated mobilization of Ca_i in these cells. The HS induced changes in hepatocyte calcium mobilization are comparable to those observed in hepatocytes from endotoxic and bacteremic shock rats indicating similarity of the cellular calcium dysfunction of hepatocytes in these models of shock.(Supported by NIH BRSG: #RR05736)

64.9

ACUTE HOST RESPONSES TO CANDIDA ALBICANS IN CONSCIOUS RATS: DETERMINANTS OF MORTALITY AND MULTIPLE ORGAN SYSTEM DAMAGE. Andrew J. Lechner, Donna Schilly*, Diane Bender*, and George M. Matuschak. Depts. Physiol. & Med., St. Louis Univ. Sch. Med., St. Louis, MO

Host inflammatory responses during sepsis-related multiple systems organ failure (MSOF) are thought to be independent of microbial taxonomy. MSOF early after C. albicans infection has been partly attributed to "canditoxins", but the time course of pathophysiologic changes after fungemia is unclear and mediation by such toxins controversial. Conscious rats instrumented with jugular venous and carotid arterial catheters were infused with 10^9 cfu live C. albicans blastospores (L) (n=9) or 0.9% NSS (S) (n=7) in 30 min after baseline hemodynamic and blood count measurements. Viability-dependent changes were assessed with 10^9 heat-killed fungi (K) (n=5). Arterial samples for fungal culture were taken at t=90, 210, and 270 min, and at death, when histopathologic changes were evaluated. 24 h mortality after L was 100% compared with 0% in S or K groups ($p < 0.0001$). Compared with baseline WBC counts, leukopenia occurred by 90 min after L (12.2 ± 1.0 to 8.2 ± 0.7 x $10^3/\mu l$, $\bar{X}$ ± SE; $p < 0.05$) and decreased further by 270 min (4.2 ± 0.5; $p < 0.0005$). Thrombocytopenia developed by 90 min after L (872 ± 64 to 689 ± 41 x $10^3/\mu l$; $p < 0.005$) and progressed by 270 min (603 ± 42; $p < 0.001$). Similar values and intravascular fungal clearance existed after K, but leukopenia and thrombocytopenia were not observed after S. Candidemia with L but not K led to severe hepatic glycogen depletion and mycelial growth in multiple organs. We conclude that 10^9 cfu live C. albicans is an LD_{100} inducing early changes in formed blood elements and glycogenolysis in this model. However, mortality and pathophysiology are critically modulated by extravascular viability-dependent factors. (Supported by NIH grants HL 37386 and GM 43513).

64.10

ACUTE HEMODYNAMIC AND PULMONARY EFFECTS OF CANDIDA ALBICANS IN CONSCIOUS RATS: RELATION TO ENDOGENOUS CACHECTIN/TUMOR NECROSIS FACTOR α. George M. Matuschak, Trevor Tredway*, Donna Schilly*, & Andrew J. Lechner. St. Louis Univ., St. Louis, MO

Tumor necrosis factor α (TNF) is thought to mediate the early stages of shock and acute lung injury during sepsis-related multiple systems organ failure. Whether shock and organ injury during candidemia proceed via TNF-dependent pathways is unknown. We studied time-dependent changes in arterial pressure (Pa), heart rate, respiratory frequency, gas exchange, and mortality in relation to circulating TNF in a conscious Sprague-Dawley rat model induced by i.v. candida infection. TNF was measured with murine L929 cells. Animals instrumented with jugular venous and carotid arterial catheters received 10^9 cfu live C. albicans blastospores (L) (n=9) or 0.9 NSS (S) (n=7) i.v. over 30 min. Viability-dependent changes were assessed with 10^9 heat-killed fungi (K)(n=5). Compared with baseline mean Pa (115 ± 4 mm Hg, $\bar{X}$ ± SE), no hypotension occurred during L infusions, at 90 min, or by 3.5 h (120 ± 5 mm Hg; p = NS). By 4 h, Pa was reduced; at 7 h remaining animals were hypotensive (53 ± 7 mm Hg; $p < 0.002$). Bradycardia paralleled Pa (390 ± 19 bpm to 201 ± 20 bpm, t=0 vs. 7h; $p < 0.01$). No hemodynamic changes occurred after K or in S. Tachypnea but not hypoxemia developed after both L and K but not S. TNF was not increased at 90 min after L (29 ± 9 pg/ml vs. 12 ± 3 pg/ml at t = 0), but rose to 412 ± 190 pg/ml by 4.5 h ($p < 0.005$). Both the magnitude and the time course of TNF changes differed between L and K. Thus, fungemia with viable C. albicans results in endogenous TNF production temporally associated with hemodynamic changes, but with different kinetics from those observed after gram-negative sepsis. Furthermore, factors inducing respiratory distress appear to be differentially regulated from those affecting gas exchange. (Supported by NIH grants GM 43513 and HL 37386).

64.11

Effect of LTB_4 Receptor Antagonists in Endotoxic Shock in the Rat. **Erik J. Li*, James A. Cook, George E. Tempel, W. Curtis Wise and Perry V. Halushka* Medical University of South Carolina, Charleston, SC 29425**

Specific LTB_4 receptor antagonists LY233978 and LY255283 (Snyder and Fleisch, 1989, Annu. Rev. Pharcol. Toxico.) were used to examine the role of LTB_4 in endotoxin (LPS) induced shock in ketamine/xylazine anesthetized rats. LY233978 was given as an infusion (10 mg/kg bolus immediately before LPS, plus 0.67 mg/kg/min for 90 minutes) and LY255283 was given i.v. bolus 10 minutes (10 mg/kg) prior to and a boost dose (5 mg/kg) 30 minutes after *Salmonella enteritidis* LPS (10 mg/kg, i.v.). Control rats received appropriate vehicles.

	LPS [6] vs LPS+LY233978 [6]	LPS [8] vs LPS+LY255283 [5]
HCT (15 min)	52.0±3.0 vs 49.4±1.8	54.0±1.1 vs 48.6±1.8*
HCT (60 min)	54.6±2.6 vs 49.4±1.0*	56.6±1.2 vs 50.9±1.4*
ΔMAP (15 min)	-35.5±8.9 vs -13.8±5.2 *	-42.9±7.1 vs -12.2±8.7 *
ΔMAP (60 min)	-51.0±11.1 vs -37.0±8.2	-58.4±10.3 vs -21.8±10.2*

HCT = hematocrit (%); ΔMAP = changes of mean arterial pressure from baselines (mmHg); [ ] = number of rats; ( ) = time post-endotoxin; * P<0.05, Fisher's Least Significant Difference following ANOVA.

LY255283 also attenuated LPS induced thrombocytopenia and lymphopenia ($P<0.05$), but failed to alter LPS induced neutropenia. The attenuation of LPS sequelae by LTB_4 receptor antagonists LY233978 and LY255283 raises the possibility that LTB_4 may contribute to these pathophysiologic responses in the rat. (Supported in part by NIH GM27673 and Eli Lilly Pharmaceutical Company.)

64.12

DEFEROXAMINE CONJUGATED TO HESPAN, AS A RESUSCITATION FLUID, ATTENUATES THE SYSTEMIC RESPONSE TO BURN INJURY. C. LaLonde, R. Demling*, J. Knox, Y.K. Youn, D. Zhu. Longwood Area Trauma Center, Boston, MA, USA, 02115.

A skin burn results in both local and systemic oxidant injury, leading to distant organ lipid peroxidation. Deferoxamine, an iron chelator, conjugated to hespan, was used as a resuscitation fluid (D+H) in an attempt to attenuate OH° release and subsequent injury. 16 female sheep 40-50kg with a 40% 3rd degree burn were studied under anesthesia. Animals were monitored for 6 hrs, then sacrificed. Group n=4. Control=C, BurnLR=BR, Burn Hespan=BH, Burn Hespan Deferox=BHD

	C.I. L/min/M^2	HR B/min	THgb %	Galac Clear ml/min	Liver MDA nmol/g	Syst Q_L % change	Net Fluid Intake(cc)
C	4.2±3	120±8	8.9±.6	1133±118	110±7	0	900
BR	3.3±.2*	150±18*	9.6±.6*	635±125*	202±59*	826*	5139*
BH	4.5±.5^t	150±18*	9.0±.4	1179±125	211±9*^{t}	741*	4016*^{t}
BHD	4.9±.4^t	120±4^t	8.7±.6^t	2943±130^t	95±26^t	1552^t	4169*^{t}

*=p<.05 compared to control t=p<.05 compared to Burn R.L.

We can conclude that deferoxamine conjugated to hespan (D+H) improves perfusion as measured by increased CI, decreased HR, decreased THgb, increased galactose clearance, increased systemic lymph flow in the presence of decreased fluid requirements compared to Burn(LR) and Burn(H). D+H also abolished the increase in lipid peroxidation MDA seen in Burn (LR) and Burn(H).

65.1

GLOMERULAR FILTRATION IMPAIRMENT BY MERCURY RELEASED FROM DENTAL "SILVER" FILLINGS IN SHEEP. M.J. Vimy*, N.D. Boyd*, D.E. Hooper* and F.L. Lorscheider. Depts. of Medicine, Pathology and Physiology, Univ. of Calgary, Alberta, Can.

In humans mercury (Hg) vapor is released from silver amalgam fillings which contain 50% Hg by wt. When such fillings are placed in sheep teeth, the kidneys will concentrate amalgam Hg at levels ranging from 5-10µg Hg/g renal tissue 4-20 weeks after placement (FASEB J. 3:2641-2646, 1989; Am. J. Physiol. 258:R939-945, 1990). In another report (publ. elsewhere) we demonstrate that the monkey kidney will likewise concentrate large amounts of amalgam Hg. For the present study occlusal fillings (12, total Hg 5100 mg) were placed in each of six adult female sheep under general anesthesia, using standard dental procedures. Glass ionomer occlusal fillings (12) were inserted in two control sheep. At several days prior to dental surgery, and at 30 and 60 days after placement of fillings, renal function was evaluated by glomerular filtration rate (GFR, inulin clearance) and by blood and urine electrolytes, urea and proteins. Average GFR of 69.5 ± 7.2 ml/min before amalgam placement was reduced to 32.3 ± 8.1 ml/min by 30 days and remained low at 27.9 ± 8.7 ml/min after 60 days. GFR did not change in controls. After amalgam placement urine [Na+] increased steadily from 24.8 ± 7.7 to 82.2 ± 20.3 mmoles/L at 60 days. Urine [K+] also increased. Levels of urea and total protein increased from 0-60 days in urine while albumin levels declined. Blood levels of Na+, K+, and urea showed moderate declines from 0-60 days after amalgam. Thus, amalgam Hg levels in kidney are sufficient to significantly reduce GFR, either by reducing renal blood flow or by alteration of the glomerular membrane. Electrolyte, urea and protein patterns in urine are also consistent with impaired renal tubular reabsorption.

65.2

MAINTENANCE OF RENAL AUTOREGULATORY CAPABILITY DURING ADENOSINE RECEPTOR BLOCKADE. A. Mariano Ibarrola*, Edward W. Inscho*, Richard C. Vari and L. Gabriel Navar. Tulane Univ., New Orleans, LA 70112

Because of the resurgence of interest in the role of adenosine as a modulator of renal hemodynamic function, experiments were conducted in anesthetized dogs to evaluate the effects of adenosine receptor blockade on autoregulation of renal blood flow (RBF). Adenosine receptor blockade was imposed by infusion of the receptor antagonist, 1,3-dipropyl-8-sulfophenylxanthine (PSPX). RBF averaged 4.04±0.1 ml/min/gKW (n=15) under control conditions, and was transiently decreased by bolus injections of the adenosine receptor agonist 2-chloroadenosine (2CA;10nmol, 41±4%; 100nmol, 66±3%). After the control period, PSPX was infused intrarenally for 45 min at 2 or 6 µmol/min (n=10 and 5, respectively). PSPX infusion increased urine flow and the fractional excretion of Na and K ($P<0.01$) while outer cortical blood flow, glomerular filtration rate and filtration fraction were unchanged. RBF increased only with the high dose of PSPX (24±6%, $P<0.02$). The vasoconstrictor responses to 10nmol 2CA were attenuated by 69% ($P<0.001$) at the low dose PSPX infusion, and by 80% ($P<0.001$) during the high dose infusion. Similarly, responses to 100nmol 2CA were inhibited ($P<0.001$) by 58 and 86%, respectively. Consistent with an inhibitory effect of adenosine on renin secretion, plasma renin activity increased from 4.0±0.6 to 8.6±1.1 ngAI/ml/hr ($P<0.001$) during PSPX infusion (2µmol/min). Autoregulation of RBF remained intact during the infusion of PSPX. At pressures above the inflection point, the slope of the pressure-flow relationship during PSPX infusion was 0.02±0.003 ml/min/g/mmHg, a value not significantly different from control (0.01±0.002). These data indicate that renal autoregulatory capability remains intact during blockade of adenosine receptors.

65.3

EFFECT OF HIGH FAT DIETS ON ANGIOTENSIN II BINDING AFFINITY OF RAT GLOMERULI. G. P. Brown, A. B. Awad, and C. S. Fink. School of Nursing and Nutrition Program, State University of New York at Buffalo, Buffalo, NY 14214.

Modification of dietary fatty acids may affect the incidence or severity of hypertension. Since angiotensin II (Ang II) has a role in some forms of hypertension, the effect of dietary fatty acids on Ang II receptor parameters was determined. Three groups of rats were fed diets containing 14% by weight of: 1) beef fat (saturated fatty acid rich), 2) fish oil (omega-3 fatty acid rich), or 3) safflower oil (omega-6 fatty acid rich), each supplemented with 2% corn oil. A 4th group of rats was fed regular rat chow which contained 6.5% fat. At the end of 8 weeks, (on 5 different days) 1 to 2 rats from each group were sacrificed, the kidneys removed, and renal glomeruli isolated using a sieving technique. Glomerular binding of Ang II was determined using ^{125}I-Ang II in a radioreceptor assay. Binding at 24°C was proportional to glomerular protein and was time dependent. Receptor affinity (K_a) and number (N), shown in the table below, were determined by Scatchard analysis of binding inhibition data. Glomerular protein concentration was lower in rats fed the high fat diets, so receptor N is expressed per number of glomeruli as well as per mg of glomerular protein.

			N (fmols)	
	µg protein/	K_a	per	X 10^4 per
Diet	100 Glom.	($10^9 M^{-1}$)	mg protein	Glomerulus
Rat Chow	8 ± 0.2	3.1 ± 0.4	838 ± 37	411 ± 24
Beef Fat	7 ± 0.4*	5.0 ± 0.5**	732 ± 32	307 ± 24**
Safflower Oil	7 ± 0.4*	4.9 ± 0.5**	852 ± 38	357 ± 11
Fish Oil	7 ± 0.4*	4.6 ± 0.3**	789 ± 30	349 ± 26

** $p<0.02$ vs. Rat Chow; * $p<0.05$ vs. Rat Chow; N=5 experiments.

The data indicate an effect of high dietary fat, whether saturated or unsaturated, to increase Ang II receptor affinity. Specific binding was greater in glomeruli from rats fed beef fat (24 ± 4 pg/mg) vs. Rat Chow (11 ± 0.4 pg/mg), so that the increased affinity offset the decreased receptor number. The increase in receptor affinity suggests possible enhanced cellular uptake and degradation of Ang II and possibly enhanced second messenger formation. Support by NIH grant HL 37451.

65.4

ANGIOTENSIN II (AII) BINDING/UPTAKE IN TISSUES OF THE RAINBOW TROUT, SALMO GAIRDNERI. J.A. Brown & C.S. Cobb, Dept. Biol. Sci., Univ. of Exeter, Exeter EX4 4PS, U.K.

Tissue slices from seawater-adapted (SW) and freshwater-adapted (FW) rainbow trout (n=3/group) were incubated with (a) ^{125}I-Asp^1 IIe^5-AII (1.71 µCi/ml, 10^{-9} M (b) ^{125}I-AII and excess unlabelled AII (10^{-5}M), (c) no AII, prior to light microscopic autoradiography and grain counting. Binding/uptake of ^{125}I-AII was significantly inhibited in all tissues by excess unlabelled AII ($P < 0.01$ - 0.05 ANOVA) with specific binding/uptake usually exceeding 60%. Specific binding/uptake of tissues from FW and SW fish were similar except in the proximal tubules (silver grains/250 µm^2, SW 88 ± 11; FW 53 ± 8; $P < 0.05$ t test) and oesophagus (silver grains/250 µm^2, FW 81 ± 4; SW 113 ± 4; $P < 0.01$ t test). There was binding/uptake by urinary bladder - epithelium & smooth muscle, intestine & oesophagus - mucosal epithelium, skin epithelium, liver, gill - lamellar epithelium, smooth muscle of filament artery. Binding to cardiac myocytes and aortic smooth muscle suggests AII receptors for regulation of cardiovascular function and/or natriuretic peptide release, binding to renal glomeruli and tubules suggests receptors for regulation of renal function and possible renal tubular uptake of AII, binding to adrenocortical tissue suggests steroidogenic receptors for AII, and binding to brain (medulla oblongata and cerebellum) may be linked to AII control of drinking and blood pressure.

65.5

EFFECT OF DOPAMINE AND CATECHOLAMINE-RECEPTOR BLOCKERS ON IN VITRO RENIN RELEASE IN THE GOLDEN-MANTLED GROUND SQUIRREL (GMGS) DURING HIBERNATION. G. A. Lopez, D. Bewernick*, A. Chang*, M. Mutuc*, D. Ruiz* and S. Tang*. Dept. of Biology, CSULA, Los Angeles, CA 90032.

We have recently reported (Lopez et al., FASEB J., 4-3: A439, 1990) that 10-4M dopamine (DOP) stimulates and 10-7M inhibits renin release (RR) in renal cortical slices from female (F), but not male (M), summer-active GMGS via an adrenergic receptor mechanism in one case (10-4M) but not the other (10-7M). Using the same preparation, we have repeated the study in hibernating GMGS, to determine if seasonal changes can modify the summer-active RR responses to dopamine challenge. Resting RR was not different between sexes. 10-7M or 10-4M DOP added alone or together with the beta-blocker propranolol (10-4M) did not alter RR in slices from M or F animals. 10-4M DOP added with 10-4M pimozide (DOP-blocker) significantly inhibited RR in the M, whereas 10-7M DOP added with 10-4M phentolamine (alpha-blocker) significantly stimulated RR in the F. These data in the hibernating GMGS indicate that: 1) in vitro resting RR is significantly lower during torpor than during activity; 2) the sensitivity of the renin-secreting cells to DOP challenge is drastically altered by hibernation and; 3) DOP-specific receptors may play a role in regulating RR during torpor in the GMGS. (Supported by NIH/MBRS #S06-RR08101).

65.6

AMMONIAGENIC ENZYMES IN MAMMALIAN RENAL TUBULE SEGMENTS: THE EFFECTS OF ACID-BASE INTAKE. P.A. Wright* and M.A. Knepper NHLBI, NIH, Bethesda, MD. 20892

The regulation of renal ammonium excretion plays a central role in the maintenance of systemic acid-base balance. To determine the sites of regulation of ammoniagenic enzyme activities, we have measured phosphate-dependent glutaminase (PDG) and glutamate dehydrogenase (GDH) activities in microdissected renal tubule segments from rat cortex and medulla. Enzyme activities were measured using fluorometric and radio-isotopic methods described elsewhere. In control rats, PDG activities were highest in the distal convoluted tubule and the cortical thick ascending limb, while GDH activities were highest in the S1, S2, and S3 proximal tubule segments. PDG and GDH activities were low in the loop of Henle and other medullary tubule segments, except PDG activities were relatively high in the inner medullary collecting duct. Chronic acid intake (0.28 M NH_4Cl in drinking water for 7 days) increased PDG and GDH activities from 3- to 6-fold in the S1 and S2 proximal tubules, but not in other tubule segments. Chronic base intake (0.28 M $NaHCO_3$) resulted in a small decrease in GDH activity in the S3 proximal tubule, but did not effect PDG activities. Conclusions: 1. The major sites of regulation of ammoniagenic enzyme activities are the S1 and S2 proximal tubule segments. 2. Inner medullary collecting ducts possess relatively high levels of PDG, however, acid or base intake did not effect PDG or GDH activities in any of the medullary segments.

65.7

GLUE SNIFFING AND DISTAL RTA; sticking to the facts.
M. Halperin, S. Donnelly, E. Carlisle, S. Vasuvattakul, S. Tobe, K. Kamel. St. Michael's Hospital, Toronto, Canada

The causes of metabolic acidosis (MAc) can be divided into 2 groups, added acids and loss of bicarbonate. Failure to excrete sufficient ammonium (AM) is prominent in the second group (<40 mmol/d). Diseases characterized by low excretion of AM are called distal RTA if the GFR is not too low. Toluene is said to cause dRTA based on urine pH, rather than AM excretion rates. A patient with MAc secondary to toluene abuse had all the features of distal RTA (plasma pH 7.34, HCO_3 15 mmol/l, anion gap 13, creatinine 84 umol/l, urea 0.5 mmol/l). There was, however, a major discrepancy in the urine. The rate of excretion of AM as estimated from the urine osmolal gap was >100 mmol/d; 8 other patients with toluene induced MAc excreted 144 $\pm$ 68 umol AM/min. A second case of toluene abuse presented with metabolic acidosis and a wide anion gap (23 mmol/l, HCO_3 3 mmol/l). The cause of the wide anion gap MAc was over-production of hippuric acid. We conclude that dRTA (excretion of AM <40 mmol/d), may not be the major cause of MAc with toluene. Overproduction of acids secondary to metabolism of toluene seems to play a more important role.

65.8

RENAL EXCRETION OF ORGANIC ANIONS BY RATS IN RESPONSE TO ACID-BASE CHALLENGE. R.K. Packer, C.A. Curry* and K.M. Brown* George Washington University, Washington D.C. 20052.

In an earlier study we showed that changes in organic anion (OA) excretion play a role in compensatory responses to oral acid and base loads in rats. Total OA excretion increases in response to base loading and decreases in acid loading. The changes in OA excretion were shown to be 40-50% as great as changes in net acid excretion. Of the many OAs found in urine, only citrate has been shown to be excreted in significant amounts by rats during base loading. To quantify excretion rates of citrate and several other OAs, rats were fed diets to which NH_4Cl (acid load), $NaHCO_3$ (blase load) or NaCl (control) was added. Total (OA) of urine was measured by titration. Urine concentrations of citrate, a-ketoglutarate, B-hydroxybutarate and creatinine were determined enzymatically. Some of the results were:

Group	pH	Total OA	Creat.	Citrate	Alpha-KG	B-OH But.
Acid	6.14	3.28	0.35	0.30	0.19	0.07
Base	7.89	11.84	0.52	0.48	0.64	0.10

Values are means. Units are uEq/q/day for OA and umol/q/day for the 4 organic anions. Excretion of all anions measured except B-hydroxybutarate changed significantly in response to dietary acid and base loads with the largest changes seen in a-ketoglutarate. The sum of the changes in the number of uEq excreted per day for citrate and a-ketoglutarate are about 50% as large as changes in bicarbonate excretion reported in an earlier study.

65.9

DEHYDROABIETIC ACID (DHAA) REDUCES BOTH *p*-AMINO-HIPPURATE (PAH) TRANSPORT AND PASSIVE PERMEABILITY IN RAT RENAL MEMBRANES. J.B. Pritchard, R. Walden*, and A. Oikari*. NIH/NIEHS, Res. Tri. Park, NC 27709 and Univ. of Joensuu, Finland

The renal organic anion (OA) transport system plays a pivotal role in elimination of potentially toxic anions. This system is driven by indirect coupling to the sodium gradient at the basolateral membrane (BLM), *i.e.* the OA enters the cell in exchange for internal glutarate (GA) and the in>out GA gradient is regenerated by Na/GA cotransport. The resin acid, DHAA, is one of several anionic xenobiotics which enter the environment secondary to pulp and paper processing. Because it is largely ionized at neutral pH (pK_a ~5), DHAA should share the OA system. Indeed, Na/GA coupled PAH uptake by renal BLM vesicles was competitively inhibited by DHAA (K_i=160 μM). Despite inhibition of initial PAH uptake, a substantial, but delayed, overshoot was observed, suggesting additional effects. Passive permeabilities to mannitol, glucose, PAH and sodium were all decreased by DHAA, consistent with a general tightening of the membrane. This decrease would extend the effective lifetime of imposed ion gradients. Thus, sodium driven GA uptake was stimulated by 200 μM DHAA, prolonging and more than doubling its overshoot. Since the immediate driving force for PAH uptake via the coupled system is the magnitude of the GA gradient, DHAA increased the driving force for PAH uptake and permitted a substantial overshoot despite the reduced rate of PAH uptake. Thus, DHAA has several distinctly different effects on the membrane. Together these effects give rise to the complex pattern of OA transport inhibition described above.

65.10

CHOLINE TRANSPORT IN RENAL BRUSH BORDERS INVOLVES SIMPLE FACILITATED DIFFUSION. S.H. Wright and T.M. Wunz. Department of Physiology, University of Arizona, Tucson, AZ 85724.

Organic cations are secreted by the proximal tubule, including an exchange for H^+ across the luminal membrane. Choline (CHO), an organic cation (OC), is typically reabsorbed. We examined this apparent paradox using rabbit renal brush border membrane vesicles (BBMV). An outwardly-directed H^+ gradient did not stimulate ^{3}H-CHO uptake, although it stimulated uptake of tetraethylammonium (TEA), a model substrate of the OC/H exchanger. Preloading BBMV with 5 mM CHO did stimulate uptake of ^{14}C-TEA, indicating CHO can serve as a substrate for the OC/H exchanger. However, though *trans*-concentrations of TEA had little effect on uptake of CHO, preloading vesicles with 5 mM CHO increased the 5 sec uptake of 125 μM CHO by 10-fold and supported a transient 15-fold "overshoot" of CHO accumulation. The 2 sec uptake of CHO was reduced 90% by 20 mM unlabeled CHO, but only 43% by 20 mM TEA; TEA uptake was reduced 94% and 84% by 20 mM concentrations of TEA and CHO, respectively. CHO uptake was saturable, with a J_{max} of 16 $\pm$ 2.1 nmol/(mg·min) and an apparent K_t of 139 $\pm$ 7.4 μM. An inside-negative membrane potential stimulated CHO uptake and supported a transient overshoot, which was blocked by 20 mM unlabeled CHO. CHO transport was extremely specific, having little interaction with a broad set of OCs. Hemicholinium-3 blocked CHO transport, with an apparent K_i of 100 μM. We conclude that the major transport pathway for CHO in the luminal membrane of proximal tubules involves simple, electrogenic facilitated diffusion, not OC/H exchange, and that this pathway is involved in normal choline reabsorption. (supported by NIH award PO1 DK41006).

65.11

ISOLATION AND CHARACTERIZATION OF BASOLATERAL MEMBRANES ISOLATED FROM SNAKE KIDNEY CELLS: COMPARISON TO BRUSH-BORDER MEMBRANES. Siribhinya Benyajati and Susan M. Bay*. Dept. of Physiology & Biophysics, University of Oklahoma, College of Medicine, Oklahoma City, OK 73190.

Relatively pure basolateral membrane vesicles (BLMV) were isolated from the garter snake (Thamnophis spp.) kidney using specific homogenization procedures and differential + Percoll gradient centrifugation. BLMV fraction (n = 11) exhibited high enrichments for the basolateral marker enzymes (Na^+-K^+-ATPase: 29 ± 7-fold, K^+-p-nitrophenylphosphatase: 19 ± 3-fold). The brush-border (BBM) marker enzymes (alkaline phosphatase and γ-glutamyl transpeptidase) were enriched only 3-fold. Other subcellular membranes showed enrichments of less than one. The BLMV protein yield was 1% and the Na^+-K^+-ATPase yield was 25 ± 7 %. Vesicular nature of BLMV was demonstrated by electron microscopy and by equilibrium osmotic space measurement. Most of the sealed vesicles (73%) were right-side-out. BLMV transport characteristics were examined by rapid filtration technique. BBM contamination of BLMV was reflected functionally by presence of phloridzin-inhibitable, Na^+-dependent D-glucose uptake. BLMV Na^+-independent D-glucose uptake was inhibited by 0.1 mM phloretin. Snake renal BLMV also exhibited specific Na^+-dependent p-aminohippurate (PAH) uptake which was inhibited by probenecid and phenol red but stimulated by very low concentration of glutaric acid. The transport characteristics and inhibitor-sensitivity of D-glucose and PAH uptake exhibited by BLMV were quite different from those observed in BBM of the snake kidney, functionally confirming the relative purity of the preparation. (Supported by NSF DCB-8702902)

65.12

EFFECT OF RENAL DECAPSULATION ON LITHIUM EXCRETION IN RESPONSE TO VOLUME EXPANSION. John A. Haas, Ali A. Khraibi, and Franklyn G. Knox, Mayo Clinic, Rochester, MN 55905

Previous studies have demonstrated that the renal capsule is essential for the full expression of the natriuretic response of acute volume expansion (VE) in rats. The objective of the present study was to establish the role of the proximal tubule in this response. Munich Wistar rats were used in this study. Fractional lithium excretion (FE_{Li}) was used as an index of fractional sodium reabsorption by the proximal tubule. The relationship between fractional sodium excretion (FE_{Na}) and FE_{Li} was determined in control rats with intact capsules (n=12) and in rats with acute bilateral renal decapsulation (n=12) during hydropenia and acute saline volume expansion. In response to volume expansion, FE_{Na} and FE_{Li} increased significantly from 0.48±.13% and 18.1±1.8% to 1.64±.23% and 32.0±2.6% in control. In decapsulated rats, FE_{Na} and FE_{Li} were 0.15±1.8% and 9.9±1.3% during control period and increased significantly to 1.16±.27% and 25.5±1.3% during volume expansion. The change in FE_{Li} was significantly greater in control rats compared with decapsulated rats (Δ+6.5±2.9%) in response to VE. The smaller response of FE_{Li} in bilateral renal decapsulation suggests that the attenuated increase in FE_{Na} observed during VE reflects a blunted decrease in proximal sodium reabsorption.

65.13

REGULATION OF RENAL PHOSPHATE REABSORPTION DURING CHANGES IN THE SUPPLY AND DEMAND FOR PHOSPHATE: ROLE OF GROWTH HORMONE. A. Haramati, M.D. Lumpkin, and S.E. Mulroney. Dept. of Physiology, Georgetown Univ. School of Medicine, Washington, DC 20007.

To study the role of growth hormone (GH) in the regulation of renal phosphate (Pi) reabsorption during growth, our laboratory has recently developed a new model of GH deficiency in the rat. Administration of a synthetic antagonist to GH-releasing factor (GRF-AN: [N-AC-TYR^1-D-ARG^2]-GRF-(1-29)-NH_2) suppressed the pulsatile release of GH, attenuated somatic growth, and decreased the tubular capacity to reabsorb Pi in immature rats. The present study further examined the role of GH in the interplay between growth and renal Pi reabsorption. Experiments were performed in male Wistar rats, 4 weeks of age, in which changes were induced in their rate of growth or dietary Pi. The animals were placed in metabolic cages and daily gain in body weight and urinary Pi excretion were measured. The effects of GH suppression with GRF-AN treatment were evaluated on the "catch-up growth" following dietary Pi replenishment to Pi-deprived rats. Rats were initially Pi-deprived for 3 days and then fed a high Pi diet for 2 days. Dietary Pi replenishment to Pi-deprived rats resulted in a significant increase in urinary Pi excretion ($U_{Pi}V$), but the rate was half that seen in control animals fed normal Pi diet. This attenuated rise in $U_{Pi}V$ was associated with an exaggerated gain in body weight. In contrast, treating Pi-deprived rats with GRF-AN significantly increased $U_{Pi}V$ in response to dietary Pi replenishment (up to the level seen in control animals fed normal Pi diet). This was associated with a significant with a reduction in body weight gain (attenuated "catch-up growth"). These results support the notion that GH plays an important role during growth by contributing not only to the demand for Pi (somatotrophic effects), but also to the supply of Pi through increases in renal Pi reabsorption.

65.14

LOCALIZATION OF HEART ANGIOTENSINOGEN AND RENIN mRNA BY HYBRIDIZATION HISTOCHEMISTRY. Kenneth M. Baker[1], Mitchell I. Chernin[2]* and Gary R. Cooper[1]*. [1]Weis Center for Research, Geisinger Clinic, Danville, PA 17822, [2]Department of Biology, Bucknell University, Lewisburg, PA 17889

Angiotensin II has recently been reported to directly stimulate hypertrophic growth in cardiomyocytes. Direct trophic effects of angiotensin II on the heart could be mediated via circulating or locally produced peptide. This study was performed to determine the presence and localization of the precursor genes for the renin-angiotensin system in cardiac tissue. Expression of the genes encoding angiotensinogen and renin in the neonatal rat heart was studied using in situ hybridization to histologic sections. Angiotensinogen and renin mRNA was detected in all four cardiac chambers and was diffusely distributed. Angiotensinogen and renin mRNA was also detected in isolated cardiomyocytes grown in culture with serum-free medium. The presence of these genes in atrial and ventricular cells in the neonatal period suggests that angiotensin II, produced by a localized renin-angiotensin system, may have a role in cardiac development. Identification of neonatal ventricular angiotensinogen and renin mRNA transcripts may also have implications with respect to the pathologic re-expression of the angiotensinogen gene in left ventricles from pressure-overloaded rats.

65.15

CALCIUM BLOCKERS ANTAGONIZE THE BARORECEPTOR MECHANISM FOR CONTROLLING RENIN SECRETION. Theresa Jones-Dombi.* SPON: Paul Churchill. Wayne State Univ, Detroit, MI 48201

Renin secretion (RS) is inversely related to transmural pressure in the afferent arteriole, or to some function of it such as stretch. It has been hypothesized that increased stretch leads to depolarization of juxtaglomerular cells, and that increased calcium influx through voltage-dependent channels mediates the inhibitory effect on RS. To test this hypothesis, isolated rat kidneys were perfused with an oxygenated Krebs-Henseleit buffer (pH 7.4) at 37°C in a single pass system. Perfusion pressure was varied between 100 and 120 mm Hg in a control period, then varied again in an experimental period during which various calcium channel blockers were added to the perfusate. Renin concentration in the venous effluent was measured and the rate of RS was calculated as the product of renin concentration and the perfusate flow rate. During the control period, RS at 120 mm Hg was 37±3% of the value at 100 mm Hg. This inhibitory effect of increased pressure was blunted by 1uM nifedipine (RS at 120 mm Hg 77±2% of the value at 100 mm Hg; p 0.001, n=15), nearly blocked by 5uM verapamil (RS at 120 mm Hg 90±3% of the value at 100 mm Hg; p 0.001, n=14), and completely blocked by 50uM diltiazem (RS at 120 mm Hg 100±7% of the value at 100 mm Hg; p 0.001, n=10). These results are consistent with the hypothesis that a depolarization-induced calcium influx mediates the inhibitory effect of increased perfusion pressure on RS.

65.16

CHARACTERIZATION OF PLATELET ACTIVATING FACTOR SYNTHESIS DURING ACUTE RENAL ALLOGRAFT REJECTION. Michael Murphy*, Martin Mangino, Charles Anderson*, and John Turk*. Washington Univ. School of Med., St. Louis, MO 63110

The synthesis and metabolism of 1-0-Alkyl-2-0-Acetyl-sn-3-glycero phosphorylcholine (PAF) was characterized in renal tissue undergoing acute cellular allograft rejection in dogs. Kidneys were transplanted between outbred mongrel dogs and allowed to reject for 5 days without adjunct immunosuppression. After 5 days, tissue slices of the renal cortex and medulla obtained from the renal allograft and native contralateral kidney were incubated in-vitro. Renal PAF production was assessed by measuring the releasee of PAF into the incubation media using gas chromatography-mass spectrometry, competitive binding immunoassay, and platelet aggregation bioassay techniques. All analytic techniques revealed dramatic increases in the cortical and medullary production of PAF and the hydrolysis product, Lyso-PAF (GC-MS) during cellular rejection. The predominant molecular species of PAF produced by renal allografts was determined to be 16:0 alkyl PAF, but 18:0 and 18:1 PAF was also detected in allograft tissue (GC-MS). Renal allograft tissue consistently produced about ten times more Lyso-PAF then PAF indicating considerable PAF inactivation during rejection. In other studies, the hydrolysis kinetics of PAF by allograft and native renal tissue revealed twice the inactivation rate by allograft tissue, relative to native renal tissue, and is consistent with enhanced Lyso-PAF production during rejection. CONCLUSION: The renal production and inactivation of PAF is increased during uncontrolled renal allograft rejection. The overall contribution of PAF synthesis to the rejection process or to renal inflammatory states in general is unclear at this time.

SEX HORMONES/REPRODUCTION/FETAL BIOLOGY

66.1

MEASUREMENT OF UMBILICAL BLOOD FLOW (UBF) AND O2 CONSUMPTION USING A TRANSIT-TIME BLOOD FLOW TRANSDUCER IN FETAL SHEEP. D. W. Boyle*, G. M. Sokol*, E. A. Liechty, and J. A. Lemons*. Indiana University School of Medicine, Indianapolis, IN 46202-5210.

Steady state diffusion methods are commonly used to determine UBF in the chronic fetal sheep preparation but may not detect minute to minute variations in UBF, potentially leading to errors in the calculation of metabolic parameters. To investigate this possibility we used a transit-time blood flow transducer to measure umbilical blood flow (UBF-FT, ml/min) continuously in 4 chronically instrumented fetal sheep on 14 separate occasions, 3 to 21 days postoperatively. These flows were compared with umbilical flows measured by the steady state diffusion method (UBF-SS, ml/min) using ethanol as the test substance. Four blood samples were drawn from the umbilical artery and vein for ethanol concentration and oxygen content. UBF-FT was measured continuously over five minutes before, during, and after blood sampling intervals. Fetal oxygen consumption (mmol/kg/min) was calculated by application of the Fick principle to the umbilical circulation using both UBF-FT and UBF-SS. The data were compared by paired t-test. Values are mean ± SEM.

	UBF-FT	UBF-SS	p
Umbilical Blood Flow	480 ± 48	622 ± 56	<0.01
O2 Consumption	0.27 ± 0.01	0.36 ± 0.02	<0.01

UBF-FT correlated with UBF-SS with an R value of 0.89. MANOVA revealed no changes in UBF-FT with respect to intermittent blood sampling. Conclusions: 1) Sampling from multiple fetal vessels does not affect UBF as measured by the transit-time blood flow transducer. 2) Although the results suggest significant differences between the two methods of measuring UBF, the O2 consumption data obtained from both methods are within the physiologic range for fetal lambs during the last trimester. We contend that transit-time methodology provides a promising alternative for measuring UBF continuously, over an extended period of time; however, further verification is necessary.

66.2

VIBRATION COUPLING ACROSS ABDOMINAL WALL. E.M. GRAHAM*, R.M. Abrams, K.J. Gerhardt*, and D.J. Burchfield*. Departments of Obstetrics and Gynecology, Communication Processes and Disorders, and Pediatrics, Univ. of Florida, Gainesville, FL 32610

Increased use of vibroacoustic stimulation as a test for fetal well-being prompted this study of transabdominal transmission of acoustic energy. Four non-pregnant sheep which had been culled for non-reproductive performance were used. Ewes were anesthetized with pentobarbital i.v. and then killed with intracardiac KCl. The stomachs and intestines were removed, flushed to remove any gas-forming bacteria and replaced with adequate saline to expand the abdominal cavity to its former size. A miniature hydrophone was placed intraabdominally 10-15 cm from the midline anterior wall of the ewe. The ewe was placed on her side and vibration excitation was effected horizontally against the midline skin by an electronic artificial larynx (EAL) or by a shaker (SHA). The vibrators were pressed against the skin with three degrees of force: (A) mild--1 cm depression; (B) moderate--3 cm depression; and (C) strong--5 cm depression. The fundamental frequency of the EAL (86 Hz) and measurable harmonics were plotted in dB sound pressure level (SPL) against frequency. The sinusoidal outputs of the SHA were also plotted in dB as a function of frequency (20-4000 Hz). With the EAL at positions B and C there were no significant differences in SPL across the range of harmonics. At position A, however, a significant decrease in sound absorption was noted ($p < 0.001$) with most of the lower SPL values occurring at frequencies > 1 kHz. SPL values created by the SHA at all three positions decreased as frequencies increased ($p < 0.001$) with all mean position A values 10 dB lower than at B and C. Conclusion: Occasional failure of the vibroacoustic stimulation test may be related in part to poor mechanical coupling between vibrator and subject's abdominal surface. Supported by HD 20084.

66.3

EFFECT OF FASTING ON UTERO-PLACENTAL (UP) AMINO ACID (AA) UTILIZATION IN THE PREGNANT EWE. E. A. Liechty, J. Kelley* and J. A. Lemons*. Dept of Peds, Indiana U. Sch of Med Indianapolis, IN 46202-5210.

In the fed state, the net utilization of most AAs by the ovine UP unit is 0. To determine if this is true for the fasted pregnant ewe also, AA concentrations were determined in 9 pregnant ewes across the Ut and Umb circulations. Net uptakes (Upt) across each circulation were calculated using the Fick Principle. Results: μmol/min, mean (SEM)

Fed	UtUpt		UmbUpt		UP	Fasted	UtUpt		UmbUpt		UP
Glu	-.65	(3.8)	-10.6	(3.8)	-9.95	.6	(5.9)	-5.9	(3)		12
Gln	28.9	(7)	22.7	(4.1)	6.2	74	(43)	37	(22)		37
Cit	9.4	(2.6)	1.1	(1.3)	8.3	14	(9.4)	4.7	(5.0)		9.3
Val	16	(1.7)	10.2	(3.7)	5.8	53	(30)	24	(14)		29
Ile	11	(1.3)	7.6	(1.5)	3.4	16	(6.0)	6.9	(2.3)		9.1
Leu	16.4	(1.7)	11.3	(.94)	5.1	34	(12)	15	(5)		19

5 AAs were found to have a consistently greater UtUpt than UmbUpt. Glu had a negative net UmbUpt, with no net UtUpt. Fasting resulted in an increase in the differences between the respective uptakes for all five AAs. No additional AAs were found to have disparate uptakes during fasting. Umb Glu uptake became less negative during fasting, but the difference between the Ut and Umb circulations remained unchanged, as the Ut circulation took up Glu during fasting. The Umb circulation took up α-KIC (.626±.18, fed), and the uptake increased during fasting (1.8±.6). Conclusions: These findings suggest that the BCAAs and Gln are utilized by the ovine UP to a greater degree than are most other AAs, and at increased rates during fasting of the ewe. These AAs, through deaminatic may be the source of UP NH_3 production, as well as serving as an energy substrate when Glucose supply is limited.

66.4

ASSESSMENT OF DYNAMIC BLOOD-TISSUE-EXCHANGE OF STEROID RECEPTOR LIGANDS USING SINGLE PASS INDICATOR DILUTION. James E. Artwohl*, Anton Scharl*, Matthias Beckmann*, John A. Holt. University of Chicago, IL 60637.

The potential of radiohalogenated steroid receptor ligands (e.g. [123I]iodoestradiol) for diagnostic and therapeutic purposes is currently under investigation. Data on the blood-tissue-exchange of these radiopharmaceuticals are critical for dosimetry. Several approaches are used for assessing blood-organ-exchange of chemicals in vivo especially on a single-pass basis. Some of them require sacrificing the animal and extirpation of the specific organ at multiple time points after administration of the radiopharmaceutical, and are therefore very time- and animal-consuming. To avoid these disadvantages, we developed a preparation that is more efficient and provides insight into the real time dynamics of blood-organ-exchange of radiopharmaceuticals at an organ level. As a general feature, the model encompasses the administration of the diffusable radiopharmaceutical together with a compound that does not escape the circulation, e.g., [99mTc]-labelled RBC, into an organ artery and subsequent drawing of arterial and venous blood samples. The course of the ratio of the activities of radiopharmaceutical/[99mTc] in the venous compared to the arterial blood of an organ provides insight into direction and volume of blood-tissue exchange of the pharmaceutical. The pulmonary and systemic circulations were studied independently, using right heart ventricle catheterization with lung vein sampling, and left heart catheterization with organ venous sampling, respectively. Because the liver plays a central role in drug metabolism, it was excluded from the circulation in these preparations by a porto-caval shunt and occlusion of the liver vessels. The pharmacokinetic processes in the capillary bed of the liver were assessed by a third preparation that included catherization of hepatic portal, venous, and arterial vessels. Swine were chosen because of the similarity in size, fat distribution, and general metabolism as man. This technic allowed successful assessment of the biodistribution of iodo-estradiol, which is used for imaging of estrogen-receptor-rich malignancies, and provided additional information on dosimetry in potential therapeutical applications. Moreover, by analyzing the blood samples for metabolites of iodoestradiol, we obtained meaningful data about its metabolism for individual organs. [Supported by R24RR029001 (JEA), CA-27476 (JAH), DFG-Scha466/1-2 (AS), DFG-Be1215/1-1 (MB), and CLIH-Mothers Aid Research Fund]

66.5

RAPID SINGLE PASS ORGAN UPTAKE AND SUBSEQUENT RELEASE OF 16ALPHA-IODO-17BETA-ESTRADIOL. Matthias Beckmann*, Anton Scharl*, James E. Artwohl*, John A. Holt. University of Chicago, Chicago, IL 60637.

LET-type radiation by Auger-electrons from [125I], when it occurs within the cell nucleus, is cytotoxic. Data from studies in vitro and in vivo, and recent human imaging have demonstrated that 16alpha-iodo-17beta-estradiol (I-E2) concentrates [125I] in the nuclei of estrogen receptor (ER) rich tissues, and has therewith the potential for single cell radiation of ER-rich tumors. The high doses of radioactivity for therapy requires careful dosimetry. To obtain insight into the dynamics of the fluxes of [125I]E2 across body organs and fluids we used a single pass indicator ([99mTc]RBC) dilution method in swine in combination with 1) right heart ventricle catheterization with lung vein sampling, 2) left heart catheterization with organ venous sampling (the liver was bypassed in preparation #1 and 2), and 3) portal vein catheterization with liver vein sampling. Blood, body fluids, and organ tissue samples were counted for [125I] and analyzed by extraction in organic and inorganic solvents, enzymatic digestion (sulfatase, glucuronidase), column chromatography, and binding to rabbit ER in vitro. **Results:** During the first pass across the capillary bed of all organs studied, a fraction of [125I]E2 that exceeded 90% of the injected dose escaped the circulation. The liver rapidly metabolized the radiopharmaceutic to [125I]E-glucuronide and -sulfate, and released the conjugate back into the circulation. Minor metabolism of [125I]E2 was observed beyond the liver; unmetabolized [125I]E2 was the principal compound released back from most organs (lung, brain, intestine, spleen, muscle, fat). Uterus and kidney retained high levels of radioactivity for at least 1h after *i.a.* injection, mainly in the form of [125I]E2. One hour after *i.a.* injection the ER-rich uterus had uptake of >0.04% of the injected dose/g tissue (%/g). Retention of the radiopharmaceutic in ER-poor organs was below 0.01%/g with exception of the kidney (0.02%/g). A similar retention pattern of the radiopharmaceutic occurred 1hr after *i.v.* administration except for a notably higher retention in the kidney (>0.05%/g). After administration of the radiopharmaceutic into the portal vein, no sequestration of [125I]E in ER-rich organs was observed. **Comment:** [125I]E2 diffuses easily throughout any organ tissue within the first pass and is sequestered in ER-rich organs. An *i.a.* route of administration appears preferable to an *i.v.* route because there is less exposure to radiation for the kidney [Supported in part by DFG-Be1215/1-1 (MB), CA-27476 (JAH), DFG-Scha466/1-1 (AS), R24RR029001 (JEA), and CLI-Mothers Aid Research Fund]

66.6

ABSENCE OF DECIDUAL CELL RESPONSE (DCR) AND ABNORMAL UTERINE RESPONSE TO ESTROGEN (E) IN THE JAUNDICED (jj) FEMALE GUNN RAT. Sandra L. Richardson*, David R. Davis*, John Harder* and Syed Saiduddin. The Ohio State University, Columbus, Ohio 43210.

Based on the lack of implantation sites observed in the mated female jj Gunn rats, experiments were initiated to study DCR to uterine trauma in pseudopregnant rats. None (n = 7) of the jj rats had DCR while 6 of 7 nonjaundiced (Jj) had a 10-fold increase in weight of the traumatized horn compared to control horn. DCR studies were also done in ovariectomized (OV_x) rats given E and P_4. Six of 11 Jj rats had DCR (5-fold increase) while only 3 of 22 jj rats had DCR (2-fold increase). We also studied the uterine response to E in OVx rats. The Jj rats showed a clear dose response to E (0.1, 0.5 and 2.5 μg/100 g BW, oil-controls) for 3 days (killed on 4th day). The jj rats showed a maximal response to 0.1 μg E and no dose response. In control rats jj uteri were larger than Jj. Rats given 2.5 μg E were also killed 1,2 and 3 weeks after E was stopped. The Jj uteri regressed to control levels by 1 wk. The jj uteri remained enlarged even 3 wks later. The lack of uterine regression following E withdrawal indicates a hyperestrogenic condition in the jj rat. In view of the published reports of a deficiency in hepatic conjugating enzyme for bilirubin in the jj rat, we speculate that a deficiency for E conjugating enzymes may coexist. Therefore, the lack of DCR and infertility in the female homozygous jaundiced Gunn rat may be due to an inability to conjugate and excrete sex steroids.

66.7

STEROID REGULATION OF PHA HYPERSENSITIVITY IMMUNE RESPONSE C. Grossman, R. Arnold*, T. O'Connell*, N. Orphanos*, S. Schrimpf*, M. Nienaber*, C. Mendenhall*, G. Roselle*. Research Srv. VAMC Biology Dept., Xavier Univ; Dept of Physiology & Biophysics, UC College of Medicine; Cincinnati, OH

Both the cell mediated and humoral immune response are greater in females than in males. To ascertain the role of sex steroids in dimorphism, male rats were castrated and steroid replacement at physiological concentrations was accomplished by subcutaneous Osmotic pumps. Cell mediated immune response was measured by the use of the Phytohemagglutinin P delayed hypersensitivity skin test. After one week of steroid replacement in comparison to buffer (B) controls; E (estrogen) depressed the response (147 mm^2 vs 179 mm^2, p=.04), T (testosterone) stimulated the response (205 mm^2, p=.07), progesterone (P), dihydrotestosterone (DHT), and E+T were similar to B, and P+E was no more effective than E alone (147 mm^2 vs 143 mm^2). These results support the immunoinhibitory role of E but not of P. The mechanism by which T acts to immunostimulate is not clear especially since the metabolite DHT does not have an effect alone. This suggests that dimorphism is not due entirely to the differences in sex steroids in males and females.

66.8

EXPERIMENTAL LEFT VARICOCELE (ELV) REDUCES IN SITU pH IN RAT TESTIS AND EPIDIDYMIS. C.R.Caflisch and T.D. DuBose, Jr. U. Texas Med. Br., Galveston, TX 77550.

Varicocele, dilation of the spermatic vein, is a vascular anomalie which is strongly associated with male infertility in humans. In the rat, ELV causes a bilateral increase in testicular blood flow and temperature and a subsequent decrease in cauda epididymidis sperm concentration and motility. However, the effect of ELV on in situ pH in the rat testis and epididymis has not been investigated previously. In this study, the effect of ELV on in situ pH was assessed in rat seminiferous tubules (ST), initial segment (IS), proximal caput (PCP), middle corpus (MCR), and proximal cauda epididymidis with glass membrane double barreled pH microelectrodes. Varicoceles (ELV) were created in five Sprague-Dawley rats by partial ligation of the left renal vein medial to the anastomosis with the left spermatic vein and the animals were prepared for micropuncture after 4 weeks. Four rats served as sham operated (SO) controls. pH values at each micropuncture site were (mean ± SEM):

	ST	IS	PCP	MCR	PCD
SO	6.91±0.02	6.79±0.03	6.58±0.01	7.19±0.06	6.89±0.02
ELV	6.79±0.02##	6.69±0.03**	6.53±0.02*	7.13±0.04	6.82±0.02#

*P<0.05;**P<0.025; #P<0.01; ##P<0.001 VS SO

Thus, pH of luminal fluid in ST, IS, PCP, and PCD was significantly more acidic after ELV of 4 weeks duration. These findings may be compatible with impairment of acid-base pathways after ELV.

66.9

EFFECTS OF THE MENSTRUAL CYCLE ON RESTING MUSCLE GLYCOGEN CONTENT. Anthony C. Hackney. Exercise Physiology Laboratory, Univ. of North Carolina, Chapel Hill, NC, 27599

A recent report suggested that the muscle glycogen content of women is affected by their menstrual cycle phase (Nicklas et al., Int J Sports Med 10: 1989). The intent of this study was to examine this issue. Ten eumenorrheic women (age = 25.0±1.6 yr, cycle length = 29.5±1.0 days; Mean±SEM) had multiple needle biopsies of the vastus lateralis performed during the midfollicular (cycle day 8±1) and midluteal (cycle day 22±1) phases of their menstrual cycle. Menstrual cycle phases were determined from daily basal body temperatures and confirmed by resting estradiol and progesterone levels in a subsample of subjects (n=6). Diet, physical activity, and sexual activity were controlled and replicated for the ~36 hours prior to each biopsy. Tissue samples were analyzed by the procedures of Bergstrom, Scand J Clin Lab Invest 14: 1962 (assay coefficent of variation ± 7.3%). The results indicate muscle glycogen content was significantly lower ($p<0.05$) in the midfollicular samples (n=13) than in the midluteal samples (n=13); 90.76±3.56 vs 102.05±4.97 umol/g w.w. muscle. These findings suggest; 1) metabolic studies should be completed in the same phase of the menstrual cycle to control for glycogen differences, and 2) endurance exercise performance may be hindered during the midfollicular phase of the menstrual cycle.

66.10

EFFECT OF MEGADOSES OF VITAMIN C ON THE REPRODUCTIVE PERFORMANCE OF SEXUALLY MATURE FEMALE GUINEA PIGS. Mark A. Kukucka* and Hara P. Misra.* (SPON: James C. Keith, Jr.) Virginia-Maryland Regional College of Veterinary Medicine, Department of Biomedical Sciences, Virginia Tech, Blacksburg, VA 24061

The scientific literature is riddled with conflicting and ambiguous information on the role of ascorbic acid in normal female reproduction. To determine if vitamin C is intimately associated with reproductive events, L-ascorbic acid was administered *per os* at a level of thirty times the recommended daily allowance (RDA) as published by the National Research Council (NRC) to female guinea pigs whose fecundity was previously determined. Following two weeks of vitamin therapy, sexually mature intact male guinea pigs were introduced to the females. The instituted vitamin regimen was continued throughout the entire length of the anticipated gestation period. Reproductive performance in terms of live, healthy guinea pig pups were recorded and analyzed for each individual female by group and by treatment. In comparison to controls, female guinea pig treated with megadoses of vitamin C delivered one fourth as many guinea pig pups. The reported data demonstrate a strong association between the oral administration of large quantities of vitamin C and consequent dramatic decreases in the reproductive performance of sexually mature female guinea pigs.

66.11

PURIFICATION AND SUBUNIT ANALYSIS OF CALF UTERINE PROGESTERONE RECEPTOR. C. B. Hurd*, C. J. Swanson and V. K. Moudgil. Oakland University, Dept. of Biological Sciences, Rochester, MI 48309 and Dept. of Biological Sciences, Wayne State University, Detroit, MI 48202.

Steroid hormone receptors are known to be composed of both hormone and non-hormone binding protein components. We have examined the protein composition of calf uterine progesterone receptor (PR) purified with the monoclonal antibody, PR6. PR from uterine cytosol was optimally precipitated with 10 µg/ml of PR6. The immuno-complexes were adsorbed to protein-A Sepharose and washed free of extraneous proteins. SDS-PAGE analysis revealed the presence of two major proteins (114 kDa and 90 kDa). Western blot analysis detected the presence of only the 114 kDa protein. The 114 kDa protein was also photoaffinity labeled with the synthetic progestin, R5020 (17, 21-dimthylpregna 4,9 (10)-diene-3, 30-dione), indicating that this subunit represents a hormone binding component of PR. PR6, which is specific only to avian PR B protein (110 kDa), may be detecting a subpopulation of PR in the uterine cytosol. The 90 kDa protein comigrated with a 90 kDa protein immunoprecipitated with AC88 (a monoclonal antibody specific for HSP-90) from the uterine cytosol. These results demonstrate that PR6 can be utilized to analyze the subunit structure of calf uterine PR, which appears to be composed of a major steroid binding protein (114 kDa) in association with HSP-90. Supported by NIH grant DK-20893, and gift of antibodies from Dr. David Toft, Mayo Clinic.

66.12

ENTEROHEPATIC CIRCULATION OF THE RADIOHALOGENATED ESTROGEN 16ALPHA-IODO-17BETA-ESTRADIOL. Anton Scharl*, Matthias Beckmann*, James E. Artwohl*, Edward J. Pavlik*, John A. Holt. University of Chicago, Chicago, IL 60637, University of Kentucky, Lexington, KY 40536.

The radiohalogenated estrogen 16alpha-17beta-iodo-estradiol (I-E2) is emerging as a diagnostic tool for imaging ER-rich malignancies with a potential therapeutic option for site-directed radiotherapy. Clinical use requires an accurate accounting of the radioactivity's biodistribution including assessment of its potential enterohepatic circulation. Enhanced biotraceability derived from radiotagging predicts more detailed insight into the dynamic physiology of the enterohepatic circulation of estrogens. Using three surgical preparations in swine we investigated the pharmacokinetics and recirculation of [125I]E2 in the enterohepatic system. In the first preparation, [125I]E2 was injected into the hepatic portal vein together with [99mTc]-labelled RBCs, the latter stay in the circulation and provide a reference to estimate blood-tissue exchange of [125I]; blood was collected continuously from the hepatic artery and vein, and the portal vein for 1h. The second preparation included i.v. injection of [125I]E2 and sampling of urine and bile for 2h (donor swine). In a third preparation, bile of a donor swine was infused into the proximal duodenum of a recipient swine, and bile, urine, and venous blood were sampled for 30 h. The samples from all preparations were counted for [125I] and [99mTc], and analyzed by extraction in organic and inorganic solvents, TLC and column chromatography, enzymatic digestion (sulfatase, glucuronidase), and in vitro binding to rabbit estrogen receptor. More than 99% of [125I]E2 was cleared from the blood by the liver during the first pass following injection into the portal vein. Within seconds, water soluble metabolites were partially released into the blood and partially excreted into the bile. The metabolized radiopharmaceutic in the blood subsequently simply passed the liver and was cleared by the kidney. More than 95% of the radioactivity in urine and bile was comprised of [125I]E2-glucuronate or -sulfate, only a very small fraction was free [125I]. Intestinal reabsorption of radioactivity was total and occurred mainly after 5-7h. The reabsorbed radioactivity was cleared immediately into the urine. [Supported in part by CA-27476 (JAH), DFG-Scha466/1-1 (AS), DFG-Bc1215/1-1 (MB), R24RR029001 (JEA), and CLIH-Mothers Aid Research Fund]

MICROCIRCULATION

67.1

ISOLATION OF CAPILLARY ENDOTHELIAL CELLS FROM THE EEL, ANGUILLA ROSTRATA. R.A. Garrick. Fordham Univ. N.Y., N.Y. 10023.

Capillary endothelial cells are the site of a number of important physiological regulatory mechanisms. Pure preparations of capillary cells are not easy to obtain from mammalian tissues. The rete mirabile of the eel is an accessible packet of capillaries which are used to study transport and metabolism. I have used the rete mirabile of Anguilla rostrata as a source for the isolation and culture of vertebrate capillary endothelial cells. The eels are anesthetized, the retia exposed and perfused with a Ca^{2+}-Mg^{2+} free salt solution. The retia are removed, the poles trimmed and the tissue minced into 0.1% collagenase in M199 and stored overnight at 4 C. The tissue is incubated at room temperature (18-20 C) for 1.5-2.0 hrs. with mixing. The tissue is filtered through 100 um nylon mesh and pelleted by centrifugation. The cells are resuspended in modified M199 and plated into gelatin coated T-25 flasks and incubated at 25 C. The cells attach and start to spread by the end of the first week. The cells have structural characteristics similar to mammalian endothleial cells. They can be used to study basic functions and comparative aspects of vertebrate capillary endothelial cells.

(Work was performed at the Marine Biological Laboratory with support from Fordham University and HL 12879).

67.2

CAPILLARITY IN AVIAN SKELETAL MUSCLE. Gregory K. Snyder. Department of EPO Biology University of Colorado, Boulder, CO 80309-0334 USA

Capillarity and diffusion distances in skeletal muscles were determined for adult birds with body masses of 10.8 g to 6,200 g. Muscle masses were closely coupled to body mass. However, there were not significant allometric relations for any of the other variables measured; numbers of capillaries per fiber, capillary density, fiber cross sectional area and diffusion distance. In addition, number of capillaries per fiber was not correlated with muscle fiber cross sectional area. Thus, capillary density decreased in a hyperbolic manner against fiber area. When normalized for fiber area, diffusion distance decreased in a hyperbolic manner against number of capillaries per muscle fiber. Red muscles had significantly more capillaries per fiber and significantly shorter diffusion distances than white muscles and the patterns were similar for avian and mammalian muscles. In both taxa capillaries are distributed in random arrays. We suggest that capillarity and the relationships between capillarity and diffusion distances in adult muscles of birds and mammals are relatively fixed; the potential for capillary growth in adult muscle, as an adaptation to increased oxygen demands or decreased oxygen supply, may be minimal.

67.3

REFLEX CHANGES IN MICROVASCULAR DIAMETERS IN STRIATED MUSCLE EVOKED BY CHEMICAL STIMULATION OF CARDIAC AFFERENTS IN RATS. Andrew M. Roberts and Irving G. Joshua. Dept. of Physiology, Univ. of Louisville, Louisville, KY 40292.

Stimulation of chemosensitive vagal afferents in the heart reflexively decreases blood pressure and heart rate. The present experiments were carried out to determine whether stimulation of vagal cardiac afferents can reflexively alter the tone of small resistance vessels in striated muscle. In pentobarbital-anesthetized male Sprague-Dawley rats with open chest, we ventilated the lungs through the lower trachea and examined the in vivo responses of 3rd order arterioles in the cremaster muscle, using closed-circuit television microscopy. Diameters of arterioles were measured as an index of microcirculatory resistance. The pericardium was opened and phenyl biguanide was applied topically to the epicardium using small pieces of filter paper soaked in test solution (10-100ug/ml). Stimulation of afferents with phenyl biguanide caused dilation of arterioles and often decreased blood pressure and heart rate. These effects were prevented by cutting the cervical vagus nerves. Constriction sometimes occurred which persisted after vagotomy. Thus, it appears that chemosensitive vagal afferents in the heart can exert inhibitory effects on the microcirculation of striated muscle. (Supported by the American Heart Association and Kentucky Affiliate of the AHA)

67.4

EFFECT OF FIBER SHORTENING ON CAPILLARY GEOMETRY IN RAT MYOCARDIUM. D. C. Poole, S. Batra, O. Mathieu-Costello and K. Rakusan. Dept. of Medicine, UC San Diego, La Jolla, CA. 92093 and Dept. of Physiology, U. of Ottawa, Ottawa, Canada K1H 8M5.

Capillary geometry in mammalian skeletal muscle changes appreciably with altered muscle length. As sarcomere length (l) decreases, capillaries become more tortuous and capillary-to-fiber surface contact increases, thereby enhancing gas exchange potential (Ellis et al. FASEB J. 2: M52, 1988). To determine whether this occurs in cardiac muscle, hearts (n=3) were arrested in situ at varying degrees of systolic contracture with calcium or barium and glutaraldehyde perfusion-fixed. Hearts were analyzed morphometrically to determine capillary orientation (tortuosity and branching; Fisher axial distribution) and l. These data were compared with diastolic hearts (Poole and Mathieu-Costello, Physiologist 32: 155, 1989). Sarcomere length in sub-epicardium (EPI) was 1.67±0.23 μm (range 1.43-2.06 μm) and 1.74±0.11 μm (range 1.64-1.93 μm) in sub-endocardium (ENDO) of systolic hearts. From these preliminary results, capillary anisotropy coefficient, c(K,0), was 1.23±0.04 (EPI) and 1.23±0.06 (ENDO). This was not significantly different from diastolic hearts: EPI, c(K,0) = 1.16±0.06 at l = 2.16±0.04 μm, ENDO, c(K,0) = 1.13±0.03 at l = 2.09±0.04 μm. Fiber cross-sectional area (XSA) was significantly greater in systolic (EPI, 355±13, ENDO, 369±11 μm^2) than diastolic hearts (EPI, 270±29, ENDO, 284±16μm^2) as predicted by the inverse relationship between l and fiber XSA at constant fiber volume. At l ~1.7 μm, capillary tortuosity and branching contributed 23% to total capillary length compared with up to ~60 to 70% in skeletal muscle. We conclude that the relationship between sarcomere length and capillary orientation is different in mammalian cardiac and skeletal muscle. It is unlikely that the gas exchange potential of the myocardial capillary bed improves during systole.
Supported by NIH (07212 and 17731) and American Lung Assoc. of CA.

67.5

ADAPTATIONS OF MATURE MICROVESSELS TO REDUCED BLOOD FLOW. D.H.Wang and R.L.Prewitt Eastern Virginia Medical School, Norfolk, VA 23501

Adaptive responses of mature arterioles were examined after a 38% reduction in total blood flow to the cremaster by unilateral orchidectomy in 12-week-old rats. Four weeks following orchidectomy, the muscle was smaller than the contralateral cremaster which did not grow during this period. Measured by closed-circuit television microscopy, the internal diameters of all orders of arterioles (1A-4A) and the number of 4A's per 3A had decreased compared to that of arterioles in the control side, but no significant change in wall cross-sectional area was observed except in 3A's. The reduced diameter of the 1A in the orchidectomy muscle resulted in unchanged wall shear rate. The length of the arcading arterioles and the number of 3A's remained unchanged. Arteriolar density increased on the orchidectomy side due to the disproportional decrease in arteriolar number and muscle mass. Therefore, adaptations of reduced internal diameter and number of mature arterioles to decreased blood flow occurred in the absence of net changes in medial tissue mass. Because the muscles were beyond their growth stage, the microvascular changes were not secondary to local changes in growth factors. (Supported by Jeffress Research Grant and NIH Grant HL-36551)

67.6

EFFECT OF TEMPERATURE ON OXYGEN DIFFUSION IN HAMSTER RETRACTOR MUSCLE. T. B. Bentley, H. Meng* and R. N. Pittman, Dept. of Physiology, Medical College of VA, Richmond, VA. 23298

In order to reconcile in vivo data on arteriolar O_2 transport with a mathematical model of O_2 diffusion, Popel et al. (AJP 256:H921,1989) have suggested that DO_2 in vivo might be an order of magnitude higher than the in vitro value previously determined at 22°C and extrapolated to 37°C (Ellsworth and Pittman, AJP 246:H161,1984). This study aimed to determine the effect of temperature on DO_2 since inaccurate estimation of the temperature dependence of DO_2 could contribute to the discrepancy between in vivo and in vitro measurements. DO_2 was measured using a nonsteady state technique by analyzing the time-course of PO_2 recorded by an oxygen electrode at the lower surface of the muscle during the transient period following step-changes in aerating gas composition above the muscle. O_2 consumption was estimated from the drop in PO_2 across the muscle once steady state was reached. The results showed that the effect of temperature on DO_2 was relatively stable between 11° and 30°C and was unable to account for the large DO_2 needed to reconcile theory and experiment. The Q_{10} for oxygen consumption was 3.5 from 11° to 23°C and decreased to 1.4 from 23° to 30°C similar to values for mammalian cardiac muscle. (NIH grant HL 18292)

67.7

MITOCHONDRIAL VOLUME DENSITY IS A PHYSIOLOGICAL VARIABLE. B. Klitzman and N. Schrader*. Plastic Surgery Research Labs and Div. Physiology, Duke University Medical Center, Durham, NC 27710

The purpose of this study was to quantify mitochondrial density in rat cremaster muscle following exposure to hypoxia or cold. Male Sprague-Dawley rats were raised for two months in chronic hypoxia (ambient PO_2= 75mmHg) or cold (4°C). Rats were then anesthetized and their cremaster muscles superfused for 10 min with buffered glutaraldehyde and paraformaldehyde, followed by muscle immersion for 60 min in fixative. Muscles were embedded and cut in cross section for electron microscopy. Electron micrographs were taken (4600X) and montages created. Using point counting, mitochondrial volume percentage was measured as mean±SE % (n).

CONTROL	HYPOXIA	COLD
2.66±0.20(173)	2.18±0.24*(108)	1.68±0.16**(88)

*p<.05, **p<.01 vs control

The mitochondrial volume density was decreased following chronic hypoxic or cold exposure. The density 10-15um from the capillaries was particularly reduced in both hypoxic and cold exposed rats. These data indicate that mitochondrial volume density is a physiological variable which can change over several weeks in response to environmental conditions.
Supported by NIH grants HL36552 and HL42444.

67.8

CRITICAL O_2 DELIVERY IN SKELETAL MUSCLE OF ANEMIC DOGS WITH AND WITHOUT PLASMA HEMOGLOBIN. G. Biro, S.E. Curtis*, P.J. Anderson* and S.M. Cain. University of Ottawa, Ottawa, Ontario Canada K1H 8M5 and University of Alabama at Birmingham, Birmingham, AL. 35294.

Homer et al. (Microvasc. Res. 22:308-323, 1981) suggested that the presence of free hemoglobin in plasma would enhance O_2 supply by reducing the large pO_2 gradient existing between red blood cells and plasma in hemodiluted animals. This suggestion was tested in resting, vascularly isolated, pump-perfused hindlimb muscles of anesthetized dogs. The systemic hematocrit was reduced by isovolumic hemodilution with dextran to 16±2%. In addition, one group of dogs received an infusion of purified hemoglobin, resulting in a plasma hemoglobin concentration of about 1 g/dl. Hindlimb oxygen uptake and delivery were determined, after stepwise reductions of blood flow. Linear regressions were fitted to the supply-dependant and supply-independant portions of the O_2 uptake/delivery relation. The critical oxygen delivery was defined as the intersection of the two regressions. The ratio of oxygen uptake at the critical oxygen delivery was defined as the critical oxygen extraction ratio. (Bredle et al., J. appl. Physiol. 66:2553, 1989). Neither of these critical parameters was significantly different between the undiluted and hemodiluted animals, or between the two hemodiluted groups. This suggests that in resting skeletal muscle, hemodilution alone does not impair and the presence of free hemoglobin in plasma does not enhance diffusive oxygen supply. There was some evidence, however, that the hemoglobin solution was vasoactive in that the pressure-flow relationship in the hemoglobin-treated group was steeper. (Supported by the Defence and Civil Institute of Environmental Medicine of Canada and by Grant HL 26927 from the National Institutes of Health).

67.9

Renin-Angiotensin Essential for Endotoxin (ENDT) Microvascular Response. C.H. Baker, E.T. Sutton*, J.R. Dietz, Dept. of Physiol. & Biophys., U. of So. Fl., Tampa, FL 33612

Response of the renin-angiotensin system may be altered by ENDT. Reactivity of cremaster muscle microvessels of pentobarbital anesthetized rats was studied using videomicroscopy. E. coli ENDT (6 mg/kg) was infused i.v. over a one hour period. Femoral arterial pressure (Pm) and arteriolar diameter changes, to i.a. bolus injections (60ng) of angiotensin II (AII) were obtained in Group I at control and at 30 and 90 min post-ENDT, and in Group II at control, 30 min after continuous infusion of saralasin (10 μg/min/kg) began, and at 30 and 90 min post-endotoxin. In Group I, the control Pm was 106±4 mm Hg, 96±4 and 89±7 mm Hg at 30 and 90 min post-ENDT. AII increased Pm 29±4% before ENDT but was significantly less ($p<0.05$) at 7±1% and 6±1% 30 and 90 min post-ENDT. In Group II the control Pm was 116±6 mm Hg, 103±5 after saralasin, 85±2 after ENDT infusion and 83±4 and 63±8 mm Hg at 30 and 90 min post-ENDT. AII increased control Pm 34±7% and only 5±2% ($p<0.05$) during saralasin infusion. Group I A_3 arterioles were constricted to 65±8% of control by AII, but Group II arterioles constricted to only 94±2% of control diameter at all stages of the experiment. Plasma renin activity averaged 5.6±1.6 ngAI/ml/hr in normal rats and 20.0±3.7 ng/AI/ml/hr in ENDT rats ($P<0.01$). The renin-angiotensin system is essential for response to ENDT even though its effects are attenuated. (USPHS grant HL-33840)

67.10

PERMEABILITIES OF ENDONEURIAL CAPILLARIES AND PERINEURIUM OF RAT SCIATIC NERVE TO ^{22}Na DURING DEVELOPMENT. Ananda Weerasuriya* (SPON: C.H. Hockman) Mercer University School of Medicine, Macon, GA 31207 and Peripheral Nerve Center, Mayo Clinic, Rochester, MN 55905

Blood-nerve transfer of ^{22}Na was measured as the permeability coefficient-surface area product (PS) of the blood-nerve interface (BNI) using the i.v. bolus injection technique, and PS of perineurium (P) with an in situ technique in 3, 6 and 12-week rats. The former was calculated using a multiple time point-graphical analysis, and the latter with a simple two compartment model with undirectional flux. The residual endoneurial plasma volume (Vp) was taken as the ordinate intercept of the graphical analysis, and PS of endoneurial capillaries (EC) was calculated from the difference between the PS of BNI and P. The results are given as mean ± S.E.M., and n is 16 to 18 for BNI and 5 to 7 for P. The relative contributions of EC

Age (weeks)	PS_{BNI}	PS_P ($ml.g^{-1}.s^{-1}$) x 10^5	PS_{EC}	Cap/Per	Vp ($\mu l.g^{-1}$)
3	29.4±6.3	2.75±0.22	26.6	9.7	73.5±20.7
6	18.6±2.7	2.67±0.26	15.9	6.0	33.6±9.2
12	9.8±1.1	1.03±0.11	8.8	8.5	24.4±9.0

and P to blood-nerve exchange of ^{22}Na, and other ions, appear to be conserved during development. Developmental decreases in PS of EC and P to ^{22}Na are largely due to reductions in their respective surface areas/gm of endoneurium. (Borchard Fund and NS-14304 to PNC, MC).

67.11

INOSINE, HYPOXANTHINE AND CREATININE IN ISCHEMIC/REPERFUSED SKELETAL MUSCLE STUDIED WITH MICRODIALYSIS David H. Lewis, Allan Sirsjö* and Bertil Kågedal*. Clinical Research Center and Department of Clinical Chemistry, Faculty of Health Sciences, University of Linköping, Linköping, Sweden

Microdialysis and HPLC were used to study extracellular levels of adenosine (Ad), hypoxanthine (Hx), xanthine (X) and creatinine (Cr) in ischemic/reperfused rabbit skeletal muscle. A dialysis probe, 10x 0.5mm, was implanted in the tibialis cranialis muscle and perfused continuously with Ringers. Dialysate was collected in 30min fractions before, during 6h total ischemia of one hindleg and after 3h reperfusion. Neither Ad nor X were detected (detection limit 1uM). In and Hx increased during final 4h of ischemia from 9.0uM and 3.0uM to 20.7uM and 6.7uM, resp. During first h reperfusion In increased two-fold (to 47.0uM) and Hx three-fold (to 17.2uM). The increase continued during second h to 67.3uM and 22.3uM,resp. At 3h the values were 80.7uM and 25.7uM. During ischemia Cr increased from 11.2uM to 25.4uM at 1h,fell to 11.9uM at 2h. During reperfusion Cr increased to 20.2uM at 1h and was 39.6uM at 3h.

These preliminary results indicate that reperfusion was associated with a marked increase in the turnover of adenine nucleotides and that microdialysis is a valuable tool in study ofmicrocirculation.

67.12

ISCHEMIA-REPERFUSION EFFECT ON CAPILLARY FLUID DYNAMICS IN AN AUTOPERFUSED RABBIT GROIN SKIN-FLAP ISLAND. T. Nomoto, N.A. Mortillaro and A.E. Taylor. Dept. of Physiology, College of Medicine, Univ. South Alabama, Mobile, AL 36688.

In anesthetized rabbits a groin skin-flap island containing the superficial circumflex iliac artery and vein was established in order to study the effects of ischemia-reperfusion on capillary fluid dynamics. The skin-flap was perfused from a carotid artery while its venous outflow was measured by a drop counter before being returned to the animal via an external jugular vein. The flap was placed on a weighing pan from which changes in weight could be measured and capillary filtration coefficient determined. For each preparation, and in addition to capillary filtration coefficient, arterial perfusion and venous outflow pressures, blood flow, capillary pressure and total vascular resistance were measured or calculated. All measurements or derived values were taken following an increase of venous outflow pressure from 0 to 10 mmhg during the control period, and 10 minutes into reperfusion following 60 and 90 minutes of ischemia. When compared to control values ischemia-reperfusion values demonstrate a significant increase in skin flap blood flow and capillary filtration coefficient while total resistance decreased. These preliminary data suggest reperfusion of the skin following a period of ischemia results in an increase in capillary permeability and/or an increase in microvascular exchange surface area. Supported by NHLBI Grant 41961.

67.13

HYALURONAN (HYA) CONCENTRATION IN FELINE INTESTINAL LYMPH AT INCREASED TRANSVASULAR AND INTERSTITIAL FLUID FLUX. R.K. Reed, M.I. Townsley, M. Morgan Smith, T.C. Laurent, A.E. Taylor. Dept. Physiol., Univ. South Alabama, Mobile, Al 36688; Dept. Physiol., Univ. Bergen, Norway; Dept. Med. and Physiol. Chem., Univ. Uppsala, Sweden.

HYA is an important structural component of the interstitium in connective tissue and is drained by the lymphatics to be metabolized in local lymph nodes and liver. Skin contains about 0.5 mg/g and HYA in prenodal lymph is 5 to 10 μg/ml. HYA concentration in intestinal lymph is 5 to 10 times higher than in skin despite 10 times lower tissue content. The physiological properties of HYA in skin and intestine therefore seem to be different and the present study was performed to investigate the properties of HYA in intestine. A postnodal lymphatic was cannulated in six autoperfused ileal segments in pentobarbital anesthetized cats. HYA concentration was analysed in lymph from each segment at normal and several levels of increased venous pressure up to 40 mmHg. Lymph flow in control averaged 89.1 (SD=145) μl/min·100g and increased to 659 (SD=213) ul/min·100g at the highest venous pressures. HYA concentration in control averaged 27.3 (SD=24.5, range 3.8 to 47) μg/ml and increased to a maximum of 40.6 (SD=30.2, range 15 to 64) μg/ml at venous pressure around 10 to 20 mmHg. At higher venous pressures HYA concentration fell and was below 5 μg/ml (average 3.0, SD=1.6) when venous pressure was raised above 25-30 mmHg. We therefore conclude that the small HYA pool in intestine can be easily mobilized and drained by the lymphatics. Supported by NIH grant HL 39045 and a NATO travel grant.

67.14

INCREASED NEGATIVE INTERSTITIAL FLUID PRESSURE GENERATES AIRWAY MUCOSAL EDEMA DURING DEXTRAN-ANAPHYLAXIS IN THE RAT. Mai-Elin Koller* and Rolf K. Reed, Dept. of Anesthesiology and Physiology, University of Bergen, Årstadv. 19, N-5009 Bergen, Norway.

Anaphylactic reactions are characterized by major fluid shifts resulting in circulatory collaps and interstitial edema. Edema in tracheal mucosa is an early and potentially fatal event during anaphylaxis. It has recently been shown that cutaneous burn injuries are accompanied by a rapid fall in interstitial fluid pressure (P_{if}) as low as -100 to -200 mmHg (Lund et al., Am. J. Physiol. 256: H940-H948, 1989). This fall in P_{if} seems to be the main mechanism behind the rapid postburn edema formation. The aim of this study was to see if similar mechanisms could contribute to the rapid edema developing in tracheal mucosa during anaphylaxis. P_{if} was measured by servocontrolled counterpressure system. Interstitial fluid volume (IFV) was measured as the extracellular and extravascular distribution volume for ^{51}Cr-EDTA after nephrectomy. Anaphylaxis was induced by giving 1ml of 6% Dextran in 0.9% saline i.v. over 20 seconds. This caused IFV in trachea to increase from 0.94 (SD 0.16) to 1.86 (SD 0.30) ml/g dry weight during the next 30 min. P_{if} was measured in seven experimental (receiving dextran as above) and five control rats (receiving 1 ml 0.9% saline i.v.). Two minutes later the rats were given hypertonic KCl to induce circulatory arrest to prevent transcapillary filtration which would otherwise mask the "true negativity" of P_{if}. Trachea was then surgically exposed. Measurements of P_{if} was performed between 10 and 120 min after administration of dextran. P_{if} in rats given dextran was reduced to -7 to -15 mmHg compared to -1 to -2 mmHg in controls. The increased negativity of P_{if} in tracheal mucosa contribute markedly to the rapid development of mucosal edema observed in anaphylaxis.

67.15

PHORBOL 12,13 DIBUTYRATE CONSTRICTS PIGLET PIAL ARTERIOLES AND INCREASES CEREBROSPINAL FLUID PROSTAGLANDIN E_2 LEVELS. David W. Busija and Charles W. Leffler. Department of Physiology and Biophysics, University of Tennessee, Memphis, TN 38163

Phorbol esters such as phorbol 12,13 dibutyrate are synthetic analogues of diacylglycerol that activate protein kinase C. However, effects of protein kinase C activation on cerebral arterioles and on synthesis of prostanoids by cerebral tissues and/or vessels *in vivo* are unknown. We examined effects of topical application of phorbol 12,13 dibutyrate (10^{-8} to 10^{-4} M) on pial arteriolar diameter and perarachnoid cerebrospinal fluid (CSF) prostanoid levels in anesthetized, newborn pigs. Piglets were equipped with closed cranial windows and arterioles measured with intravital microscopy. CSF levels of PGE_2 were determined by radioimmunoassay. Baseline arteriolar diameter was 152 ± 12 μm, and constricted with the phorbol ester to 130 ± 18 μm at 10^{-8} M, 125 ± 13 μm at 10^{-7} M, 109 ± 11 μm at 10^{-6} M*, 120 ± 13 μm at 10^{-5} M*, and 118 ± 16 μm at 10^{-4} M* (n = 6). Baseline PGE_2 level was 2,933 ± 666 pg/ml, and increased with the phorbol ester to 7,249 ± 2,590 pg/ml at 10^{-8}, 11,906 ± 7,118 pg/ml at 10^{-7} M, 15,562 ± 5,851 pg/ml at 10^{-6} M*, 16,070 ± 5,113 pg/ml at 10^{-5} M*, and 19,422 ± 4,944 pg/ml at 10^{-4} M*. Addition of the vehicle, dimethyl sulfoxide, had minimal effects on arteriolar diameter and CSF PGE2 levels. We conclude that activation of protein kinase C with phorbol 12,13 dibutyrate constricts piglet pial arterioles and stimulates PGE_2 production. *p < 0.05, compared to baseline. Supported by NIH HL-30260 and HL-34059.

PULMONARY CIRCULATION AND FLUID BALANCE

68.1

DETERMINATION OF PULMONARY MICROVASCULAR REFLECTION COEFFICIENT IN SHEEP BY VENOUS OCCLUSION. T. Isago*, L.D. Traber*, D.N. Herndon, and D.L. Traber. University of Texas Medical Branch and Shriners Burns Institute, Galveston, TX 77550

The microvascular permeability to protein is a determinate of the effective oncotic pressure and is represented in the Starling equation as the oncotic reflection coefficient (σ). This has previously been determined in the ovine lung lymphatic preparation by elevating the microvascular pressure utilizing a balloon in the left atrium. Inflating a balloon in the left atrium can result in unstable hemodynamic conditions and is frequently associated with arrhythmias. In spite of heparinization, clotting still occurs during the experimental procedures.

In order to evaluate the reflection coefficient of the lung microcirculation of sheep without general heparinization, we devised a technique that permitted elevation of pulmonary pressures in unanesthetized sheep (N=6) by occluding their pulmonary veins. Using this technique we raised pulmonary capillary pressure (Pc) from a baseline of 13.2±2.2 to 35.3±5.1 mm Hg. This caused an increased lung lymph flow (8.8±2.7 to 53.1±13.9 ml/hr). We estimated σ and found it to be 0.82 ± 0.05 (SD). The filtration coefficient (Kf) was 0.019 ± 0.005 (SD) ml / (mm Hg x min). During the period of increased pressure, the animals had stable arterial pressures and cardiac outputs. No animals developed blood coagulation problems.

These data illustrate the usefulness of pulmonary venous occlusion to elevate pulmonary microvascular pressure to obtain plasma to lymph protein concentration ratios independent of flow, allowing for the calculation of σ. Supported by GM33324.

68.2

TNF PRIMES THE ISOLATED LUNG TO FMLP INDUCED EDEMA. Arnold Johnson, Denise C. Hocking* and Thomas J. Ferro. Dept. of VA Medical Center and Albany Medical College. Albany, New York 12208

We investigated the effects of FMLP (300nM) in lungs from TNF treated ($3.2x10^3$ U/kg given i.p. 18 hrs prior to lung isolation) guinea pigs. The lung was perfused with an acellular Ringer's solution containing albumin (0.5GM%) and glucose (5.5mM). Pulmonary capillary pressure (Ppc) and lung weight gain (dW) were measured during baseline and 60 min. FMLP was given after baseline. In separate groups lungs were treated with PAF antagonist WEB-2086 (37μM) before FMLP. The results are ±SEM. *=diff. from baseline; §=diff. from TNF+FMLP.

	Ppc (cmH_2O)		dW (g)
	Baseline	60 min.	60 min.
TNF+FMLP	5.2±0.7	10.9±0.7*	2.3±0.4*
FMLP	5.4±0.2	7.2±0.4*§	0.6±0.1§
TNF	5.8±0.3	8.3±0.7*§	0.4±0.2*§
WEB+TNF+FMLP	5.0±0.1	8.6±1.7*§	0.6±0.5*§

In lungs isolated from TNF treated animals FMLP increases Ppc and lung weight which is attenuated by WEB-2086. TNF sensitizes the lung to FMLP possibly in part via a PAF dependent mechanism. Dept. of Veterans Affairs, AHA, ALA and HL-07194.

68.3

A POROELASTIC MODEL OF THE PERIALVEOLAR INTERSTITIUM OF THE LUNG. J. Sachs, T. Ford, J. Grotberg and M. Glucksberg. Biomedical Engineering Dept., Northwestern Univ., Evanston, IL 60208.

We recently reported a new technique (FASEB J. 4(4):4095, 1990) to characterize the flow-deformation properties of the pulmonary interstitium in the septal junctions of the isolated rat lung. Briefly, one bevelled glass micropipette is used for measuring pressure in the subpleural interstitium by the servo-null technique while a second micropipette is used to inject 10-40nl of 3.5g% albumin solution into the interstitium 10-50μ away from the pressure measuring micropipette. The ensuing pressure transient is recorded as a spike followed by an exponential decay.

We model the subpleural perialveolar interstitium as a linear poroelastic material which behaves according to the constitutive equations:

$$\tau_{ij} = 2G\epsilon_{ij} + \delta_{ij}(\lambda\epsilon_{kk} - P)$$

$$\vec{\nabla} P = -b\vec{V}$$

where τ_{ij} is the stress tensor, ϵ_{ij} is the small strain tensor, G and λ are elastic moduli, P is the fluid pressure, $\vec{V}$ is the velocity of the fluid relative to the solid and b is the Darcy resistivity. We approximate the geometry of the subpleural interstitium as a radially symmetric sheet of finite thickness and infinite extent. The injected bolus establishes a pressure distribution which is a function of position and time. The model predicts the exponential decay observed in the experiment and shows that the time constant represents the product of the resistance (R) and the compliance (C) of the interstitium where $R = b\,l^2/\phi_o$ and $C = 1/2(G + \lambda)$, and ϕ_o is the porosity and l is the length scale of the bolus. Support: MG and TF-Whitaker Foundation, Am. Lung Assn.; JS and JG-NIH Grants HL41126, HL01818.

68.4

PERFUSION HETEROGENEITY IN INJURED LUNGS ESTIMATED USING FLUORESCENT ZINC-CADMIUM SULFIDE (ZCS) AGGREGATES. James C. Parker, Paula J. Coker*, Lucrecia A. Hernandez, and John A. Freeman*. Depts. of Physiology and Biology, Univ. of South Alabama, Mobile, AL 36688

Acute lung injury is characterized by focal damage with heterogeneous regional perfusion and capillary derecruitment. We estimated the amount of unperfused lung tissue in control lungs (C) and after injuries due to oleic acid (OA), high peak pressure (45 cmH2O) ventilation (HV), and detergent lavage with dioctyl sodium sulfosuccinate (OT) in isolated perfused lungs of 0.8-1.3 kg rabbits. At the termination of the experiments the lungs were infused with 0.5g of ZCS in 50 ml normal saline, inflated to 30 cmH2O and air dried. The lungs were then cut into 1 cm thick slices, placed under a transparent grid and UV light. ZCS fluoresces a bright yellow, so the percent of each slice receiving no blood flow was determined by point counting the slice and expressing as a percent of the whole lungs (n=4) as follows:

GROUP	C	OA	OT	HV
X (%)	2	43	30	24
SE	1.5	9.4	7.7	6.8

These data indicate a significant fraction of derecruited capillaries after severe microvascular injury.

68.5

EFFECT OF TRANSPULMONARY PRESSURE ON PERIALVEOLAR INTERSTITIAL RESISTANCE AND COMPLIANCE IN THE ISOLATED RAT LUNG. T. Ford and M. R. Glucksberg. Northwestern University, Biomedical Engineering Department, Evanston, Il 60208.

We have used our recently described technique (FASEB J. 4(4):4095, 1990) to determine the resistance-compliance characteristics of the perialveolar pulmonary interstitium. In 4 excised blood perfused rat lungs held at constant airway pressure, we used micropuncture techniques to characterize the local mechanical properties of the perialveolar interstitium at different transpulmonary pressures (Ptp). We used one micropipette (2μ tip OD) to measure pressure by the servo-null technique in the interstitium at an alveolar junction (Pjct) and a second micropipette (4μ tip OD) to inject a 10-20nl bolus of 3g% Evan's blue albumin solution into the junctional interstitium some 20-50μ away from the pressure-measuring micropipette. Injection of the Evan's blue albumin caused a spike in Pjct followed by an exponential decay asymptoting to a new baseline. Peak pressure and the time constant (K) of decay are shown below (mean ± SD).

Ptp (cmH_2O)	Peak Pjct (cmH_2O)	K (seconds)
5	4.1±0.3	3.1±0.9
10	8.0±1.1	2.0±1.2
15	10.7±1.6	1.6±0.7

Peak Pjct and K were significantly increased and decreased respectively with increased Ptp. We interpret the time constant to be the product of the resistance the compliance of the interstitial matrix. We believe that peak Pjct is a measure of the compliance alone. Our data suggest that compliance decreases with increased Ptp while resistance remains unchanged. (Support: Whitaker Foundation, American Lung Association).

68.6

EFFECT OF EMBOLISM ON PULMONARY VASCULAR PERMEABILITY TO PROTEIN. I.C. Ehrhart, H.J. Ocasio and W.F. Hofman. Medical College of Georgia, Augusta, GA, 30912-3000.

Glass beads, 105 um, were injected into the artery supplying the left lower lung lobe of the dog (n=6). Controls received only the bead vehicle (n=6). The lobe was removed and pump perfused with recirculating autogenous blood (300 ml/min). Lobe weight change and arterial (Pa) and venous (Pv) pressures were continuously recorded. A solvent drag reflection coefficient (σ), a measure of vascular permeability to protein, was obtained from the concentration of plasma proteins relative to red cells during fluid filtration at Pv = 20 Torr. At elevated Pv, embolism increased Pa from 22.5±0.8 to 53.5±10.2 and increased double occlusion pressure from 21.2±0.8 to 27.0±1.4 Torr, P<0.05. Embolism decreased σ from 0.86±0.07 to 0.53±0.03, P<0.05. Since σ is not decreased during elevated vascular pressure (FASEB J. 3:A566, 1989), the embolism induced increase in vascular permeability is likely independent of vascular pressure elevation. (Supported by the American Lung Association of Georgia.)

68.7

INTERDEPENDENCE OF EXTRAALVEOLAR ARTERIES AND PARENCHYMA IN NEWBORN PIGLET LUNGS. Anthony L. Mansell and Allison L. McAteer. Brown University, Providence, R.I. 02902

As piglet lungs grow and mature postnatally, the volume density of amorphous elements decreases in the interstitium, while the volume density of elastin and other formed elements increases. Such a change in composition of the interstitium surrounding extraalveolar blood vessels might cause differences in the behavior of the vessels as newborn and mature lungs are compared at various degrees of inflation. To test this hypothesis, we filled extraalveolar pulmonary arteries of excised lobes with a radioopaque silicone rubber compound (Microfil) and measured radiographic dimensions of the vessels. Transpulmonary pressure (P_L) and vascular pressure relative to pleural pressure (Pv-Ppl) were controlled independently. Results from 80-90 day old piglets (n=3) agreed with published results from mature lungs: at any given Pv-Ppl between 0 and 25 cm H_2O, diameters of the pulmonary arteries were larger at P_L=25 than at P_L=5 cm H_2O and axial dimensions of the arteries changed in proportion to the cube root of lung volume. Results from 3 day old piglets (n=4) were unique: at any given Pv-Ppl, arterial diameters were smaller at P_L=25 than at P_L=5 cm H_2O and axial dimensions of the arteries did not change significantly with lung volume. Thus, mechanical coupling between extraalveolar arteries and the surrounding interstitium appears to cause compression rather than distention of the vessels as newborn piglet lungs are inflated.

68.8

ANALYSIS OF ARTERIAL AND VENOUS OCCLUSION: INSTANT OF OCCLUSION?. T.S. Hakim, G.F. Nieman and A.M. Paskanik*. Dept.of Surgery, SUNY Health Science Center, Syracuse,NY 13210.

Criteria for analysis of the arterial (AO) and venous (VO) occlusions are not well defined. Conceptually flow can be stopped for a "short period" of time (Δt) across one segment of the vasculature without changing the flow across the other segments. This study was designed to find out if "Δt" is discernable following AO and VO. To accomplish this the left lower lobe of dog lungs were perfused(~500ml/min)in situ from an arterial reservoir and drained passively into another reservoir. The arterial (Pa) and venous (Pv) pressures, as well as the blood flow rate into (Qa) and out (Qv) of the lobe were monitored, digitized at 200HZ,and computer stored. AO and VO were accomplished using a clamp with a microswitch on it to provide a zero reference time (t=o). The pressure data between 0.2 to 1.5 sec post-occlusion were fitted to an exponential ($P_t=P_o*e^{st}$)and extrapolated to t-o. The results show that during baseline when Qa is abruptly stopped,Qv remains constant for 162±23msec (=Δt). Likewise when Qv is abruptly stopped,Qa remains constant for 129±19msec (=Δt). The pressures on the exponential at t=o and t=Δt (conceptually both are valid) were different by up to 2 mmHg. Thus the arterial and venous pressure gradients can be miscalculated by poor selection of instant of the occlusion.

68.9

FREQUENCY OF DISRUPTIONS IN THE PULMONARY BLOOD-GAS BARRIER AT HIGH VASCULAR PRESSURE. R. Prediletto, A. Elliott, O. Mathieu-Costello and J.B. West. Dept. of Medicine, UCSD, La Jolla, CA 92093.

We reported that increased transpulmonary capillary pressure causes disruptions of the pulmonary capillary endothelium and alveolar epithelium, and interstitial pulmonary edema (FASEB J. 4:A969, 1990). In this study, we further investigated the extent of structural damage of the blood-gas barrier at high vascular pressure. We used the same material as in our previous study, i.e. lungs of rabbits perfused with their own blood at capillary transmural pressures of 12.5, 52.5 and 72.5±2.5 cm H_2O and processed for electron microscopy. Using image analysis, we quantified the number of disruptions per mm boundary length of endothelium and epithelium, as well as the thickness of endothelial, epithelial and interstitial layers in the blood-gas barrier. One sampling site, taken randomly in one stratum (perpendicular to the cranial-caudal axis, about 1/3 the distance from the bottom of either side lower lobe) was analyzed in 2 animals at each pressure (total, 23-44 micrographs/animal). We found no evidence of endothelial nor epithelial discontinuity at 12.5 cm H_2O pressure (total 1,595 μm endothelium and 1,280 μm epithelium boundary length examined in 2 animals). We found up to 10.8±4.1 (endothelium) and 10.2±3.4 (epithelium) breaks/mm at 52.5 cm H_2O pressure, and 39.8±8.9 (endothelium) and 6.7±3.6(epithelium) at 72.5 cm H_2O. However, there was substantial variability between animals. The thickness of the blood-gas barrier increased with the increased vascular pressure, mainly as a result of increased interstitial space (interstitial edema). Our results, which are preliminary, indicated 1)large variability in the extent of disruptions within samples, suggesting a possible clustering of structural damage, e.g. in capillaries situated near their supplying arteriole, 2) large variability in the blood-gas barrier vulnerability to increased pressure in different animals at the chosen sampling site, and 3) clear evidence of interstitial edema at 52.5 and 72.5 cm H_2O pressures. It remains to be determined whether or not the large variation found at 52.5 cm H_2O pressure and above is related to intra-lung heterogeneity,i.e. focal responses of the lung, or inter-animal variability. Supported by NIH Program Project HL17731-16.

68.10

SPACEFLIGHT AND TAIL-SUSPENSION AFFECTS LUNG ULTRASTRUCTURE IN RATS. A.R. Elliott, O. Mathieu-Costello, and J.B. West. Dept of Med. Univ. of Calif. San Diego, La Jolla, CA 92093.

There have been no previous studies on the effect of microgravity exposure during spaceflight on lung tissue. We examined the ultrastructure of the left lungs of 5 Czechoslovakian Wistar male rats flown on the 13 day, 19+ hr. Cosmos 2044 mission and compared them to controls (5 male vivarian control rats at 1G conditons and 5 male rats exposed to 14 days of tail-suspension). When the flight animals were inspected immediately post-landing the rats were active and in good condition. The flight animals were sacrificed 5 hrs post-landing near the recovery site. All tissues were removed and immersed in 3% glutaraldehyde in 0.1M phosphate buffer (pH= 7.4). Samples from both dorsal and ventral portions of the lung in a slab taken perpendicular to the cranio-caudal axis, approximately 2mm below the hilum, were processed for both light and electron microscopy. No significant perivascular or peribronchial cuffing was present in the samples. In all five flight and five tail-suspended rats, edema and red blood cells (RBC) were present in the alveolar spaces. The frequency of alveolar edema and RBC flooding was larger in the dorsal than in ventral (gravity dependent) regions of the lung in all animals. In two of the vivarian control animals, some alveolar edema and RBCs were found in the dorsal samples only. In conclusion, pulmonary hemorrhage, of unknown origin and alveolar edema occurred to a greater extent 1) in both flight and tail-suspended animals, and 2) in the dorsal regions of the lung. The cause of these changes in both groups of animals requires further investigation. Supported by NASA grant NAG-2-616. We gratefully acknowledge Dr. A.S. Kaplansky and the Soviet dissection team at the Institute for Biomedical Problems, Moscow, USSR.

68.11

REGIONAL PULMONARY PERFUSION FOLLOWING WOOD SMOKE INHALATION (SI). G.F. Nieman, T.S. Hakim, A.M. Paskanik*, W.R. Clark*, and C.E. Bredenberg. Dept. of Surgery, SUNY Health Science Center, Syracuse, N.Y. 13210

Previously we have shown that SI increases alveolar surface tension (ST) and blood flow (Q) to lung regions damaged by smoke. This study compares the effects of SI and high ST on regional pulmonary Q. Mongrel dogs were anesthetized and intubated with a split endotracheal tube separating ventilation to each lung. A flow probe was placed on the left main pulmonary artery and cardiac output (CO) was measured by thermo-dilution. In Group I (n=8), one lung was subjected to 5min of SI and in Group II (n=4), ST was increased in one lung by aerosolizing diocytl sodium sulfosuccinate (OT) detergent. The contralateral lung in both groups served as a control. The Q in the injured and control lungs were measured at 5,30,60, and 120 min after injury. The Q in the injured lung as % of CO is shown in the Table:

	BL	5	30	60	120 min
SML	51±8	52±10	55±8	59±7	63±5*
OTL	50±13	53±15	56±13	54±15	52±14

*=p<0.05 vs Baseline (BL); SML=Smoke Lung; OTL=OT Lung

These data suggest that there is an increase in blood flow in the smoke injured lung independent of changes in surface tension.

68.12

TUMOR NECROSIS FACTOR-ALPHA (TNFα) INCREASES PULMONARY VASCULAR REACTIVITY IN RATS. T. Stevens, D.A. Diesel, P.L. Janssen and A. Tucker. Colorado State University, Fort Collins, CO 80523.

Female VAF Sprague-Dawley rats, weighing 175-225 g, were used to determine if acute or long-term administration of TNFα (recombinant human) alters pulmonary vascular reactivity. Rats treated acutely received either saline (CON, n=6) or TNFα (40 μg/kg in saline) (Acute-TNF, n=9) through a catheter in the left jugular vein. 20 min after treatment, the lungs were isolated, perfused with Earles salt solution (+ 4 g% Ficoll), and tested for vascular reactivity with acute hypoxia (3% O_2) and angiotensin II (AII; 0.025-0.40 μg). Rats treated chronically received i.p. injections of either saline (CON, n=8) or TNFα (250 μg/kg in saline) 2 times per day for 7 days (Chronic-TNF, n=8). Lungs of Chronic-TNF rats were isolated and evaluated (as described above) on Day 8. Chronic-TNF rats had lower body weights and hematocrits than CON rats. Vascular responses to hypoxia and AII were not different between the two CON groups, so their data were combined. Pulmonary pressor responses to hypoxia were greater ($P<0.05$) in both of the TNF groups (8.2±0.7 and 8.1±1.4) compared to CON (5.2±0.9). AII responses were increased ($P<0.05$) in Chronic-TNF rats compared to the other rats (e.g. with 0.20 μg AII: Chronic-TNF, 15.9±2.7; Acute-TNF, 11.8±1.4; CON, 7.5±0.7). Long-term treatment with TNFα enhanced pulmonary vascular reactivity (both hypoxic and AII responses), whereas acute TNFα treatment increased hypoxic, and slightly increased AII, responsiveness. Results suggest that pulmonary vascular reactivity may be increased during inflammatory responses when TNFα is released.

68.13

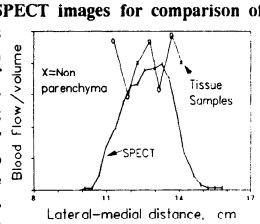
EFFECT OF HYPOXIA AND OTHER CONTRACTILE AGENTS ON SMOOTH MUSCLE CELLS ISOLATED FROM PULMONARY AND CEREBRAL ARTERIES. Maithili Subramanian and Jane A. Madden, Zablocki V.A. Medical Center and The Medical College of Wisconsin, Milwaukee, WI 53295.

Pulmonary arteries contract when exposed to hypoxia both *in vivo* and *in vitro* and the magnitude of the response is dependent upon artery size. In contrast, cerebral arteries do not exhibit such a response to hypoxia. Whether the response to hypoxia is a function of the arterial smooth muscle cells (SMC) alone has not been determined. Pulmonary arteries of <200μm, 200-400μm, 400-600μm, and >800μm , and the anterior and middle cerebral arteries were isolated from cat lung and brain, respectively. The SMC from these arteries were dispersed by collagenase enzyme. Cells were plated on polylysine coated coverslips and incubated at 95%O_2/5% CO_2. Cells were used for studies within 72 hours of plating. The contractile responses of SMC were measured by video microscopy. SMC varied in the response to hypoxia depending upon the source and the size of the artery. SMC from 200-400μm diameter pulmonary arteries contracted by 25% to hypoxia ($P< 0.001$). Cells obtained from >800μm arteries showed only a minimal contractile response to hypoxia, about 0.5-1%. Cells from the <200μm arteries contracted by 12% and those from the 400-600μm, 20% ($P<0.05$ and 0.01, respectively). In contrast, cells from the cerebral arteries did not contract upon exposure to hypoxia. Pulmonary and cerebral artery SMC were also exposed to serotonin (5-HT), norepinephrine (NE), indomethacin (IND) histamine (HIST) and prostaglandin F2α (PGF2α) in order to assess their ability to contract to these known contractile agonists. Cells from 200-400μm pulmonary arteries responded significantly to 5-HT, NE, IND, HIST and PGF2α ($p<0.01$ for all). Cerebral artery SMC showed significant contractions to 5-HT, NE and IND ($p<0.01$)but not to HIST or PGF2α. Results of these studies indicate that SMC isolated from pulmonary and cerebral arteries respond to known contractile agents and the contraction to hypoxia seen in pulmonary artery SMC depends upon the size of the arteries from which the cells were isolated.

68.14

REGIONAL PULMONARY BLOOD FLOW IN DOGS USING HIGH RESOLUTION SPECT. **K.C. Beck, M.K. O'Connor,* M.A. Schroeder.* Mayo Clinic & Foundation, Rochester, MN 55905**

We injected 15μ diameter microspheres labelled with Co-57 into the vena cava of prone anesthetized dogs. The lungs were removed and air-dried; the distribution of radioactivity was obtained by single photon emission computed tomography (SPECT, 128 x 128 matrix, 128 views at 15-20 min/view). The lungs were sliced (5 mm), and small (4 mm D) tissue samples were removed in rows along the lateral to medial aspect of slices. Samples were inspected for presence of non-parenchymal structures. Using anatomical landmarks and external ink markers, the locations of the physical slices were identified in the SPECT images for comparison of profiles of radioactivity across slices (figure). Ratios of radioactivity from central to extreme peripheral samples of pure parenchyma were not significantly different from 1.00 (0.98 ± 0.13, N=5 animals). This contrasts with SPECT profiles which exhibited central to peripheral gradients in profiles that were less than about 5 cm across (figure). Direct tissue sampling does not confirm central to peripheral blood flow gradients, although such gradients are often evident in SPECT images of narrow lung cross-sections. Supported by HL-30937.



68.15

THE ROLE OF CATECHOLAMINES DURING ACUTE HYPOXIA. Robert J. Porcelli and Philip Devine* Veterans Affairs Medical Center, Northport, New York 11768.

This study examined plasma norepinephrine (NE) and epinephrine(E) levels during acute hypoxia and if systemic hypoxia releases NE from the lung. We collected temporally identical samples of pulmonary arterial blood and measured serum NE and E by HPLC in two groups of seven animals: Sham operated controls and animals exposed to systemic hypoxia ($FIO2=0.08$). We also measured NE in venous effluent from Ringers perfused lobes in animals that were systemically hypoxic but lobar normoxic. NE input was zero in the perfusate and outflow levels reflected lobar nervous activity. Since NE and E levels vary widely between animals, levels are expressed as ratios of experimental to control (x/c):

	SHAM	HYPOXIA	LOBE
NEx/NEc	1.4 ± 0.2	1.6 ± 0.2	0.38 ± 0.15@
Ex/Ec	1.6 ± 0.4	1.5 ± 0.5	(@ = p<0.05)

These data indicate that hypoxia has no effect on plasma catecholamines. Since systemic hypoxia inhibits release of lobar NE, such release does not mediate hypoxic vasomotion. Such sympathetic down regulation may be one way hypoxia modulates vascular function. Support: Department of Veterans Affairs.

68.16

METHYLENE BLUE POTENTIATES NITROGLYCERIN-INDUCED VASODILATION IN THE DOG LUNG. W.F. Hofman, H.A. El-Kashef* and I.C. Ehrhart. Dept. of Physiology and Endocrinology, Medical College of Georgia, Augusta, GA. 30912.

Nitroglycerin (NG) is hypothesized to induce vasodilation via activation of guanylate cyclase (GC). We examined the effect of methylene blue (MB), a putitive inhibitor of GC activation, on nitroglycerin-induced vasodilation in the isolated dog lung lobe (n=6). Intraarterial bolus doses of 100, 200 and 500 ug NG were administered at basal tone (pulmonary arterial pressure, Pa=14.8±0.7 cmH_2O) before and after cyclooxygenase inhibition (COI) with 45 uM meclofenamate (Pa=16.0±0.9 cmH_2O). Vascular tone was then increased by infusion of either the thromboxane A_2 analogue, U46619 (0.5 ug /min; Pa =34.1±0.7 cmH_2O) or by adding 30 mg MB followed by a 0.5 mg /min infusion (Pa=34.6±1.2 cmH_2O). Vasodilation to NG at basal tone or after COI was negligible. When tone was raised by U46619, NG elicited a marked, dose related decrease in lobar vascular resistance (LVR) of 6.6±0.8, 10.4 ±0.6 and 14.2±0.5 cmH_2O/L/min, respectively. After MB, NG produced a greater decrease in LVR ($P<0.05$) than that during U46619 infusion. Our data indicates that MB does not inhibit NG-induced vasodilation in the isolated dog lung. We conclude that MB is either an ineffective inhibitor of GC activation or NG-induced vascular relaxation occurs via a mechanism other than GC activation in dog lung. (Supported by HL-40488)

68.17

THE ROLE OF FREE RADICALS DURING REPERFUSION INJURY IN ISOLATED RAT LUNGS. Deborah G. Ho*, R. Lance Johansen*, Shrikant Mishra* and Hara P. Misra*. (SPON: James C. Keith, Jr.) Virginia-Maryland Regional College of Veterinary Medicine, Department of Biomedical Sciences, Virginia Tech, Blacksburg, VA 24061

Recent evidence has shown that upon reperfusion, tissue damage occurs. During reperfusion, there is a series of single electron transfers that generate highly reactive free radical intermediates. Tissue damage caused by reperfusion may be mediated to a large degree by the production of these free radicals. The effects of the following compounds on reperfusion injury in isolated rat lungs were studied: 1) a spin trapping agent, N-t-butyl-α-phenylnitrone (PBN), 2) an iron chelator, deferoxamine mesylate and 3) two of the reactive oxygen scavengers, superoxide dismutase (SOD) and catalase (CAT). Lungs were subjected to a 90 minute period of ischemia followed by a 20 minute period of reperfusion. Control lungs were perfused with a Krebs-Henseleit solution containing 4% bovine serum albumin (KH-BSA). Experimental lungs were perfused with the KH-BSA solution plus one of the aforementioned compounds. Negative control lungs were perfused with KH-BSA without an ischemic period. The lung wet to dry weight ratios, an index of edema, were compared. There was a significant difference ($p< 0.01$) in wet to dry weight ratios between non-ischemic and post-ischemic lungs. PBN at 10 mM caused some protection against reperfusion injury. SOD-CAT, however, did not seem to affect reperfusion injury. The effect of deferoxamine mesylate was inconclusive. A PBN-hydroxyl radical was detected in post-ischemic reperfused lungs using EPR spectroscopy and spin trapping techniques. The apparent protective effects of PBN on reperfusion injury and the identification of a spin adduct supports the evidence that tissue damage caused by reperfusion may be mediated by free radicals in the lungs. (Supported in part by NIH HL-42009 and Sigma Xi).

MEMBRANE TRANSPORT

69.1

Neutral Amino Acid Transport in Vascular Endothelial Cells: Effect of Serum. N. Escobales and M. M. Rivera-Correa*. Department of Physiology, Univ. of Puerto Rico School of Medicine, San Juan, P.R., 00963

Amino acid transport in bovine aortic endothelial cells (BAEC) was investigated under basal conditions, in serum-deprived cells (SD) and in SD+Serum cells (SD+S). In addition, the effect of forskolin (50μM), theophyline (1mM) and phenylephrine (10μM) was evaluated. BAEC were found to transport neutral amino acid (0.15mM) by systems similar to the A, ASC, N and L systems which have been characterized in other cell preparations. System A was identified by the initial rate of the Na^+-dependent α(methylamino)-isobutyric acid (mAIB) uptake and the Na^+-dependent alanine uptake was taken to represent system ASC. Similarly, the Na^+-dependent glutamine entry was taken as an index of system N activity. The activity of system L was defined by the entry of leucine in a Na^+-free media. Competition experiments indicated that in BAEC substantial overlapping in substrate transport exists among Na^+-independent and Na^+-dependent transport pathways. Thus, glutamine transport occured both through System N and L. However, glutamine transport through System L ocurred with an activity 54% larger that that of system N. Furthermore, the transport of alanine through System A was largely inhibited by the presence of 5mM glutamine, leucine and mAIB in the incubation media.

SD marginally reduced amino acid transport through these systems when compared to control cells. However, in SD+S cells a significant and strong activation of system ASC, N and A was observed. System L, however, was not affected by serum. Intracellular Ca^{++} and/or cAMP appear to be involved in the activation of amino acid transport by serum since phenylephrine, which is known to affect the levels of these second messengers, markedly abolished its stimulatory effect. In addition, agents such as forskolin and theophylline, significantly stimulate systems A and ASC by about 21% under basal conditions. These findings suggest that activation of amino acid transport in vascular endothelial cells, possibly via changes in $[Ca^{++}]_i$ and/or cAMP, is necessary for the induction of cell growth and proliferation by serum. This work was supported by UPHS-NIH grant #RR-08224-04.

69.2

HETEROGENEITY OF OUABAIN-INSENSITIVE K-ATPASE ALONG THE INNER MEDULLARY COLLECTING DUCT (IMCD). Lal C. Garg and Neelam Narang*. Univ. of Florida College of Medicine, Gainesville, FL 32610

Recently we reported the presence of a ouabain-insensitive K-ATPase in the cortical and outer medullary collecting duct segments of the rabbit. The enzyme is inhibited by omeprazole and SCH 28080 (inhibitors of gastric H-K-ATPase but not by ouabain (an inhibitor Na-K-ATPase). To determine if this K-ATPase is also present in the IMCD which is an heterogenous segment, we measured the enzyme activity in the IMCD segments microdissected from different positions along the axis of the inner medulla of the rabbit kidney. ATPase activity was measured by a fluorometric microassay in which ATP hydrolysis is coupled to the oxidation of NADH. Ouabain-insensitive K-ATPase is the difference in ATPase activity in the presence and absence of KCl but in the presence of ouabain and is expressed as $pmol \cdot min^{-1} \cdot mm^{-1}$.

$IMCD_1$ (initial 1/3rd)	$IMCD_2$ (middle 1/3rd)	$IMCD_3$ (terminal 1/3rd)
9.2 ± 1.4	14.5 ± 2.7*	7.9 ± 2.5

Values are mean ± SEM of 5 rabbits. * $P< 0.05$ vs $IMCD_1$ and $IMCD_3$.

K-ATPase activity in the $IMCD_1$ and in $IMCD_3$ was similar to that of the OMCD reported previously. On the other hand, K-ATPase activity was higher in $IMCD_2$ than in the OMCD or in the other IMCD subsegments. K-ATPase activity in all 3 subsegments was completely inhibited by SCH 28080. It is concluded that: a) all IMCD subsegments have measurable K-ATPase activity that could potentially drive the active K transport in these segments; and b) there is an axial heterogeneity in the the rabbit IMCD with respect to K-ATPase activity.

69.3

MECHANISM OF RELEASE OF PRODUCT FROM MUCUS GRANULES. Ingrith Deyrup-Olsen and Arthur W. Martin. Univ. of Washington, Seattle, WA 98195.

An important step in the formation of mucus, an epithelial cell product serving crucial protective functions, is the release of mucins and other substances from the granules in which they are stored. It has been suggested that mucus secretion occurs by exocytosis, but countering this hypothesis are cases of giant mucus granules formed by hagfish (Cyclostomata) and land slugs (Pulmonata, Mollusca). In hagfish the granules are released intact by aposecretion, and break down on contact with sea water (Downing, S.W., et al. 1981 Science 212: 326-328). Our experiments with Eptatretus stouti show that this results from inrush of water and ions through granule membranes that are freely permeable to cations and to anions smaller than sulfate. In the land slug Arioliimax columbianus mucus granules are also released intact. They are invested with two membranes, the inner presumably derived from Golgi membranes, and the outer from the cell membrane. Their lysis is triggered specifically by adenosine triphosphate (10^{-6}M and below). Since this lytic process is blocked by nigericin and cyclooxygenase inhibitors (indomethacin, salicylate) we infer that its mechanism involves proton/potassium exchange through a cyclooxygenase derived product of arachidonic acid.

69.4

RYANODINE BINDS TO INTERNAL MEMBRANE RECEPTORS AND INHIBITS CALCIUM TRANSPORT IN RAT VAS DEFERENS SMOOTH MUSCLE. Zhen-Du Zhang,* Chiu-Yin Kwan* and E.E. Daniel. Dept. Biomed. Sci. McMaster Univ. Hamilton, Ont. Canada.

Our recent study indicated that ryanodine (RYA) inhibited agonist-induced contractile response of rat vas deferens (RVD) in Ca-free medium (Bourreau et al, FASEB, 1990). We tested whether specific binding sites were present in endoplasmic reticulum (ER) of RVD and whether RYA inhibites Ca transport by ER. We employed the subcellular membrane fraction technique. Radioligand binding study using ^{3}H-RYA showed that RYA was capable of binding to RVD membranes with a high affinity (K_d=6 nM) in a saturable manner. Dissociation of ^{3}H-RYA occurred on dilution but not on addition of cold RYA. The RYA receptors were localized in the ER based on the marker enzyme distribution in various subcellular membrane fractions. RYA (10 uM) inhibited the ATP-dependent Ca-transport in crude microsomal fraction known to contain ER vesicles in a time dependent manner. No inhibtion was observed during the first 5 minites of Ca-transport and a gradual decline of Ca-accumulation followed reaching 25% inhibition at 20 min. Our results are consistent with the view that RYA interacts with internal membranes and depletes Ca from the intracellular store in RVD. Such an action may account for the functional effects of RYA on the contractile response of RVD in Ca-free medium.(Supported by the Heart and Stroke Foundation of Ontario)

69.5

ENDOGENOUS AMILORIDE-SENSITIVE SODIUM UPTAKE BY XENOPUS OOCYTES. David W. Towle and Adrienne Baksinski*. Lake Forest College, Lake Forest, IL 60045.

To determine the existence of endogenous amiloride-inhibitable sodium transport systems in Xenopus oocytes, stage IV and V oocytes were defolliculated with mild collagenase treatment followed by manual removal of the loosened follicle. Incubation of 4-6 oocytes in 0.1 ml of a modified Barth's medium containing 100 mM choline chloride and 4 mM ^{22}NaCl yielded a linear uptake of isotope during the 90-minute incubation. The addition of 5 x 10^{-4} M amiloride to the incubation medium inhibited uptake by 55%, while 1 x 10^{-5} M amiloride had no effect. The presence of an amiloride-sensitive Na^+/H^+ antiporter, rather than a Na^+ channel, is therefore indicated.

Supported by National Science Foundation (DCB-8996137 and REU Supplement).

69.6

SPECIFIC ^{125}I-BH-NPY BINDING TO INTACT CULTURED BOVINE ADRENAL MEDULLA CAPILLARY ENDOTHELIAL CELLS. P. Sanabria and W. I. Silva*. Departments of Physiology and Pharmacology, Universidad Central del Caribe, School of Medicine, Cayey, P.R., 00634

A modulatory role in adrenal medulla secretion has been suggested for neuropeptide Y ((NPY) which is co-stored and co-released with norepinephrine in cultured chromaffin cells. In this study high affinity binding sites for NPY were detected on cultured capillary endothelial cells derived from bovine adrenal medulla. Equilibrium binding assays were conducted on intact cells with ^{125}-I Bolton-Hunter labeled NPY (^{125}I-BH-NPY) using 1 μM of unlabeled synthetic porcine NPY to define specific binding. Scatchard analysis of the binding data indicated the existence of high affinity binding sites with a Kd (±SE) value of 13.03 (± 3.24) nM and a B_{max} of 334 (± 57.56) fmol/10^6cells. Competition experiments were performed with cold NPY and two other members of the PP-fold peptide family, peptide YY (PYY) and avian pancreatic polypeptide (APP). NPY and PYY displayed IC_{50} (± SE) values of 8.40 (± 0.08) nM and 7.54 (± 0.21) nM, respectively. APP was unable to compete with ^{125}I-BH-NPY in the concentration range of 0.001-1μM. The present study suggests the possibility of endothelial cell involvement in mediating NPY's post-junctional actions at the adrenal medulla.

TEMPERATURE REGULATION

70.1

THERMAL BALANCE IN YOUNG RHESUS MONKEYS AT MODERATE TEMPERATURES AND LOW VAPOR PRESSURE. S. H. Constable and C. J. Sherry*. USAF School of Aerospace Medicine & *Systems Research Laboratories, Brooks AFB, TX 78235

Thermal balance profiles were conducted on six restrained, female Macca mulatta monkeys (wt = 3.98 ±0.55 kg) at 3 environmental temperatures (T_{db} = 25, 30 & 35 °C) and constant vapor pressures of ~5 Torr. Core temperature (T_{re}), mean weighted skin temperature ($\overline{T}_{sk}$), respiratory water loss (E_{resp}), metabolic rate (M) and heart rate (HR) were recorded after physiological equilibration at each T_{db}. No significant differences were observed in T_{re} (38.6, 38.6, 38.7 °C), HR (173,171, 171 bpm) or E_{resp} (3.5, 4.0, 4.4 W/m^2) between any of the three environmental conditions, respectively. Mean responses at 25, 30 & 35 °C T_{db} for the following variables were: $\overline{T}_{sk}$ (34.9±0.5, 36.0±0.9, 38.7±0.2°C); M (62.1±9.5, 54.3±9.4, 44.5±3.3 W/m^2); K (17.5±3.8, 16.6±3.1, 23.8±3.2 W/[m^2·°C]), respectively. Significant differences could be observed between selected ambient temperatures in these variables. Total evaporative heat loss (E_{tot}), as determined by gross estimates of weight loss was inconsistent, possibly due to measurement error. Comparisons of these variables in a repeated set of experiments conducted at 30 °C T_{db} indicated that the reliability of those measures was quite good. Previous, complete thermal balance studies in male rhesus monkeys at moderate absolute humidities have established a thermal neutral zone (TNZ) of between ~ 25 & 30 °C T_{db}. The present, limited studies suggest that the TNZ may be higher for juvenile females in dry, moderate environments.

70.2

LOCAL SWEATING RESPONSES OF UNACCLIMATED MEN BEFORE AND AFTER A TWO MINIMAL ERYTHEMAL DOSE (MED) OF ULTRA-VIOLET RADIATION EXPOSURE. **R.R. Gonzalez, K.B. Pandolf, W.A. Latzka*, K.K. Kraning, R.W. Gange*, and I.H.Blank. US Army Rsch Inst Envir Med, Natick, MA 01760, Wellman Lab of Photomedicine/ Massachusetts General Hospital, Harvard Medical Sch, Boston, MA 02118.**

Sunburn is an inflammatory reaction to UVL photons (UV-B, 280-320 nm) absorbed within the skin that results in damage to skin cells. To date, the thermoregulatory implications of such exposure are little understood. Responses were investigated during 50-min cycle ergometer exercise (≈53 % $\dot{V}O_2$max) in the heat (T_a=49°C; 20 %rh; 1 m/s wind) in 10 unacclimated, male subjects before (CONB) and 24-h after 2 MEDs of UV-B radiation (SUNB) covering ≈85% of the body surface area. In 7 subjects, esophageal temperature (T_{es}, °C) was recorded; in all 10 subjects, 4-site skin temperatures, back, left forearm, and shielded (12 cm^2 area) right forearm sweating rates [$\dot{m}_{sw}$, mg/(min·cm^2)] were recorded at 15s intervals; venous blood was collected before and after exercise. Pre-and post- exercise values of hematocrit, hemoglobin, plasma protein, % Δ in plasma volume (Δ of -6.4±2.8SD, CONB vs Δ-6.5±3.3SD, SUNB), and plasma osmolality (mO$_s$/kg: 289.7±4.0 SD, CONB vs 289.5±4.8SD, SUNB) were not affected (P >0.05) by SUNB. Analysis of CONB and SUNB data showed that: the T_{es}-intercept for sweating (37.06°C vs 37.03°C, P>0.05) was unaffected but the $\dot{m}_{sw}$:T_{es} and final $\dot{m}_{sw}$ from the left forearm ($\dot{m}_{sw}$:T_{es}, 0.24 ±0.04 vs 0.17 ±0.01, P<0.003) were significantly reduced. Variable subject pigmentation on the back sites resulted in mixed $\dot{m}_{sw}$:T_{es} responsiveness (0.43±0.08 vs 0.36±0.02, P<0.052). Since the protected right forearm $\dot{m}_{sw}$ was not impeded by SUNB, decrements in sudomotor drive and level of hydration were not factors in the response. The data suggest that following SUNB there is an effect, locally mediated, on both the responsiveness and capacity of the sweat gland.

70.3

THERMOREGULATORY AND RESPIRATORY RESPONSES OF BROWN BULLHEAD CATFISH TO CADMIUM ION STRESS. Brenda P. Moffitt, Norma Rae*, and Michael Rizzi*. Lehman College of CUNY, Bronx, NY 10468.

As cadmium ions have been shown to increase ventilation rates of several species of fish, and as elevation of ambient temperature has similar effects, these studies were conducted (a) to see if cadmium ion exposure affected the final thermal preferendum (T_{pref}) of these fish, and (b) to observe its effects on ventilation rate (f_v). Brown bullhead catfish (Ictalurus nebulosus) were obtained commercially and acclimated to 22.0±1.0 C for several weeks. Food was witheld for three days proir to experimentation. The T_{pref} of some fish was determined before and after exposure for 24 h to Cd^{++} at four different concentrations. Fish were tested individually and used only once. The f_v of other fish, habituated to confinement in small baths maintained at 22.0 ± 1.0 C, was determined before and either immediately or 24h after exposure to Cd^{++}. T_{pref} was increased from 29.5±0.95 C by a maximum of 4.0±1.98 C. The response was not dose-dependent. F_v was significantly decreased in a dose-dependent fashion in both experimental scenarios after exposure to Cd^{++}. The results suggest that the higher T_{pref} of the Cd^{++}- exposed fish may compensate for the ion's depressant effects on ventilation.

(Supported by NIH grant # T34 GM08182-05)

70.4

ADRENERGIC MODULATION OF THE LHRH INDUCED FLUSH RESPONSE IN RATS. Michael J. Katovich and James W. Simpkins, Dept. Pharmacodynamics, University of Florida, Gainesville, FL 32610

There are numerous reports of a temporary relationship between LH secretion and a subsequent flushing response in menopausal women. We have developed a morphine-dependent animal model to study the mechanisms of the hot flush. We have recently reported (Brain Res 494:85, 1989) that central administration of an LHRH agonist produces a marked rise in tail skin temperature (TST) i.e., produces a flush response. We concluded that the temperature response is mediated by a central mechanism and involves a LHRH neuronal network. The purpose of this study was to evaluate the effects of α-adrenergic agents on the TST response to LHRH since these agents have previously been shown to be effective in attenuating the TST response to naloxone in our animal model (Brain Res 426:55, 1987). Ovariectomized rats were administered phentolamine (50 ug/5 ul, icv) thirty minutes prior to administration of an LHRH agonist. The 5°C rise in TST was abolished in the phentolamine treated group. A similar study was performed utilizing clonidine instead of phentolamine. Central administration of clonidine also abolished the TST rise to LHRH. Collectively these data suggest that the adrenergic neuronal system may mediate the temperature response initiated by administration of LHRH.

(Supported by NIH Grant HD18133)

70.5

EVAPORATIVE COOLING IN THE CICADA OKANAGODES GRACILIS (HOMOPTERA: CICADIDAE). Allen F. Sanborn*+, Maxine S. Heath*, James E. Heath, and Polly K. Phillips*. University of Illinois, Urbana, IL. 61801 and +Barry University, Miami Shores, FL. 33161.

Okanagodes gracilis Davis inhabits the salt flats of the Sonoran Desert. O. gracilis uses evaporative cooling to suppress body temperature and continue activity when ambient conditions would otherwise restrict activity. Body temperatures of O. gracilis in the field were as much as 4.3C below ambient. The regression of body temperature on ambient temperature (Y=.142X+34.63) intersects the isothermal line at 40.35C, which is less than two standard errors from the upper thermoregulatory point measured in the laboratory (41.16 ± .409C; $\bar{X}$±s.e., n=34). In the laboratory, animals lose weight (H_2O) faster at higher than at lower temperatures. Pores in the dorsal thorax are probably the site of H_2O loss. Dead O. gracilis cool at a rate of .320C/min°C gradient. To maintain a 4.3C gradient below ambient, O. gracilis needs to evaporate 1.6mg H_2O/min or the equivalent of 40.97% of live body weight per hour. The animals replenish water lost during evaporative cooling by continuously feeding during activity.

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CARDIAC DYNAMICS AND METABOLISM

71.1

CARDIAC VENTRICULAR VOLUME (VV)-EJECTION FRACTION (EF) PLOTS IN EVALUATING RESPONSE TO ANTERIOR VERSUS INFERIOR MYOCARDIAL INFARCTS. M.K. Karimeddini*, C.J. Homs*, R.P. Spencer. Univ. Connecticut Health Center, Farmington, CT 06032.

Using the assumption that there is an attempt to maintain constant cardiac output (VV x EF = C), plots can be made of log End Diastolic Volume Index (EDVI) or log End Systolic Volume Index (ESVI) versus log EF. This produces lines with downward slopes in most populations. The formulation was used to compare 15 patients sustaining anterior wall myocardial infarcts (AWMI) and 15 with inferior wall infarcts (IWMI), both immediately after the events and 2 weeks later (data from McKay et al, Circulation 74:693, 1986). Initially, AWMI showed a disordered pattern in which the log EDVI-log EF plot actually sloped upward, while the log ESVI-log EF graph had only a minimal downward slope. Two weeks later, AWMI plots revealed a nearly normal pattern. A graph of IWMI data showed a less disturbed pattern immediately post-infarction, with a reordering in two weeks. Such information is consistent with the more ominous significance of AWMI than IWMI. An extension of the approach would be from classes of patients, to individual cases, to determine if the plots of log EDVI or log ESVI versus log EF have prognostic significance. Of interest was the observation that, in each of the categories, ESVI values gave better correlation coefficients than did the EDVI information. Hence, systolic function indicators might have particular value in evaluating prognosis.

71.2

CARDIOVASCULAR RESPONSES TO TWO MINUTES OF SUSTAINED MAXIMAL ISOMETRIC CONTRACTIONS OF THE FINGER FLEXORS. D.L. Smith,* J.E. Misner,B.H. Massey, D. Bloomfield, and L.K. Essandoh. (SPON: A. Katz). Univ. of Illinois at Urbana-Champaign, IL 61820;*Skidmore College, Saratoga Springs, NY 12866.

The purpose of this study was to investigate the cardiovascular responses to two minutes of sustained isometric contraction of the dominant finger flexors in healthy women. Twenty young females (mean age=26.4 years) participated in this study. Subjects were tested in a semi-reclined position while in the postabsorptive state. Measurements of heart rate (HR), blood pressure (BP) and stroke volume (SV) were made every 30 seconds during two minutes of rest, during two minutes of maximal handgrip exercise and during two minutes of recovery. SV was calculated using Doppler echocardiography. SV was defined as the product of resting aortic diameter (2D echocardiography) and time velocity integrals (Doppler). The table below summarizes the cardiovascular responses to sustained maximal isometric contraction of the finger flexors:

	Maximal Contraction Time (Sec)				
	Rest	30 sec	60 sec	90 sec	120 sec
HR (b/min)	63.4	104.3	99.4	98.6	98.9
MAP (mmHg)	87.9	103.2	111.2	118.1	120.5
SV (ml)	127.6	126.3	125.6	135.8	135.7

During recovery HR and BP returned to resting values whereas SV increased significantly above resting and exercise values.

71.3

THE MECHANISM OF IN VIVO DEPRESSION OF CARDIAC CONTRACTILITY INDUCED BY ANGIOTENSIN I. David B. Kozlov and Richard M. Raymond Depts. of Surgery and Physiology Loyola University Shock Trauma Institute, Maywood, IL 60153

In a previous study we reported that angiotensin I (A1) resulted in a depression of contractility. The present study was undertaken to test the hypothesis that the negative inotropic effect was mediated via a baroreceptor response. Mongrel dogs were anesthetized, intubated and ventilated against 5-7 cm H_2O. Animals were surgically instrumented to measure left ventricular pressure (LVP), mean arterial pressure (MABP), and coronary flow (Q). Coronary vascular resistance (CVR) was calculated. A pneumatic occluder was placed around the aortic arch and used to alter the loading conditions on the heart. Left ventricular minor axis internal diameter was determined using the transit-time technique. LVP-diameter loops were separated via partial occlusion of the aorta (3-5 sec) while the respirator was stopped at end-expiration. The slope of the end-systolic pressure-diameter relationship (Ees) was used as our index of contractility. Following basal cardio- and hemodynamic measurements, A1 (0.1 μg/kg) was infused intra-arterially and data were collected over a five minute period. Similar measurements were made following ß-blockade.

	CONTROL		ß-BLOCKADE (BB)	
	BASAL	A1	BASAL	A1
Ees	21±3	16±1	19±2	13±2
MABP	88±7	100±7	92±4	101±10
Q	47±3	37±9	41±6	37±8
CVR	1.9±.3	2.8±1	2.5±1	3.5±1

These data indicate that A1, used to alter loading conditions, is inappropriate in assessing contractility. Further, reductions in Q in the face of increased pressure work weigh strongly against this event being baroreceptor mediated, and suggest either relative ischemia and/or direct negative inotropic effects of A1.

71.4

DEPRESSED CARDIAC RESPONSIVENESS TO CATECHOLAMINES IN CONSCIOUS DOGS WITH DILATED CARDIOMYOPATHY. R.P. Shannon*, K. Komamura*, W.T. Manders*, B.S. Stambler*, S.F. Vatner Dept of Cardiovascular Medicine, Harvard Medical School and New England Regional Primate Research Center, Southborough, MA 01772

To determine whether impaired inotropic responsiveness in dilated cardiomyopathy (DCM) is specific to catecholamines, we studied 8 conscious dogs, chronically instrumented with left ventricular (LV) pressure gauges, aortic and left atrial catheters, and ultrasonic dimension crystals, at control (Con) and after the development of DCM induced by rapid ventricular pacing (240 min^{-1}). DCM was associated with significant increases in LVEDP (+18±2 from 8±3 mmHg, p<0.01), an 18±2% increase in LV mass (p<0.05), LV cavity dilatation (Con: 40.1 ±0.4 mm; DCM: 46.5±1.1 mm, p<0.01), and depression in baseline LV dP/dt (Con: 2804±107 mmHg/sec, DCM: 1346±126 mmHg/sec, p<0.01) and ejection fraction (EF)(Con: 48±3%, DCM: 27±3%, p<0.01). The LV dP/dt response to norepinephrine (0.4 μg/kg /min) was depressed (Con: +1544±173 mmHg/sec; DCM: +396+114 mmHg/sec, p<0.01) as was the response to isoproterenol (0.4 μg/kg/min)(Con: +4831±427 mmHg/sec; DCM: +911±170 mmHg/sec, p<0.01) but was maintained to ouabain (20 μg/kg)(Con: +636±204 mmHg/sec; DCM: +584±77 mmHg/sec, NS). A similar pattern was observed with EF. Thus, in conscious dogs, DCM induced by chronic pacing is associated with depression in inotropic responsiveness to ß-adrenergic stimulation, but preserved responsiveness to a cardiac glycoside.

71.5

EFFECT OF LOADING CONDITIONS AND HEART RATE ON INDICES OF CONTRACTILITY. J.D. Schipke and G. Heusch. Dept. of Experimental Surgery, Univ. Düsseldorf and Dept. of Pathophysiology, Univ. Essen, Germany

Contractility (C) is a major determinant of ventricular function. Thus, erroneous interpretation of C endangers correct assessment of ventricular function. We investigated on 5 isolated, blood-perfused canine hearts the effects of preload (P), afterload (A), heart rate (HR) and C on 3 global and 3 regional indices of C. The end-systolic pressure-volume relationship was chosen as the standard of C. Data were analysed using stepwise multiple linear regressions; the table shows the partial and multiple (sum) correlation coefficients:

Index	C	P	A	HR	sum
dP/dtmax	0.657	0.263	0.012	0.016	0.940
dP/dtmax/Pmax	0.817	0.017	0.013	0.071	0.881
EF	0.770	0.016	0.074	0.012	0.872
δT	0.538	0.074	0.062	0.025	0.699
v	0.566	0.047	0.092	0.061	0.766
T90	0.861	0.000	0.007	0.099	0.967

n = 75; Pmax: peak syst. pressure; EF: ejection fraction; δT: relative syst. wall thickening; v: mean syst. wall thickening velocity; T90: wall thickness at end-syst. pressure of 90 mmHg

Of the global indices, dP/dtmax exhibits the best multiple correlation with C; the preload-dependency of this index is lost after normalizing by Pmax. T90 correlates best with C; both other regional indices exhibit considerable dependency on P, A and HR. **Conclusion:** Changes in indices of contractility reflect true changes in contractility to a different degree.

71.6

DIASTOLIC STUNNING IN REPERFUSED MYOCARDIUM

G. Heusch and J.D. Schipke. Dept. of Pathophysiology, Univ. Essen and Dept. of Experimental Surgery, Univ. Düsseldorf, Germany

The consequences of reversible ischemia on regional ventricular function were investigated in 13 anesthetized dogs using sonomicrometry. The early (E) thinning velocity (V) during the isovolumic relaxation phase, i.e. the time between dP/dtmin and mitral valve opening (LVP 5 mmHg above EDP), and the late (L) V during diastasis and atrial contraction (time between LVP 5 mmHg above EDP and EDP) were determined during control, after 15 min coronary occlusion, and 10 min, 4 h and 8 h after onset of reperfusion. EV and LV were compared to the systolic wall thickening velocity (SYS):

	control	occlusion	10 min	4 h	8 h
SYS	11.7±5.0	-1.8±3.4	3.7±3.5	6.5±3.9	7.8±4.6
EV	-7.2±5.1	7.2±6.3	5.8±5.1	-0.5±5.8	-0.6±6.3
LV	-15.6±5.7	-1.5±7.2	-11.6±7.6	-8.6±6.5	-6.1±8.4

The correlations between SYS and EV (r=-0.67) and SYS and LV (r=-0.67) were significant but not between EV and LV. **Conclusion:** Not only systolic function but also diastolic function is impaired after reversible ischemia. The processes of relaxation and ventricular filling appear to be impaired independently from each other, suggesting that both active relaxation processes and geometric reconfiguration of the left ventricle might be affected by postischemic dysfunction.

71.7

ISOLATED HEART FUNCTION DECLINES WITH INCREASING AGE. Leslie J. Kohman and Linda J. Veit*. SUNY Health Science Center, Syracuse, New York 13210.

The literature contains conflicting reports on the relative susceptibility of neonatal and adult myocardium to ischemia. "Neonate" has encompassed ages from 1 to 30 days, which may account for some of the variability in results. We tested the function of isolated rabbit hearts of various ages before and after 10min of global normothermic ischemia. The results are listed in the table (Mean±SEM):

	2 weeks (n=4)	4 weeks (n=6)	6 weeks (n=4)
AF			
Pre	14.3±2.8	11.7±1.4	6.1±1.5
Post	8.1±2.3	7.0±0.7	4.3±0.9
CO			
Pre	21.2±3.1	14.2±1.7	8.2±1.3
Post	15.9±2.7	9.1±0.7	5.9±0.9
SV			
Pre	.10±.02	.07±.003	.04±.007
Post	.08±.02	.05±.003	.03±.006

Aortic flow (AF) cardiac output (CO), and stroke volume (SV) all expressed as ml/min/gm. wet wt., were progressively lower as age increased, both before (pre) and after (post) ischemia. This shows that strict attention must be paid to the age of "neonatal" animals when evaluating cardiac function.

71.8

SELECTIVE PLASMENYLETHANOLAMINE BIOSYNTHESIS MEDIATED BY ETHANOLAMINE PHOSPHOTRANSFERASE IN RABBIT CARDIAC MICROSOMES AND MYOCYTES. David A. Ford, Kimberly B. Rosenbloom and Richard W. Gross, Molecular and Cellular Cardiovascular Biochemistry, Washington Univ. Sch. of Med., St. Louis, MO 63110

Recently, we have demonstrated that ethanolamine glycerophospholipids in myocardial sarcolemma and sarcoplasmic reticulum are markedly enriched in plasmenylethanolamine molecular species. Incubation of rabbit myocardial microsomes with [^{14}C-ethanolamine] CDP ethanolamine resulted in the selective incorporation of radiolabel into plasmenylethanolamine molecular species (16:0-20:4 >18:1-20:4 >18:0-20:4 >18:1-18:2 (sn1-sn2 plasmenylethanolamine molecular species)) in comparison to phosphatidylethanolamine molecular species. This plasmalogen subclass specificity was manifest despite the nearly 100-fold molar excess of endogenous microsomal diacyl glycerol compared to 1-O-alk-1'-enyl-2-acyl-sn-glycerol in microsomes. In contrast, incubation of [^{3}H]-ethanolamine with rabbit myocardial microsomes or incubation with isolated rabbit cardiac myocytes resulted in the preferential incorporation of [^{3}H]-ethanolamine into phosphatidylethanolamine molecular species (predominantly 18:0-20:4 and 18:0-18:2 (sn1-sn2 phosphatidylethanolamine molecular species)) which is presumably mediated by base exchange. Collectively, these results demonstrate that rabbit myocardial plasmenylethanolamine is synthesized through condensation of 1-O-alk-1'-enyl-2-acyl-sn-glycerol with CDP ethanolamine and that virtually no plasmenylethanolamine biosynthesis occurs through base exchange reactions.

71.9

BIVENTRICULAR WORKING MODEL FOR ISOLATED PERFUSED RAT HEARTS. Todd L. Demmy*, George J. Magovern*, and Race L. Kao. Allegheny Gen. Hosp./Allegheny-Singer Res. Inst., Pittsburgh, PA.

The isolated working left heart of small animals has been extensively used for metabolic and physiologic studies. However, using only the left side of the heart gives imperfect evaluations due to ventricular septal shifting and an inactive right heart. This study demonstrates the establishment of a biventricular working model for isolated perfused rat hearts. The oxygenator and atrial reservoirs have their height independently adjusted for separate control of left and right atrial filling pressures (preloads). The compliance chamber provides dynamic impedance to the aortic output. The aortic resistance (afterload) is easily regulated by the air pressure within the compliance chamber. Pulmonary resistance is adjusted by the height of the pulmonary outflow column. A total of 33 hearts from Sprague-Dawley rats (body weight 350-400 g) were used for this study. After aortic cannulation and preliminary perfusion, the left atrium, pulmonary artery, and right atrium were cannulated. With consistent preload (9.5 mmHg) and afterload (aorta 80 mmHg, pulmonary artery 18 mmHg), the following hemodynamic performance was observed: aortic output 39.3+1.4 ml/min, coronary flow 23.8+1.6 ml/min, aortic systolic pressure 138+3 mmHg, pulmonary artery systolic pressure 36+1 mmHg, and heart rate 241+10 beats/min. For 7 consecutive hearts that were perfused for 3 hours, the aortic output (95±5%), coronary flow (83±7%), aortic systolic pressure (97±3%), pulmonary artery systolic pressure (94±7%), and heart rate (104±4%) were well maintained as compared to initial levels. Myocardial ATP (36.5±2.9 umol/g protein) was also maintained at normal physiologic concentration after 3 hours of perfusion.

71.10

COMPARISON OF FIVE CARDIOPLEGIC SOLUTIONS AT 16° C FOR MYOCARDIAL PROTECTION. Race L. Kao, Todd L. Demmy*, Jeanne Park*, and George J. Magovern*. Allegheny-Singer Res. Inst. and Allegheny General Hospital, Pittsburgh, PA 15212.

With an increasing percentage of patients for open-heart surgery that are elderly or have depressed cardiac function, interest in myocardial protection has been renewed. A modified St. Thomas solution (used clinically at this institution), Bretschneider solution, Plegisol (Abbott Lab., North Chicago, IL), Allegheny solution, and Cryomedical solution (Cryomedical Sci., Bethesda, MD) were used to arrest isolated perfused working rat hearts for three hours at 16° C. Each group of hearts (N=6) was arrested by multidose cardioplegia and freeze clamped at the end of crossclamp or after 60 min of reperfusion. The biochemical parameters at the end of elective cardiac arrest and after reperfusion as well as the hemodynamic recovery for each group of hearts are summarized as follows:

	St. Th.	Bretsch.	Pleg.	Alleg.	Cryomed.
ATP - End Crossclamp	25+3	10+2	27+1	29+2	16+1
ATP - Reperfusion	12+1	6+1	16+2	21+3	19+3
AO (ml/min)	10+4	3+2	15+5	29+8	24+5
Developed Pressure	15+5	17+7	34+8	47+5	39+9
Heart Rate (beats/min)	161+45	138+31	229+12	233+17	227+10

ATP in umol/g protein. AO = Aortic Output.

Developed Pressure = systolic pressure - diastolic pressure in mmHg.

From the biochemical and hemodynamic data, we conclude that the Allegheny solution is the better cardioplegic solution for the rat heart. Further investigation of selected solutions in large animals under cardiopulmonary bypass will clarify the findings.

71.11

ANIMAL MODEL WITH COMPROMISED LEFT VENTRICULAR FUNCTION FOR DYNAMIC CARDIOMYOPLASTY. James A. Magovern*, Ignacio Y. Christlieb*, Race L. Kao, and George J. Magovern*. Allegheny General Hospital and Allegheny-Singer Res. Inst., Pittsburgh, PA 15212

Electrically conditioned skeletal muscle has been used in experimental and clinical studies to power circulatory assist devices and to improve left ventricular function. Improvement of hemodynamic function by dynamic cardiomyoplasty in animals with normal cardiac function has not been successful. This study was designed to produce chronic left ventricular dysfunction using dogs as an experimental animal model. Mongrel dogs (25 to 32 kg) purchased from a licensed vendor and under humane care were used for the study. After proper anesthesia and sterile surgical preparations, the heart was exposed through a left thoracotomy. A catheter filled with heparin solution was positioned in the left main coronary artery and connected to a vascular access port (Norfolk Medical Products). The location and patency of the catheter were confirmed initially by methylene blue injection and subsequently by roentgenograph with Renografin infusion. Five doses (10 mg/dose/week) of Doxorubicin Hydrochloride were given at a rate of 1.1 ml/min for 55 minutes by a Harvard infusion pump (Model 975). The ejection fraction decreased from 46.3±0.9% to 36.4±2.9% and the cardiac output was lowered from 6.05±0.54 L/min to 4.72±1.02 L/min. Controlled infusion of Doxorubicin Hydrochloride directly into the left main coronary artery of dogs produces compromised left ventricular function which can be used as a model to evaluate hemodynamic changes following cardiomyoplasty. Supported by NIH Grant HL-38078

79.1

QUANTITATIVE ANALYSIS OF IMMUNOGLOBULINS FROM NORTHERN ELEPHANT SEALS *(Mirounga angustirostris)*. John L. Sanders* and C. L. Ortiz, Department of Biology and Institute of Marine Sciences, University of California Santa Cruz, Santa Cruz, CA 95064

Immunoglobulins from sera of Northern elephant seals, were analyzed to establish determinant homology among the immunoglobulins of humans, Northern elephant seals, and terrestrial mammals. IgG, IgM, and IgA were isolated from the sera of adult males, and from the sera and milk of adult female elephant seals. Immunoglobulins were purified by precipitation, gel filtration and ion exchange chromatography. Purity of the isolated fractions was checked by immunoelectrophoresis and SDS-PAGE. Determinant homology was established by immunodiffusion using antisera specific for human IgG, IgM, and canine IgG. These antisera showed excellent cross-reactions with elephant seal immunoglobulins and sera from other terrestrial and marine mammals. Rabbit anti-elephant seal sera was used for quantitative analysis. SDS-PAGE molecular weight determinations showed IgG heavy and a light chains were 55 Kd. and 29 Kd. respectively. IgM heavy and light chains were 61 Kd. and 29 Kd. IgA had a molecular weight of 320 Kd. These results suggest that the physiochemical properties of the immunoglobulins from this marine mammal species are quite similar to those of humans and many terrestrial and marine mammals. These observations provide a first glimpse into the immune systems of these unique marine mammals, and will serve as a foundation for future research in maternal/neonatal immunology in this species. **(Supported by Minority Biomedical Support Program NIH RR-08132 and GM34-07910)**

79.2

THE EFFECT OF PHOTOPERIOD AND MELATONIN ON FREEZING TOLERANCE IN THE WOOD FROG, *RANA SYLVATICA*. M.L. O. Edwards, K.B. Storey, and E.B. Pivorun, Erskine College, Due West, SC 29639; Carleton Univ., Ottawa, Ontario, Can K1S 5B6; Clemson Univ., Clemson, SC 29634.

In a variety of vertebrates photoperiod and melatonin have been shown to be regulators of seasonal activities including hibernation and torpor in mammals. This study exposed wood frogs to either long (12L/12D) or short (2L/22D) photoperiods to determine the effect on freezing tolerance. Additional groups of *R. sylvatica* were treated with melatonin dissolved in an ethanol/water solution or were treated as controls and injected only with ethanol/water. Frogs were very solidly frozen at -2.5°C and thawed at 3°C using an established protocol. All frogs survived but demonstrated significant differences in the levels of cryoprotectant synthesized. Frogs were double pithed and blood and liver samples were collected. Blood glucose levels were found to be significantly lower in frogs treated with 0.47 μg melatonin/g frog when compared to the control and 4.7 μg melatonin/g frog groups. In this same group of frogs, liver glucose and glycogen levels were also significantly reduced when compared to the other two treatment groups. Glucose and glycogen levels in frogs exposed to different photoperiods are also compared.

79.3

GLUCOSE REGULATION IN FASTING AND FEEDING NORTHERN ELEPHANT SEALS LESS THAN 1 YEAR OF AGE. V.L. Kirby* and C.L. Ortiz, Biology Dept, University of California, Santa Cruz, CA 95064

Models of fuel homeostasis predict that the adaptations to fasting are the same as those to high dietary fat intake, i.e. glucose intolerance, hypoinsulinemia, hyperglycemia and increased body fat. Earlier studies in neonate northern elephant seals reported that they exhibited the above characteristics during suckling and a post-weaning fast. Suckling pups increase their fat mass to >45% at weaning on a high milk fat diet whereas fasting weanlings catabolize endogenous fat stores. It is not known if these adaptations are restricted to neonate development or may occur in other age classes as an adaptation to being a carnivore. To test this, the regulation of glucose homeostasis was compared in seals that were either 3 month old fasting weanlings captured just prior to their initial departure to sea or 6-8 month old seals just returned from feeding at sea. All seals were induced to eat herring for 3 weeks and received IVGTT (0.5 g glucose/kg body wt) or IVITT (0.1 U insulin/kg body wt). Body composition was determined from tritum determinations of total body water. All seals were glucose intolerant, had impaired insulin response, insulin:glucagon ratios <1.0. and baseline glucose levels of 120-135 mg%. Changes in body fat had no effect on glucose/insulin responses. After 3 weeks of mass gain on fish, weanlings reduced their body fat from 45% to 28% by increasing lean mass. Body fat levels were constant (25-30%) in seals captured after 2-3 months of feeding at sea as well as the recovery program seals. Thus, glucose intolerance, hypoinsulinemia, hyperglycemia are not restricted to neonate development and are normal for seals on a high fat diet in which up to 85% of the calories may come from milk fat or fish fat or entirely from endogeneous body stores during fasting.

79.4

REGIONAL HETEROGENEITY IN ATP LEVELS IN THE ANOXIC TURTLE BRAIN. Alexis Alfaro* and Peter L. Lutz, Marine Biology and Fisheries, RSMAS, University of Miami, Miami, Florida 3314 9

The turtle brain has a remarkable capacity for conserving energy during anoxia. Even after eight hours of anoxia, global ATP levels are maintained at normal values, however, it is unknown if ATP is maintained uniformly throughout the brain or if some regions are preferentially protected. For example, recent data (Nilsson in pre.) suggest that adenosine is released in the striatum after the first 15 minutes of anoxia. Regional changes in APT concentration of the brain of the turtle Pseudemys scripta have been studied after 15, 30, 60, 120, 180 and 240 minutes of anoxia. A bioluminescence technique using luciferin-luciferase in a magnesium buffer was applied to 14 micron frozen sections of turtle brain. For the 15 minute group we report a considerable drop in ATP in the olfactory bulb with maintained levels of ATP in the telencephalon. The cerebellum and the optic lobes maintained ATP levels throughout the 240 minutes of anoxia. The glycolitic activity in the anoxic brain appears to favor the telencephalic structures in the striatum and those responsible of limbic control over the olfactory nuclei.

79.5

QUANTITY OF TRANSLATABLE mRNA IN *ARTEMIA FRANCISCANA* EMBRYOS DOES NOT CHANGE DURING ENTRY INTO ANAEROBIC DORMANCY. Gretchen E. Hofmann* and Steven C. Hand. Univ. of Colorado, Boulder, CO 80309-0334.

Previous results with *Artemia* embryos clearly indicate that protein synthesis is inhibited upon entry into anaerobic dormancy [Hofmann and Hand (1990) Amer. J. Physiol. 258: R1184], but the mechanisms involved in this biosynthetic arrest are not understood. We have developed an in vitro translation system using rabbit reticulocyte lysate that translates *Artemia* mRNA. Phenol-chloroform extraction was used to isolate total RNA from aerobic (control) embryos and from embryos exposed to 4 h of anoxia. mRNA from 1 g of anaerobically dormant embryos directed the incorporation of ^{35}S-methionine into TCA-precipitable protein at a rate of 35.0 ± 4.9 x 10^6 cpm/h (± SE; n=3) versus 33.0 x 10^6 cpm/h for mRNA from 1 g of aerobic embryos. However, the numerous polysome peaks observed in aerobic embryos (density gradient centrifugation) were markedly diminished in anoxic embryos. Thus, the amount of mRNA apparently does not limit protein synthesis across this transition, but rather, regulation may occur at the level of translation. [NSF grant DCB-8702615]

79.6

GLUCOSE, ARGININE, PALMITIC ACID, AND OLEIC ACID STIMULATE SOMATOSTATIN-25 SECRETION FROM ISOLATED RAINBOW TROUT BROCKMANN BODIES. Carmen D. Eilertson and Mark A. Sheridan. North Dakota State University, Fargo, N.D. 58105

Humoral regulation of somatostatin-25 (SS-25) secretion was studied by perfusing isolated rainbow trout Brockmann bodies. Two to three Brockmann bodies were placed on a bed of Sephadex G-25 in a mini-column and perfused with gassed (100% O_2) Hanks salts containing 0.24% bovine serum albumin and 2.0 mM glucose, pH 7.6 (basal medium). The tissue was perfused at a flow rate of 15 ml/h. Somatostatin-25 was measured in the effluent fractions by ELISA. The ELISA was sensitive to 5.0 pg of peptide per 75 ul of sample. Glucose (either 10 mM or 25 mM) stimulated SS-25 secretion over basal levels. Arginine (either 10 mM or 25 mM) was also a potent secretagogue of SS-25 release. In addition, arginine-stimulated SS-25 release was augmented at a higher glucose concentration (5.5 mM). Both palmitic acid (16:0) and oleic acid (18:1) at 25 mM stimulated SS-25 release. These results indicate that pancreatic SS-25 secretion is regulated by a variety of nutrient molecules. (Supported by NSF DCB 89-01830 to M.A.S.)

79.7

HEPATIC LIPID MOBILIZATION IS MODULATED BY BOTH GLUCAGON AND INSULIN. Jamie S. Harmon and Mark A. Sheridan. North Dakota State University, Fargo, ND 58105.

The effects of nutritional state, glucagon and insulin on the lipid metabolism of rainbow trout, Oncorhynchus mykiss, was assessed both in vitro and in vivo. In nutritional state experiments, fish were either fed continuously (except 24 hr prior to experimentation) with commercial trout chow or fasted for 3-4 weeks. Hormones were injected into anesthetized fish (fed continuously except 24 hr prior to injections) in 10 µl of saline/g body weight. Doses ranged between 10 ng/g body weight to 100 ng/g body weight. Tissue and plasma were sampled 1 and 3 hr after injection. Plasma fatty acid (FA) levels in fed fish were 0.39 ± 0.4 µEq/ml and increased 30% in fasted animals. The hyperlipidemia of fasted fish was supported, in part, by elevated hepatic lipolysis as indicated by triacylglycerol lipase activity. Administration of salmon glucagon (100 ng/g) resulted in hyperlipidemia 3 hr after injection. Salmon insulin (100 ng/g) resulted in depressed plasma FA concentration and reduced hepatic lipase activity. In vitro interactions of nutritional state and hormone treatment were evaluated by incubating liver and adipose tissue pieces in Hanks-MEM. Lipase activity in liver tissue isolated from fasted fish was greater than that in tissue isolated from fed fish. The presence of glucose (5.55 mmol/L) in the incubation medium accentuates lipolytic activity in both liver and adipose tissue. Glucagon ($2x10^{-6}$M) directly stimulated lipid breakdown in both liver and adipose tissue. These actions were manifested by enhanced FA and glycerol release into the culture medium and by elevated lipase activity. Insulin ($2x10^{-6}$M) generally appeared antilipolytic, as this agent inhibited glucagon-stimulated lipase activity and glucagon-stimulated FA release. Furthermore, insulin (in the presence of glucose) reduced lipolysis, as indicated by glycerol release, compared to control cultures. These results indicate that nutritional state, glucagon and insulin are important modulators of lipid metabolism in rainbow trout. (Supported by NSF DCB 8901380.)

79.8

INSULIN INCREASES CARBOHYDRATE PRODUCTION IN HEPATOCYTES OF TWO TELEOST FISHES. Glen D. Foster* and T.W. Moon. Dept. of Biology, University of Ottawa, Ottawa, Ont. CANADA. K1N 6N5.

The functions of insulin on carbohydrate homeostasis in teleost liver were examined in hepatocyte suspensions of eel and sea ravens. Insulin is generally considered to be an anabolic hormone in mammals, where one of its actions is to increase glycogen synthesis. It also decreases glucagon-stimulated gluconeogenesis in isolated hepatocytes. Recently evidence has been reported indicating a role for insulin in increasing glycogen content of the liver using C_3 precursors as substrates in the absence of glucagon. In fishes the role of insulin on these parameters is poorly understood. In sea raven and eel hepatocyte preparations, insulin (Scombroid and/or porcine) acted additively to (sea raven) or had no effect on (eel) glucagon-stimulated gluconeogenesis. When added alone insulin increased C_3 (serine, alanine, lactate) flux to glucose and glycogen (sea raven) or glycogen (eel). The hormone increased PFK-1 sensitivity to ATP (eel, sea raven), increased amino acid uptake (sea raven), decreased %GPase a (eel), and had no effect on PEPCK V_{ppt} or any measured aspect of PK kinetics (sea raven). These data indicate that in eel and sea raven liver cells, insulin a) does not function in a counter-regulatory fashion with glucagon on gluconeogenesis, and b) functions in increase carbohydrate production from C_3 precursors with a key regulatory point at PFK-1.

79.9

EFFECTS OF INDUCED COLD TORPOR AND HYPOXIA UPON CYTOCHROME OXIDASE (COX) ACTIVITY, PHOSPHOLIPID CONTENT, AND ULTRASTRUCTURE IN CARDIAC MITOCHONDRIA OF THE FRESH WATER TURTLE, PSEUDEMYS SCRIPTA. Albert J. Rotermund and George Demos*. Loyola University, Biology Dept., Chicago, IL 60626.

Turtles were divided into three groups: room temperature controls, and experimentals which were acclimated to 5°C cold or cold-hypoxia for two weeks. Arrhenius plots of COX activity of controls had an activation energy (E_a) of 10.77 kcal/mole (5-35°C), whereas those of both cold-acclimated groups showed discontinuities at 30°C. E_as of turtles adapted to cold alone were 10.99 kcal/mole (5-30°C) and 5.155 kcal/mole (30-35°C), while those of cold-hypoxic animals were 11.25 kcal/mole (5-30°C) and 2.14 kcal/mole (30-35°C). Lubrol-treated mitochondria exhibited no such "breaks". These results suggest that COX activity is viscotropically regulated during cold adaptation. Mitochondrial levels of phosphatidyl ethanolamine decreased significantly in both cold-acclimated groups ($P = 0.001$), whereas cardiolipin increased significantly in animals acclimated to cold alone ($P = 0.005$). Morphometric analysis showed non-ischemic, significant increases of mitochondrial area within both cold-adapted groups ($P = 0.001$), with no alterations of shape.

79.10

A STUDY OF THE PHYLOGENY OF THE CETACEA USING HPLC ANALYSIS OF MYOGLOBIN. D.L. Hayteas* and D.A. Duffield* (SPON: L.I. Crawshaw). Portland State University, Portland, OR 97207.

Myoglobin from 15 species of cetaceans was extracted, purified, and digested with trypsin. The resulting peptide mixture was separated by reversed-phase high pressure liquid chromatography (HPLC), producing a characteristic peptide map for each species. The maps were compared, the number of retention time differences tabulated, and a difference matrix constructed. Phylogenetic relationships were determined using a "maximum liklihood" genetic distance computer program. Results agreed with traditional cetacean phylogenies, except a close relationship was indicated between the harbor porpoise, Phocoena phocoena, and the beluga, Delphinapterus leucas. Since each species exhibits a distinctive peptide map, HPLC analysis of peptide mixtures has application in phylogenetic reconstructions, as well as for tissue identification in wildlife forensics.

79.11

DISTRIBUTION OF OPINE DEHYDROGENASES IN BRACHIOPODS AND MOLLUSKS. Carl S. Hammen and Robert C. Bullock. Univ. of Rhode Island, Kingston, RI 02881.

The opine dehydrogenases catalyze the reductive condensation of pyruvate with various amino acids to form products resembling octopine (N-Carboxyethyl arginine). They are widely distributed among marine invertebrates, and function in metabolism in the place of lactate dehydrogenase, which often has very low activity, especially in mollusks. The reaction of pyruvate with either alanine, arginine, ß-alanine, or taurine, catalyzed by tissue extracts of various species, was measured by decrease in absorbance of NADH. The 27 species examined were brachiopods, bryozoans, and a wide variety of mollusks, including a scaphopod, two amphineurans, and species representing the five sub-classes of bivalves and three orders of prosobranch gastropods. Activities were coded 0-5, with 5 assigned to rates greater than 5 µmol/min-g. These numbers were entered by species into a program that performed average linkage cluster analysis. Results of this analysis were transformed into a branching tree diagram. The pleisiomorphic state was defined as the presence of the total array of opine enzymes, and the loss during evolution of one or more was taken as apomorphic. The resulting cladogram has some features in common with standard phylogenetic trees based on morphology and development, and a few departures that require interpretation.

79.12

INTRACELLULAR PIGMENT GRANULES IN THE GILLS OF LUCINA FLORIDANA CATALYZE THE OXIDATION OF SULFIDE. Amy E. Anderson* and Steven C. Hand. Univ. of Colorado, Boulder, CO 80309.

Lucina floridana is a eulamellibranch bivalve that lives in sulfide-rich seagrass beds and contains chemoautotrophic sulfur bacteria in 'bacteriocytes' within its gills. A striking intracellular feature of the bacteriocytes is densely staining 'pigment granules' which range from 1-16 um in diameter. Energy dispersive X-ray analysis showed the inorganic fraction of purified pigment granules to be 80% quartz, with hornblende and feldspar comprising the remainder. These minerals are embedded in an organic matrix containing a heme compound. Interestingly, a similar inorganic composition is observed for large (25-60 um) extracellular concretions associated with the adductor muscles, except these structures also possess an outer laminar coat of calcium carbonate. Pigment granules catalyze the oxidation of sulfide (HS^-) at a rate of 0.38 nmoles/ nmole heme-min. in 5 mM sulfide. High speed supernatants (granule free) of gill homogenates show maximum HS^- oxidation (SOx) activities of 6.18 nmoles sulfide/nmole heme-min. in 5 mM HS^-. Supernatant SOx accounted for 70% of the total activity in crude homogenates (2.47 IU/g gill tissue), and 28% was found in the pellet fraction. In contrast, extracellular concretions do not oxidize HS^- nor contain detectable heme. Thus, there are at least two sources of SOx in gill tissues. Both activities likely contribute to sulfide detoxification in this clam. [NSF grant OCE-8900107]

79.13

CHARACTERIZATION OF LEUKOTRIENE C_4 BINDING SITES IN BULLFROG VENTRICULAR MEMBRANES

M.J. Chiono*, J.J. Andazola*, and C.A. Herman. Department of Biology, New Mexico State University, Las Cruces, NM 88003

Previous results from our laboratory demonstrated leukotriene (LT)C_4 affects contractility in the isolated perfused bullfrog heart. This study characterizes specific binding sites for $^3HLTC_4$ on membrane preparations from bullfrog (Rana catesbeiana) heart ventricles. Binding assays were done in the presence of serine (5 mM) borate (10 mM) for 30 min at 23°C. Under these conditions, no metabolism of LTC_4 to LTD_4 occurred. Specific binding of $^3HLTC_4$ reached steady state within 1 min, remained constant for 60 min and was reversible with the addition of 1000 fold excess unlabeled LTC_4. Scatchard analysis of the binding data indicated a single class of binding sites with a K_d of 27.2 nM and B_{max} of 42.2 pmol/mg protein. Competition binding studies revealed an order of potency of LTC_4> LTD_4> LTE_4> glutathione with K_i values of 49, 2/80, 9714, and 44700 nM, respectively. Two mammalian LTD_4 antagonists, L-649,923 and LY171883, failed to inhibit specific binding of $^3HLTC_4$, suggesting that the LTC_4 receptor is distinct from the LTD_4 receptor. Neither guanosine 5'-triphosphate or guanyl-5'-yl-imidodiphosphate affected specific binding of $^3HLTC_4$, indicating that, like mammalian LTC_4 receptors, a G_i protein is not involved in the transduction mechanism. LTC_4 acts on bullfrog hearts through specific membrane receptors and is similar to its mammalian counterpart. (Supported by NSF Grant DCB-8702228)

79.14

GLUTAMINE OXIDATION BY MITOCHONDRIA ISOLATED FROM FISH SKELETAL MUSCLE. M.E. Chamberlin and J.S. Ballantyne. Ohio Univ., Athens, OH 45701 and Univ. of Guelph, Guelph, Ontario, N1G 2W1, Canada

Amino acid metabolism was examined in the muscles of three species of fish, representing divergent taxonomic groups. Mitochondria were isolated from the lateral red muscles of the lake char, *Salvelinus namaycush* (Teleostei), the bowfin, *Amia calva* (Holostei), and the little skate, *Raja erinacea* (Chondrichthyes:Elasmobranchii). These mitochondrial preparations were characterized by high respiratory control ratios and, in all three species, glutamine was oxidized more rapidly than any other amino acid tested. Glutamine oxidation was significantly lower in mitochondria isolated from the lake char compared to that from the bowfin or the skate. Mitochondrial glutaminase activity was correspondingly higher in the skate and bowfin compared to that of the char. Aminooxyacetate inhibited the oxidation of glutamine by about 20% in all three species, indicating that glutamine oxidation occurs primarily *via* glutamate dehydrogenase. The activity of glutaminase in extracts of skate red muscle was nine times higher than that in bowfin and the teleost. Red muscle glutamine synthetase activity was very low in all three species. The high glutaminase/glutamine synthetase ratio indicates that fish muscle, unlike mammalian muscle, does not synthesize and release glutamine. Instead, this high ratio indicates that glutamine oxidation may be an important source of energy in fish muscle. The very high glutaminase activity as well as the high rate of glutamine oxidation in skate mitochondria indicate that glutamine may be a particularly important energy source in the elasmobranch red muscle. This research was funded by the Natural Sciences and Engineering Research Council of Canada.

79.15

DOES FUEL PREFERENCE DEPEND ON AEROBIC CAPACITY? FAT AND CARBOHYDRATE OXIDATION IN RUNNING COYOTES, DOGS, AND GOATS. T.J. Roberts*, J.-M. Weber, and C.R. Taylor. Museum of Comp. Zoology, CFS, Harvard University, Old Causeway Rd., Bedford, MA 01730.

Dogs and coyotes are highly adapted for endurance exercise, with aerobic capacities approximately 2.5 and 3.5 times greater than goats. These high metabolic rates require both an increased capacity for oxygen delivery and an increased rate of metabolic fuel supply. We asked whether rates of carbohydrate and fat oxidation scale directly with $V_{O_2}max$, or if the relative contributions of each fuel change. Endurance-adapted animals could utilize proportionately more fat to spare limited carbohydrate stores. Fat and carbohydrate oxidation were calculated from oxygen consumption and carbon dioxide production in 4 goats (30 kg), 3 dogs (30 kg), and 3 coyotes (12 kg) running on an inclined treadmill. Substrate utilization was compared in the three species at three equivalent intensities: 40%, 60%, and 85% of $V_{O_2}max$. For each species, fat oxidation increased to a steady level which was independent of exercise intensity; at higher intensities additional energy was supplied by carbohydrates. The relative proportions of fat and carbohydrate oxidized were the same for all species at equivalent exercise intensities: dogs and coyotes consumed approximately 2.5 and 3.5 times more fat than goats. We conclude that nature's endurance athletes have not exploited relatively higher rates of fat oxidation as an adaptation for sparing carbohydrates. However, they rely to a far greater extent on fat metabolism at any given speed because they operate at a lower percentage of $V_{O_2}max$. This work was supported by NSF grant DCB-8918371.

79.16

RESPIRATORY COUPLING OF SULFIDE OXIDATION TO ATP PRODUCTION IN MITOCHONDRIA OF THE BIVALVE *SOLEMYA REIDI*. John O'Brien and George N. Somero. Scripps Inst. of Oceanography, La Jolla, CA. 92093

The bivalve *Solemya reidi* lives in reduced sediments where its symbiotic sulfur-oxidizing bacteria have a rich supply of hydrogen sulfide. Mitochondria of this clam oxidize sulfide to thiosulfate via the respiratory chain. Electrons enter the respiratory chain at cytochrome c and pass through cytochrome c oxidase to oxygen. The process supports ATP synthesis with approximately one ATP produced per sulfide molecule oxidized. This stoichiometry is about one half that expected for the transfer of four electrons through site III of the mitochondrial respiratory chain. The reduced ATP coupling efficiency may improve the mitochondrion's ability to protect itself from sulfide poisoning by reducing the thermodynamic "backpressure" against sulfide oxidation and hence increasing its rate. The reduced coupling efficiency also reduces the dependency of sulfide oxidation on cellular ATP demand. Protonophoric uncoupling of respiration by sulfide does not appear to be the cause of the low coupling efficiency. Instead, a lower proton pumping stoichiometry for *S. reidi* cytochrome oxidase than is observed in other mitochondria may account for the discrepancy. Supported by NSF OCE-86-10513.

79.17

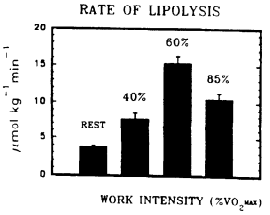
ISOLATION AND CHARACTERIZATION OF ANOXIA TOLERANT HEPATOCYTES FROM THE WESTERN PAINTED TURTLE. Leslie T. Buck and Peter W. Hochachka. Univ. of British Columbia, Dept. of Zoology, Vancouver,B.C. V6T 2A9

The difficulties of studying cellular anoxia tolerance in an intact animal system are obvious and at present there are no good cell systems available. Presented here is a method for the isolation of hepatocytes from Chrysemys picta in a 10 - 20 % yield. Adenylate energy charge is stable at 0.90 over a 24 hr period at 20 C under normoxic conditions. Trypan Blue staining remains at 0% and LDH leakage into the medium increases from 1 to 2% over the same time course and conditions. Over a 10 hr period of anoxia energy charge is maintained at approx. 0.90, Trypan Blue staining remains at 0% and LDH leakage increases two fold. A test of metabolic competence - gluconeogenesis was measured and a rate of 0.2 μmoles/gm/hr was obtained. PEPCK was determined to be entirely mitochondrial suggesting lactate is the perferred gluconeogenic substrate. These data suggest that hepatocytes isolated from this animal provide a good experimental system to study anoxia tolerance at the cellular level. This work is supported by NSERC Canada.

79.18

MAXIMAL FAT MOBILIZATION IN EXERCISING GOATS. J.-M. Weber, T.J. Roberts*, and C.R. Taylor. CFS, Harvard University, Bedford MA, 01730.

Because lipid metabolism usually depends on both intensity and duration of exercise, it is not clear at what work rate and after how long maximal mobilization of fat reserves is achieved. To answer this question, we measured glycerol production by continuous infusion of 2-^{3}H-glycerol in goats exercising on a treadmill at 40, 60, and 85% VO_2max for 120, 60, and 15 min respectively. Lipolysis (=R_a glycerol) increased very rapidly at the onset of work but did not change significantly thereafter. The response was not proportional to exercise intensity and maximal glycerol production occurred at the intermediate work rate (60% VO_2max). At 40% VO_2max, the goat response was 2.5 times lower than what has been reported for dogs having a 2.5-fold higher VO_2max, suggesting that fat mobilization is scaled directly with aerobic capacity. Supported by NSF grant DCB-8918371.



79.19

ASPECTS OF THE ENERGETIC METABOLISM OF ISOLATED CELLS FROM BLUE CRAB HEPATOPANCREAS IN SIMULATED HYPOXIC OR POST-EXERCISE CONDITIONS. François H. Lallier* and Patrick J. Walsh. Univ. of Miami, RSMAS, MBF, Miami, FL 33149.

The fate of lactate ions and the occurrence and importance of gluconeogenic processes are still controversial in Crustacea. The cellular approach, using isolated cells, seemed appropriate to address this problem Cells isolated from the hepatopancreas of blue crabs, *Callinectes sapidus*, were suspended in solutions reproducing as closely as possible actual *in vivo* acid-base and respiratory conditions during four different situations: control (C, pH=7.6, CO_2 = 0.25%, O_2 = 21%, [L-lac] = 0.5 mM, [Ala] = 0.5 mM), hypoxia (H, 7.9, 0.1%, 2%, 0.5 mM, 0.5 mM), post-exercise (E, 7.2, 1%, 21%, 15 mM, 5 mM) and recovery (R, 7.6, 0.25%, 21%, 5 mM, 5 mM). We measured the production of CO_2 and glucose from ^{14}C-lactate and ^{14}C-alanine, and the production of CO_2 from ^{14}C-glucose. In addition, the activities of 8 enzymes involved in these processes were assayed on hepatopancreas homogenates. CO_2 production from lactate was low in C (0.11 μmol.g^{-1}.h^{-1}) and H (0.05) conditions but increased dramatically in E (0.41) and R (0.45) conditions. Similar trends with lower levels were found for CO_2 production from alanine. Glucose synthesis was evidenced from lactate, but not from alanine, in E (0.06 μmol.g^{-1}.h^{-1}) Surprisingly, no lactate dehydrogenase activity could be detected in this tissue. We discuss the role of the hepatopancreas in the removal of lactate after exercise in the blue crab.

COMPARATIVE PHYSIOLOGY: HEART AND CIRCULATION

80.1

COELIAC ARTERY BLOOD FLOW IN THE ESTUARINE CROCODILE, *CROCODYLUS POROSUS*. Michael Axelsson*, Regina Fritsche*, Susanne Holmgren*, David Grove* and Stefan Nilsson. (SPON: A.P. Farrell). Nuffield Fish Laboratory, School of Ocean Sciences, Marine Science Laboratories, UCNW, Menai Bridge, Wales, UK.

In crocodiles, there is a complete separation of the left and right ventricle. In addition to the systemic (right) aorta from the left ventricle, a separate aorta (left aorta) runs from the right ventricle. There are two points of communication between the left and right aorta, the first via *foramen Panizzæ*, an aperture in the intra-aortic septa immediately outside the aortic valves and a second at an abdominal anastomosis located in the abdomen. It has recently been shown that the net blood flow in the left aorta is low compared to the right aortic blood flow, with a complex flow profile showing both anterograde and retrograde blood flow during each cardiac cycle. It was concluded that blood flow in the left aorta emanates from the right aorta via *foramen Panizzæ*. Gut blood flow may occur via two routes; either via the left aorta, which continues as the coeliac artery posterior to the arterial anastomosis or from the right aorta via the arterial anastomosis. In this study simultaneous recordings of left and right aortic, coeliac and carotid artery blood flow were performed. Coeliac artery blood flow was substantial and continuous throughout the cardiac cycle and did not show the complex flow patterns of the left aorta. It is suggested that the coeliac artery blood flow is derived from the right aorta via the aortic anastomosis. After feeding the animals, there was an increase in the coeliac arterial and left aortic blood flow. During "fright" dives there was a developing bradycardia and a reduction in the recorded blood flows. The decrease in the carotid artery blood flow appeared smaller than the decrease in coeliac arterial and right aortic blood flow. A largely unimpaired carotid artery blood flow was also maintained after epinephrine injection, although coeliac arterial flow decreased.

80.2

THE INFLUENCE OF CHEMORECEPTIVE DRIVE IN LONG DURATION VOLUNTARY DIVES IN MUSKRATS. Paul F. McCulloch and Nigel H. West. University of Saskatchewan, Saskatoon, Saskatchewan, S7N 0W0, CANADA.

In previous studies investigating voluntary diving in muskrats I have measured heart rates in short duration (less than 30 seconds) voluntary dives. This short duration precludes possible chemoreceptive influence upon the diving bradycardia. In escape dives lasting up to 60 seconds, the dive bradycardia intensifies at about 30 seconds, suggesting chemoreceptor involvement. The objectives of this study were to determine if a similar drop in heart rate occurs at about 30 seconds into voluntary dives, and if chemoreceptive influence is responsible for this decline. Muskrats were implanted with an ECG transmitter and trained to swim underwater through a 16 m round trip long maze to obtain food, and to dive only upon signal. Voluntary dives lasting 60 seconds were recorded, and the heart rate response to long duration voluntary dives are presented. Alteration of pre-dive gas mixtures determined the extent of chemoreceptive influence upon the heart rate towards the end of these long dives.

Research supported by Medical Research Council of Canada.

80.3

AUTONOMIC NERVOUS CONTROL OF BLOOD PRESSURE AND HEART RATE DURING HYPOXIA IN THE ATLANTIC COD, *GADUS MORHUA*. Regina Fritsche and Stefan Nilsson. Dept. of Zoophysiology, Univ. of Göteborg, Sweden.

In the Atlantic cod, rapidly induced hypoxia produces increased ventral (P_{va}) and dorsal (P_{da}) aortic blood pressure, increased systemic resistance (VR_s), bradycardia and increased plasma concentrations of catecholamines. In the present study, the autonomic nervous and possible adrenergic humoral control of blood pressure and heart rate during hypoxia, 4.0-5.3 kPa (30-40 mmHg), was investigated in the Atlantic cod. Bretylium, known to prevent transmitter release from adrenergic nerve endings, was used as a chemical tool to differentiate between neuronal or humoral adrenergic control of blood pressure and heart rate (f_H) during hypoxia. The hypoxia-induced increase in P_{va} and P_{da} was strongly reduced in bretylium-treated cod, which suggests that adrenergic nerves are responsible for the hypoxic hypertension. In addition, a small contribution by circulating catecholamines to the adrenergic tonus affecting P_{va} during hypoxia is suggested by the decrease in P_{va} induced by injection of the α-adrenoceptor antagonist phentolamine into bretylium-treated cod. The cholinergic and adrenergic tonus affecting heart rate were estimated by injections of atropine and the ß-adrenoceptor antagonist sotalol. The experiments demonstrate an increased cholinergic as well as adrenergic tonus on the heart during hypoxia.

This work was supported by the Swedish Natural Science Research Council, the Hierta-Retzius Foundation, the Längmanska Cultural Foundation, the Royal and Hvitfeldtska Foundation and the Magn. Bergvall Foundation.

80.4

PRESSURE-FLOW RELATIONSHIPS IN A PERIPHERAL VASCULAR BED OF THE LOBSTER, Homarus americanus. George B. Bourne and Pollie Lumby*. The University of Calgary, Calgary, Alberta, Canada, T2N 1N4.

Pressure-flow relationships were used to establish functional attributes in the abdominal circulation of the lobster, Homarus americanus. In situ preparations were made by cannulating the dorsal abdominal artery via the ventricle. After allowing some time for the preparation to stabilize, repeated pressure-flow profiles were made using a modified version of the vertical-tube technique of Nichols et al. (Am. J. Physiol. 164: 330-344 [1951]). Experiments were carried out at 10°C using artificial seawater as the perfusate. Over the 90 min time course of an experiment, there was a small tendency for flow to decrease. Under conditions of unchanging output pressure, flow became relatively constant at higher input pressure. This maintenance of constant flow indicated that there are inherent mechanisms for adjusting hydraulic resistance in this region of the lobster circulatory system. Since lobster arteries appear to lack muscle, regulating hydraulic resistance by this means of reducing vessel diameter appears unlikely. Based on current anatomical knowledge, we suspect that these changes are mediated neurally by altering the degree of closure of an (some) unidentified valve(s). (This research was supported by NSERC and the University of Calgary.)

80.5

BLOOD PRESSURE DURING THERMAL AND HYPOXIC STRESS IN PIGEONS. A. D. Bustamante*, R. A. Furilla*, and M. H. Bernstein. NM State Univ., Las Cruces, NM 88003

Most available blood-pressure (BP) data in birds are variable and inconsistent, and few data are available for combined hypoxic and thermal stress. We therefore measured resting BP in pigeons (Columba livia, mass 0.6 kg) with a brachial-artery catheter connected to a small pressure transducer near the point of skin exit. This minimized damping and hysteresis artifacts. After recovery, the bird was placed in a dark chamber at constant air temperatures (T_a) of 6, 25, or 40°C and at constant, normobaric PO_2 of 138, 85, or 65 Torr. In normoxic birds, steady-state systolic and diastolic pressures (P_S and P_d) varied inversely with T_a, ranging from 133 to 147 Torr and from 93 to 110 Torr, respectively. Pulse pressure ($PP = P_S - P_d$) and mean arterial pressure (MAP) increased with decreasing T_a. The derivative of arterial pressure (dP/dt) did not vary with T_a, suggesting constant cardiac contractility. During hypoxia, P_S increased with decreasing T_a; however, P_S decreased with decreasing PO_2. The same was true of P_d and MAP; dP/dt decreased with decreasing PO_2 only. P_S, MAP, and PP were highly correlated with dP/dt in hypoxic birds. The data suggest that at high altitude the effects of decreased T_a might offset those of decreased PO_2, thereby minimizing changes in BP. (Supported by NSF grant BSR-8806604.)

80.6

REDISTRIBUTION OF CARDIAC OUTPUT IN RESPONSE TO HYPOXIA IN THE CRAYFISH. Carl L. Reiber. Dept. of Zoology, Univ. of Mass., Amherst MA 01003.

While crayfish regularly encounter waters of reduced oxygen tension, the hemodynamic responses to this stress have not been investigated. Restrained crayfish (*Procambarus clarkii*) maintained at 25 °C were exposed sequentially to 150 mm Hg O_2 (control), followed by PO_2s of 25, 40, 75, and 115 mm Hg. A pulsed Doppler system was used to simultaneously record hemolymph flow velocities in three major arteries (anterior aorta, sternal artery, posterior aorta) leading from the heart. Heart rate, cardiac output and tail movements were also monitored. Hemolymph flows and heart rate stabilized within 20 minutes following exposure to lowered PO_2. Heart rate decreased from 150/minute under control conditions to 60/minute at 25 mm Hg. Hemolymph flow through the anterior aorta was conserved at all levels of hypoxia. Flow in the posterior aorta flow was unchanged at 115 mm Hg but declined dramatically at lower PO_2s. Mean sternal artery flow increased during moderate hypoxia, but with severe hypoxia (25 mm Hg) sternal artery flow decreased. Tail movements declined from 18 flips/h during control and moderate hypoxia to 1 flip/h at more severe levels of hypoxia. During tail flips, flow through the sternal artery increased from 2 to 10 fold, likely due to an increased venous return. The circulatory response to hypoxia in the crayfish defends hemolymph flow to the anterior regions of the animal. This is accomplished through the redistribution of cardiac output, resulting in a greater proportion of the hemolymph being pumped anteriorly in the animal. Supported by NSF grant DCB-8916938 to Warren Burggren.

80.7

SIMULTANEOUS DETERMINATION OF BLOOD VOLUME AND EXTRACELLULAR FLUID SPACES IN FISH WITH TWO GAMMA-EMITTING NUCLIDES. M.D. Kellogg, D.W. Duff, D.E. Kullman and K.R. Olson. Dept. Biol. Sci., U. Notre Dame,and Ind. U. Sch. Med., South Bend Ctr., U. Notre Dame, Notre Dame, IN 46556.

Methods for measuring blood volume (BV) and extracellular fluid space (EFS) in fish have employed B-emitting or monovalent nuclides. The former necessitate tissue digestion and liquid scintillation spectrometry; the latter may be influenced by osmoregulatory processes. In the present study ^{51}Cr-tagged red cells (Cr-RBC) and ^{60}Co-chelated to ethylenediamine-tetraacetate (Co-EDTA) were injected into fresh water (FW) or sea water (SW) adapted rainbow trout (*Salmo gairdneri*; 200-500 g) to determine BV and tissue red cell space (RCS; both with Cr-RBC method) and EFS and tissue extracellular space (TES; both with Co-EDTA method). Dorsal aortic blood was taken at 1, 2, 4 and 8 h after injection of ^{51}Cr-RBC and ^{60}Co-EDTA and tissue samples at 8 h. BV and EFS stabilized by h 4. At 8 h BV in 6 FW and 5 SW trout was 39.5±5.2 and 38.2±4.3 ml.kg^{-1}; mean+SE, respectively; EFS was 257±60 and 262±18 ml.kg^{-1} for FW and SW, respectively. RCS and TES were tissue specific. These results show that this method is a quick and reliable procedure with which to measure blood and fluid spaces in fish. Supported by NSF Grant No. DCB 8616028.

80.8

VASCULAR EFFECTS OF ENDOTHELIN IN TROUT. K. R. Olson, M. D. Kellogg, and J. F. Villa. Indiana U. Sch. Med., South Bend Center, U. Notre Dame, Notre Dame, IN 46556.

Endothelin-1 (ET-1) is one of the most potent vasoconstrictors in mammals. The present study describes the cardiovascular effects of ET-1 in vivo and in a perfused trunk preparation from rainbow trout, *Salmo gairdneri* (unknown strain), and in vascular rings from steelhead trout, *S. gairdneri* (Skamania strain). In vivo: Dorsal aortic blood pressure (DAP) was monitored in unanesthetized trout during graded ET-1 injections. Perfused trunk: Skeletal muscle and kidney were perfused via the dorsal aorta (PDA) and splanchnic tissues perfused via the celiacomesenteric artery (PCA). Vascular rings: Rings were cut from the celiacomesenteric artery (CA) and anterior cardinal vein (CV) and mounted in muscle chambers. In vivo, 10^{-8} M ET-1 produced a transient (10 min) 9 mmHg decrease in DAP (n=7); 10^{-9} and 10^{-10} were ineffective. ET-1 (10^{-6} M) increased PDA resistance from 0.36±0.07 to 0.88±0.15 and PCA resistance from 2.4±0.3 to 7.5±1.1 mmHg.ml^{-1}.min^{-1} per 100 g body wt (n=4). Threshold responses were observed in PDA and PCA at ET-1 levels <10^{-12} M (n=4).Both CA and CV (n=8) exhibited dose-dependent contractile responses to ET-1 (EC50 = 2x10^{-9} M and 7x10^{-9} M for CV and CA, respectively. Threshold contractions were seen at <10^{-10} M. These results show that ET-1 is a potent vasoconstrictor in trout in vitro. Supported in part by NSF Grant No. DCB 8616028.

80.9

VASCULAR COMPLIANCE OF TROUT VESSELS. **D.J. Conklin and K.R. Olson. Dept. Biol. Sci., U. Notre Dame and Ind. U. Sch. Med., South Bend Ctr., U. Notre Dame, Notre Dame, IN 46556**

Anterior cardinal veins (ACV; length 5-8.5 mm) and efferent branchial arteries (EBA; length 4-7 mm) were isolated from 300-600 g rainbow trout (*Salmo gairdneri*) and intraluminal pressure (P) was monitored during incremental volume (V) expansion. Compliance (C; [$\Delta V/\Delta P$]) was measured in control vessels and vessels stimulated with epinephrine (Epi; 10^{-10}, 10^{-8}, 10^{-6} M), norepinephrine (Nepi; 10^{-10}, 10^{-8}, 10^{-6} M) and angiotensin II (AII; 10^{-9}, 10^{-8}, 10^{-7} M). C (mean±s.d.) was 21 fold greater in ACV than EBA (2.05±0.99 and 0.098±0.027 µl/mmHg, N=14,13, respectively). ACV compliance curves were non-linear, whereas EBA curves were linear at physiological pressures. Epi had no effect on C in ACV. Epi (10^{-8} M) significantly (P<0.05) lowered C in EBA to 0.078±0.029 µl/mmHg (N=11). Epi (10^{-10} or 10^{-8} M) increased C in 80% and 66% of EBA examined. Nepi had no effect on C in ACV. Nepi (10^{-6} M) significantly (P<0.05) lowered C in EBA to 0.061±0.005 µl/mmHg (N=4). Nepi (10^{-10}, 10^{-8} M) had no effect on C in EBA. AII had no effect on C in either ACV or EBA. Venous:arterial compliance ratios are similar in trout and mammals (21:1 and 24:1, respectively). In trout, catecholamines appear to change arterial compliance in an apparent biphasic pattern. **Supported in part by NSF Grant No. DCB 8616028.**

80.10

PREOXYGENATION DELAYS ONSET OF THE CUSHING RESPONSE IN A BLUEFISH. A.B. DuBois, S.H. Fox*, and C.S. Ogilvy*. John B. Pierce Laboratory, New Haven, CT, 06519.

Arterial hypertension (the 'Cushing response') of bluefish begins 4 sec after intracranial pressure is increased. Theoretically the onset could be due to cerebral hypoxia, hypoglycemia, or lowered pH caused by external compression of cerebral blood vessels. To distinguish between these, we used a method adapted from Carlisle, Lanphier, and Rahn (J. Appl. Physiol. 19:914-918, 1964), who compressed the eyeball and found visual blackout beginning in 4 sec when breathing air, but delayed to 50 sec when breathing O2 at 4 atm. We presaturated a bluefish with oxygen dissolved in cool seawater, and found a delay in the onset of the Cushing response amounting to 21 sec. Air dissolved in cool seawater or oxygen in warm seawater did not cause such a delay. The tentative conclusion is that cerebral ischemia led to cerebral hypoxia which produced peripheral vasoconstriction, causing a compensatory rise in blood pressure. It is by no means certain that the vasomotor hypoxic response would be dominant in mammals, because their ventilation and cerebral blood flow are responsive to arterial CO2 tension whereas CO2 tension in fish is kept low through loss of CO2 from the gills while arterial oxygen levels in fish are more marginal.

80.11

CHARACTERIZATION OF Na/Ca EXCHANGE IN THE MYOCARDIUM OF RAINBOW TROUT. Glen F. Tibbits and Haruyo Kashihara*
Simon Fraser University, Burnaby, B.C., CANADA

Na/Ca exchange (Na/CaX) is the primary mechanism of Ca efflux across the sarcolemma (SL) and contributes therefore to mechanical relaxation in the mammalian heart. This study sought to compare trout myocardial Na/CaX (T-Na/CaX) with that from mammals (M-Na/CaX). In SL isolated from the ventricles of cold-adapted trout and purified 15 fold, the apparent Km (Ca) and the Vmax were 13 µM and 7.7 nmol/mg/s respectively at 21°C. T-Na/CaX was stimulated by 167% in the presence of 5 µM valinomycin, indicating that it is electrogenic as is M-Na/CaX. Antibodies raised against dog heart Na/CaXer cross-reacted with trout SL on Western blots with bands of 70, 120 and 160 kDa as in mammals. Chymotrypsin stimulated T-Na/CaX by 200% and increased the intensity of the 70 kDa band. T-Na/CaX was studied over a temperature range of 7-37°C in both the native (NV) and asolectin reconstituted (RV) vesicles. At 10 µM Ca, T-Na/CaX velocity was 4.1 and 8.4 nmol/mg/s in RV at 7 and 21°C respectively. The rates of T-Na/CaX in both NV and RV at 7°C are many fold higher than M-Na/CaX. These data suggest that the relative insensitivity of T-Na/CaX to cold is an intrinsic property of the exchanger itself. Although T-Na/CaX is similar in in many respects to that in mammals, the unique temperature dependence may be an important adaptation maintaining cardiac function in cold water.

Supported by NSERC

COMPARATIVE PHYSIOLOGY: KIDNEY/NITROGEN EXCRETION

81.1

EFFECTS OF MESOTOCIN ON RENAL FUNCTION IN THE DOMESTIC FOWL. Pat Marks* and T. I. Koike, Univ. of Arkansas for Med. Sci., Little Rock, AR 72205.

In chickens, plasma levels of Mesotocin (MT), the avian oxytocin-like neurohypophysial peptide, is increased by infusing a hypotonic saline solution and decreased by hypovolemia. In this study graded doses of MT (0.46, 0.92 and 1.84 ng/min/kg) were infused to determine their effects on renal function in conscious, hydrated cockerels. Glomerular filtration rates were not significantly altered by the elevations in plasma MT. Urine flow (V) and sodium excretion ($U_{Na}V$) were increased during infusion of the high MT dose (P<0.05).

	Low MT Dose		Medium MT Dose		High MT Dose	
	C	Exp.	C	Exp.	C	Exp.
P_{MT}	47.8	89.8	41.6	123.4	43.4	207.7
(pg/ml)	±2.5	±5.7**	±2.5	±9.4**	±3.	±14.4**
V	0.13	0.15	0.11	0.16	0.18	0.24
(ml/min)	±0.02	±0.02	±0.02	±0.02	±0.02	±0.03*
$U_{Na}V$	4.8	6.7	4.9	7.7	4.9	9.1
(µEq/min)	±0.7	±1.4	±1.1	±1.2	±0.5	±0.7*

**P<0.01, *P<0.05

The natriuresis and diuresis observed appears to be due to tubular actions of MT. (Supported by NSF DCB86-17476 and UAMS Graduate Research Fund).

81.2

FACTORS INFLUENCING THE SCALING OF RENAL STRUCTURE AND URINARY CONCENTRATING ABILITY IN MAMMALS. Carol A. Beuchat. Univ. of Arizona, Tucson, AZ 85724

The urinary concentrating ability of the mammalian kidney varies substantially among species. Some of this variability in concentrating ability is accounted for by differences in body size: maximum urine concentration declines with increasing body mass even though the length of the loop of Henle increases. To explore the contribution of other factors to differences in concentrating ability, I compiled a data base on over 350 species of mammals that includes information on renal morphology, maximal urine concentration, and several ecological and phylogenetic variables. For animals of a given body mass, concentrating ability increases with length of the loop of Henle, as would be predicted from counter-current multiplier theory. In turn, some of the interspecific variability in loop length reflects the influence of habitat: species from arid environments generally have the longest loops, and are also generally the best concentrators, followed by species from mesic, freshwater, and marine environments. Furthermore, most of this variability across habitats in total loop length reflects variability in the length of the thin ascending limb, while the length of the thick ascending limb varies little. In some instances, it is apparent that diet can override the influence of habitat: the poorest concentrator, Sanborn's long-nosed bat, occurs in the desert, but it is nectarivorous and probably has little need to conserve water. The gross morphology of the mammalian kidney varies enormously among species, from the unipapillary kidney typical of rodents to several types of multipapillary kidneys in larger mammals. The scalings of loop length and concentrating ability vary with kidney type, but the reason these different types of kidneys are necessary remains unclear. Concentrating ability varies strikingly among species when sorted by taxon. For example, artiodactyls can produce a more concentrated urine than rodents of the same body mass. Surprisingly, however, there are no parallel patterns in the scaling of loop length that might account for these differences. (Supported by NSF DCB 88-96203 and NIH BRSG 328728).

81.3

EFFECTS OF CHRONIC AND SHORT-TERM WATER RESTRICTION ON DRINKING AND KIDNEY FUNCTION IN BOBWHITE QUAIL. David L. Goldstein and Christine C. Ellis*. Wright State Univ., Dayton, OH 45435.

Water restriction during growth of bobwhite quail causes decreased whole-body growth, but kidney mass is not reduced and the renal medulla hypertrophies. In the present study, we infused polyethylene glycol, PEG, via implanted osmotic pumps to examine the renal response to changing water availability in birds raised with either restricted (DEH) or unrestricted (HYD) water. Given unrestricted water, DEH birds drank copiously (70 ml/48 hrs) compared with HYD birds (35 ml/48 hr). The elevated drinking persisted for at least one week, though body mass stabilitzed within 24 hr. Glomerular filtration rate, (GFR, 42 ml/hr) did not differ between the two groups with unrestricted water, but urine flow rate was higher (UFR, 1.9 vs. 1.2 ml/hr) and urine osmolality lower (U_{osm}, 306 vs. 426 mmol/kg) in DEH birds. Kidney function was tested during both short-term water restriction (4 days of restricted drinking) and acute dehydration (30 h with no water). GFR was reduced by similar extents in the two dehydration regimens, dropping to approximatly 21 ml/hr in both DEH and HYD birds; the pattern of response in GFR did not differ in the two groups (ANOVA). In contrast, the pattern of response in urine to plasma PEG ratio (U/P) did differ in the two groups. This was primarily the result of the response to short-term water restriction, when DEH birds had higher U/P values (98, vs. 53 in HYD) and consequently lower UFR (0.26 vs. 0.58 ml/hr). This occurred in the absence of any difference in plasma osmolality (359 vs. 358 mmol/kg in HYD and DEH birds). This study demonstrates that chronic water restriction during growth enhances drinking in bobwhite and alters certain renal responses to changing water availability.

81.4

REGULATION OF REPTILIAN RENAL FUNCTION BY VASOACTIVE HORMONES. Stanley D. Yokota. Department of Physiology, West Virginia University, Morgantown, WV 26505.

An isolated perfused ophidian kidney preparation was developed using the common garter snake (Thamnophis sirtalis) to investigate the dose-response relationships of renal function to controlled vasoactive hormone concentrations. Kidneys were perfused with an physiological solution containing complete salts, glucose, amino acids and 1% bovine serum albumin and Cr-EDTA as a glomerular filtration marker. Dual constant pressure perfusion of the kidney was accomplished by the cannulation of the dorsal aorta (40 mmHg) and of both renal portal veins (10 mmHg) by a pump-overflow system. Arterial renal perfusion was monitored continuously with an in-line electromagnetic flowmeter. Renal vascular resistance was calculated as the AV pressure gradient divided by the arterial perfusion rate. Volume reabsorption was determined by the $(U/P)_{Cr\text{-}EDTA}$. Arginine vasotocin (AVT, 1-1000 fmol/ml) and norepinephrine (NE, 10-10,000 pg/ml) both elicited glomerular antidiuresis at high concentrations but both may be diuretic at low concentrations. NE-induced diuresis was associated with decreasing fractional volume reabsorption as well as an increase in GFR. Since renal vascular resistance consistently increased with increasing concentrations of AVT and NE, post-glomerular resistance probably was disproportionately increased at low concentrations. The EC50 for renal vascular resistance was about 200 pg/ml for NE and quite variable for AVT (20-200 fmol/ml). Vasoactive intestinal peptide (VIP) caused a diuresis when administered to kidneys receiving perfusion with a high concentration of NE. This approach allows the precise evaluation of renal vascular, glomerular and tubular regulation by controlled concentrations of vasoactive hormones. (Supported by Am. Heart Assoc. WV Affiliate.)

81.5

THE ONTOGENY OF NITROGENOUS EXCRETION IN CHIROMANTIS XERAMPELINA (AMPHIBIA, ANURA). J.P. Loveridge* (SPON: V.H. Shoemaker). Dept. Biol. Sci., Univ. of Zimbabwe, P.O. Box MP 167, Harare, Zimbabwe.

Adults of the Central African frog, Chiromantis xerampelina, are uricotelic. Eggs are laid within a foam nest which is constructed above a temporary water body. Upon hatching the larvae drop out of the foam nest and complete development (until metamorphosis) in the water. The ontogeny of nitrogenous excretion was studied in eggs before hatching (Shumway stages 23-25) and from hatching to metamorphosis (Taylor & Kollros stages I-XXII). Ammonia production was initially high (at egg stage 24-25 81±21 μg NH_3 nitrogen $g^{-1}h^{-1}$ with some samples as high as 170 μg), falling off rapidly to 25 μg NH_3 nitrogen $g^{-1}h^{-1}$ at tadpole stage V and dropping slowly thereafter to 9 μg NH_3 nitrogen $g^{-1}h^{-1}$ at stage XXII. Urea production was never very great, rising from undetectable levels at egg stage 23 to 5 μg urea N $g^{-1}h^{-1}$ between tadpole stages VII-XX. Urate production was undetectable or low (<5 μg uric acid N $g^{-1}h^{-1}$) throughout. Urate was only produced in any quantity once the newly metamorphosed frogs fed on insect food.

/Supported by the University of Zimbabwe Research Board/.

81.6

UREA ACCUMULATION IN LARVAL SALAMANDERS: ROLE OF UREA CONSERVATION. Charles J. Costa and Brian T. Miller. Eastern Illinois Univ., Charleston, 61920 and Middle Tennessee St. Univ., Murfreesboro, 37130

Larval salamanders (Ambystoma tigrinum melanostictum) living in saline, alkaline ponds (300 mosm, pH 10) accumulate urea as a source of solute used to maintain normal osmotic balance. Ambystoma larvae produce urea using urea cycle enzymes with activities that are independent of exposure to saline water (SW) but may depend on alkaline conditions. Since urea synthesis appears not to be activated by SW exposure, urea accumulation must be mediated by limiting urea loss from the body. The route(s) of urea loss were determined in larvae acclimated to conditions favoring the establishment of high blood urea concentrations. Prior to the experiment, the animals were prevented from voiding urine by cloacal ligature then exposed to either fresh water (FW) or SW. Urea efflux across the skin was measured by monitoring the bath and renal urea loss was determined from urine removed from the bladder. An approximation of urine volume was made by measuring weight gain during the experimental period. Larvae in both FW and SW lost similar amounts of urea across the skin. The major route of urea loss in FW was via the kidney - salamanders in FW produce 5-8 times more urine than do animals living in SW. Thus, no complex mechanism needs to be postulated to account for the observed urea accumulation in saline conditions.

HIBERNATION AND HYPOTHERMIA

82.1

THE BIOCHEMICAL ADAPTATIONS OF THE LIPIDS PRODUCED FOR HIBERNATION BY GROUND SQUIRRELS. Craig L. Frank. Univ. of California, Irvine, CA 92717

Ground squirrels are small herbivores common to the alpine meadows of North America. These rodents hibernate during the winter and prior to hibernation, body mass increases dramatically. One important nutritional/physiological limitation on prehibernatory fattening and winter survival may be the melting point of the stored fat, since lipids must be fluid to be metabolizable. Most mammalian fats have melting points of about 30 C, and are thus inadequate to support hibernation since they cannot be utilized at low body temperatures. The melting point of a lipid decreases with increasing unsaturation in the fatty acid portions of the molecule. Depot fat samples were taken from captured golden-mantled squirrels (Spermophilus lateralis). Analyses reveal that these fats are three times more unsaturated than those of other mammals, containing mostly plant-produced polyunsaturated fatty acids. Their melting points were thus 3 to 5 C. This indicates that the extent to which ground squirrels can hibernate depends largely on diet composition.

82.2

TISSUE-SPECIFIC METABOLISM DURING NORMOTHERMY AND DAILY TORPOR IN DEER MICE. James R. Nestler. Univ. of Colorado, Boulder, CO 80309-0334

Glucose metabolism was measured in tissues from normothermic deer mice (T_b 36.3±1.4 °C) and mice in daily torpor (T_b 21.8±2.1 °C). Heart and skeletal muscle were each incubated in one of three media with in vivo metabolite levels (glucose, palmitate, lactate, acetoacetate, β-hydroxybutyrate) and acid-base conditions. The first medium (NORM37) emulated normothermic conditions (37 °C, pH 7.37, pCO_2 43 torr). The second medium (NORM25) was maintained at 25 °C, with temperature-corrected normothermic pH (7.56) and pCO_2 (26 torr). The third medium (TORPOR) resembled torpor conditions (25 °C, pH 7.38, pCO_2 55 torr). Total glucose metabolism (μmol/g·h; mean±SE) was calculated by trapping $^{14}CO_2$ oxidized from ^{14}C-glucose and determining glucose specific activity in the tissues.

	NORMOTHERMIC MICE (n=5)		TORPID MICE (n=4)	
	Heart	Muscle	Heart	Muscle
NORM37	0.54±0.05	0.60±0.06	1.06±0.06	0.55±0.04
NORM25	0.96±0.09	0.20±0.05	0.58±0.05	0.31±0.04
TORPOR	1.17±0.07	0.30±0.06	0.62±0.06	0.17±0.02

Glucose metabolism in normothermic heart was increased in response to decreased temperature, suggesting some type of tissue-specific compensation. In contrast, skeletal muscle showed a reduction in glucose metabolism, with torpid muscle undergoing a further decline under torpor conditions. This further reduction may be a possible mechanism to spare low endogenous carbohydrate levels during dormancy in skeletal muscle.

82.3

NEW EVIDENCE FOR THE HIBERNATION OF BEARS: EFFECTS OF CHANGE IN CLIMATE. G. Edgar Folk, Jr., Jill M. Hunt* and Mary A. Folk*. Univ. of Iowa, Iowa City, IA 52242

Some physiologists still deny that bears hibernate; the evidence for this hibernation will be reviewed. The principle of a changing TR set-point (Hammel) applies easily to the hibernation of small mammals; rapid physiological changes can occur. The principle must be applied differently with animals weighing 130 k to 450 k where body temperature changes would take days. T_c of bears in hibernation is reduced only by 7° or 8°C. But rapid changes occur in heart rate; three species of bears have a sleeping summer heart rate between 40 to 50 bpm but in hibernation the rate is reduced to 8 to 10 bpm. In the EKG, small hibernators are known to have a very short QT interval both when normothermic and hibernating. Thus repolarization of the ventricle occurs rapidly after contraction. We reported earlier that the QT intervals of hearts of summer sleeping bears are physiologically similar to those of small hibernators (marmot .15 sec ±.03 SE, HR 90 bpm; polar bear .14 ±.01 SE, HR 48; man .45, HR 60). New experiments show that with the same heart rates (84-94 bpm), small hibernators and bears both increased QT interval in Winter (W): woodchuck Summer (S).07 ±.01, W .08 ±.01; marmot S .14 ±.03, W .17 ±.06; grizzly bear S .20 ±.04 W .30 ±.03; black bear S .21 ±.01, W .22 ±.01; polar bear S .13 ±.01, W .15 ±.01. The effects of climate change on ice-transported polar bears of Hudson Bay will be discussed. (Supported by NSF and ONR).

82.4

BODY TEMPERATURE VARIATION IN HIBERNATING RATTLESNAKES. Charles R. Peterson and Vincent A. Cobb.* Idaho State University, Pocatello, ID 83209.

Although many species of temperate ecothermic vertebrates spend a considerable amount of time hibernating, surprisingly little is known about body temperature (T_b) selection during this period. To measure body temperature variation and associated movements during hibernation, we surgically implanted temperature-sensitive radiotransmitters into seven, adult Western Rattlesnakes (*Crotalus viridis*). We captured the snakes in September of 1989 at a den site in the desert on the INEL National Environmental Research Park in southeastern Idaho and released them by mid October. Body temperatures were measured once per week and environmental temperatures were measured every 30 minutes using thermocouples and a datalogger. Most of the snakes entered hibernation during late October and all were hibernating by mid November. Mean body temperatures decreased from approximately 12°C in mid November to a minimum of 6°C in late February and then increased to approximately 7.5°C by late April. The lowest T_b experienced by any of the snakes was 4.2°C. During the winter, differences in T_b's among individuals measured at the same time were as great as 4.2°C. Dates of emergence ranged from May 4th to May 22nd. These results indicate considerable interindividual variation in body temperature selection by hibernating snakes. Future research should focus on the consequences of this variation and its relationship with the physiological condition of the individual snakes.

82.5

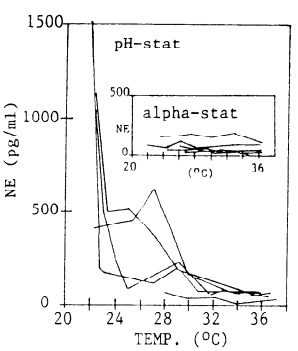
ARTERIAL ACID-BASE STATE DURING ENTRANCE INTO FASTING-INDUCED HYPOTHERMIA IN PIGEONS (*COLUMBA LIVIA*). Chris Jensen* and Claus Bech. Dept. Zool., Univ. Trondheim, N-7055 Dragvoll, Norway.

Low body temperature during torpor and hibernation in mammals is followed by a relative acidosis, which has been interpreted as having an inhibitory effect on the metabolic rate. No comparable studies exists for birds. We studied the respiratory and acid-base changes occurring during the entrance into fasting-induced nocturnal hypothermia in pigeons. Minimum nocturnal body temperatures reached was 35-38°C. Q_{10}, relating oxygen uptake to body temperature, was high (>4.0) at the very beginning of entrance into hypothermia. Both total ventilation and oxygen consumption decreased with a reduced body temperature. The ventilatory requirement, however, did not significantly change. Arterial pH and pCO_2 (measured at constant temp. of 40°C) was significantly reduced (0.016 units/°C) and increased (-2.0 torr/°C), respectively, with a decreased body temperature. The data shows that hypothermia in pigeons is paralleled by a relative acidosis. It also seems that there is an active metabolic inhibition at the beginning of the hypothermic period, but the data do not necessarily allow us to link this inhibition to the acidotic state.

82.6

PROFOUND ELEVATION OF NOREPINEPHRINE CONCENTRATION DURING HYPOTHERMIA WITH pH-STAT REGULATION. David C. Willford, Richard M. Garden*, Esther Hill, and Walter Schaffartzik*. Dept. Medicine, M-023A, UCSD, La Jolla, CA 92093.

We previously noted elevated norephinephrine (NE) concentration with pH-stat acid-base regulation during moderate (29 C) hypothermia (Physiologist 32:203, 1989). We have now extended our measurement of NE in 10 immature domestic pigs during cooling to approximately 23 C. In 5 pigs cooled with pH-stat management (constant pH = 7.4 in vivo at all temperatures), NE concentrations increased an average of 19-fold between 37 C and 23 C with pH-stat management (Figure to left). In 5 pigs cooled with alpha-stat pH management (i.e. an in vivo pH that increases 0.014 pH units/ C decrease), the corresponding increase in NE concentration was less than 50% (Figure insert). The NE response with pH-stat appears to be similar to that with acidosis. Supported by NIH HL 17731 and the Parker B. Francis Foundation.



82.7

SHORT-TERM EXPOSURE TO TEMPERATURES LESS THAN 10 °C DOES NOT INCREASE CAPILLARY PERMEABILITY IN THE ISOLATED CAT HINDLIMB. L.P. Porter* and M.B. Wolf. Physiology Dept., Univ. of South Carolina, Columbia, SC 29208.

We determined the albumin solvent drag reflection coefficient (σ_f) using the IMB method (Wolf, et al., Am. J. Physiol., 253:H194, 1987) after lowering limb temperature to ~6 °C by cooling the blood perfusing the limb at constant flow and reducing the ambient temperature. To prevent edema at this low temperature, venous pressure had to be lowered to just above venous collapse and the flow to < 10 ml/min/100g. We theorized that low temperature caused a tissue injury with an increase in microvascular permeability (decrease in σ_f). However, we found that after exposure of the limb to temperatures under 10 °C for ~60 min, σ_f was not decreased from the 37 °C control. Total vascular resistance increased by > 4 times at ~6 °C which was similar to the increase in postcapillary resistance we found previously at this temperature (Zhang et al., FASEB J., 4:A1278, 1990). Hence, the tendency for edema formation was likely caused by an increase in capillary hydrostatic pressure. We conclude that short-term exposure to very cold, but above freezing, temperatures does not cause increases in capillary permeability in this preparation. However, it is possible that the permeability-increasing effect of tissue damage does not occur until rewarming. Sup. by the Nav. Med. Res. and Dev. Cmd. Combat Casualty Care Prog. and NIH grant HL 39691.

82.8

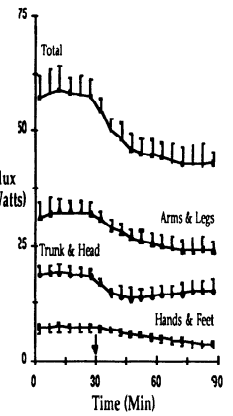
TISSUE TEMPERATURE SENSITIVITY IN THE NINE-BANDED ARMADILLO (*DASYPUS NOVEMCINCTUS*). Martha E. Heath PRL, University of California, San Diego, CA 92093

The purpose of this study was to evaluate the temperature sensitivity (TS) of the skin (STS), hypothalamus (HTS) and total body (TBTS), to cold in the nine-banded armadillo (n=12). TS was assessed as the relationship between tissue or whole body temperature and rate of heat production (HP; in Watts/kg)). Measurements included skin (T_{sk}: head, back, belly, tail, leg), rectal (T_{re}: > 8 cm past anal opening) and hypothalamic (T_{hy})temperatures monitored with thermocouples, and rate of O_2 consumption measured in an open-circuit system utilizing a dual channel Applied Electrochemistry O_2 analyzer. Prior to doing experiments, a 4-tube thermode array with a central thermocouple re-entrant tube was implanted to straddle the pre-optic and anterior regions of the hypothalamus. Surgical procedures were done in sterile conditions while animals were under general anesthesia. For assessment of STS, HTS and TBTS, T_{sk} was altered by changing ambient temperature, T_{hy} was altered with the water-perfused thermode, and total body temperature was lowered using heat exchangers introduced in the lower intestinal tract. STS was -0.39 W/kg per °C. HTS was -0.45 W/kg per °C. TBTS averaged -1.74 W/kg per °C. Resting metabolic rate averaged 1.2 W/kg. These values are lower than those reported for other eutherian (placental) mammals of similar body mass. But when these TS values are standardized by expressing them as a percent of each animals RMR, they are comparable to values found in other eutherian mammals. It is concluded that the afferent temperature signals driving the armadillo's thermoregulatory mechanism are similar to that found previously in other eutherian mammal species. (Support: 5 F32 NS06516).

82.9

THERMOREGULATORY VASOCONSTRICTION MINIMALLY DECREASES CUTANEOUS HEAT LOSS. DI Sessler, A Moayeri,* R Støen,* B Glosten,* and J McGuire.* UCSF, San Francisco, CA 94143

With IRB approval, we determined the extent to which thermoregulatory vasoconstriction decreases heat loss to the environment in 5 minimally clothed volunteers in a 30.8 ± 0.1°C environment. Vasoconstriction was induced by central venous infusion of cooled fluid. The infusion decreased tympanic temperature ≈ 1.5°C and provoked shivering. Finger blood flow (venous-occlusion plethysmography) decreased 15 fold. However, blood flow in skin covering the trunk (laser Doppler) only decreased 40%. Total heat loss (sum of area-weighted loss from ten thermal flux transducers), and loss from the arms and legs decreased ≈ 25% (15.5 ± 0.3 watts). Heat loss from the trunk and head decreased only 17%, whereas, loss from the hands and feet (10.5% of the body surface area) decreased ≈ 50%. Thermoregulatory vasoconstriction appears to only minimally decrease cutaneous loss of metabolic heat to the environment.



82.10

THE ROLE OF LIGHT EXERCISE ON THE ONSET AND INTENSITY OF SHIVERING IN COLD EXPOSED HUMANS. L. E. Wittmers, D. Israel* and R.G. Hoffman* Hypothermia and Water Safety Laboratory, Depts. of Physiology and Behavioral Sciences, University of Minnesota-Duluth School of Medicine, Duluth, MN 55812.

One response to cold exposure is shivering, which produces heat to maintain core temperature. It would seem reasonable that if cold exposure was coupled with exercise, the extra heat produced might affect shivering. In order to investigate this possibility, 13 lightly dressed male volunteers were exposed to 1°C air for three hours. Surface EMG activity was monitored on seven muscle groups. Rectal and skin temperatures were monitored throughout the experiment. Two 12 minute exercise periods were scheuled during the first hour of exposure. During exercise the subject maintained his heart rate at 70% of the predicted maximum. Thirty second EMG samples were obtained, at a predetermined time, via analog to digital conversion and the root mean square (RMS) voltage computed as an estimate of shivering intensity. In the protocols containing the exercise components the onset of shivering is delayed well into the second hour, in contrast to the first half hour in the nonexercise protocols. By the end of the second hour shivering in the exercise protocols exceeded that demonstrated in the controls. Rectal temperatures in the exercise experiments rose during exercise up to 60 minutes (+0.6 0°C) then decreased, reaching comparable values to the controls by the end of the experiment. Skin temperatures were not significantly different when the exercise and non exercising protocols were compared. The increased core temperature resulting from the exercise could have overridden the peripheral input at the hypothalamic level,resulting in a delayed shiver onset. (Supported in part by U.S. Army Medical Research Support Grant#DAMD17-88-C-8054 and U. S. Naval Medical Research Command Grant#N00014-88-k0582).

82.11

MECHANISMS OF DIISOPROPYL FLUOROPHOSPHATE (DFP)-INDUCED HYPOTHERMIA IN THE RAT. C.J. Gordon, L. Fogelson, and J. Highfill. U.S. EPA, Research Triangle Park, NC 27711.

DFP is a potent, irreversible inhibitor of acetycholine esterase and induces hypothermia along with other toxicological effects. To understand the mechanisms of DFP-induced hypothermia, metabolic rate (MR), evaporative water loss (EWL), body temperature (T_a), tail skin temperature (T_t), and motor activity (MA) were measured following 0 to 1.5 mg/kg (s.c.) DFP at ambient temperatures (T_a) of 10, 20, and 30 °C. DFP at doses of ≥ 1.0 mg/kg induced hypothermia at all three T_a's, but the effect was attenuated at 30 °C. MR was reduced at 20 °C following 1.5 mg/kg DFP, unaffected at 30 °C, and slightly stimulated at 10 °C. EWL was significantly increased at 30 °C following 1.5 mg/kg DFP. MA was reduced following ≥ 1.0 mg/kg DFP at 20 and 30 °C and 1.5 mg/kg DFP at 10 °C. T_t was elevated by DFP at 30 °C and reduced at 10 °C. In another study, rats were injected with DFP and placed in a temperature gradient while selected T_a, MA, and T_b were monitored. T_b and MA were significantly depressed at 1.0 and 1.5 mg/kg DFP while selected T_a was similar to that of the controls. However, DFP treated animals failed to select warmer T_a's in the temperature gradient which would have attenuated the DFP-induced hypothermia. These data demonstrate that T_a can significantly affect the toxicological efficacy of DFP and further suggest that DFP may elicit a reduction in set-point.

REGULATION OF EPITHELIAL FUNCTION BY ENVIRONMENTAL FACTORS

83.1

SUCRASE AND LACTASE ACTIVITY DURING EARLY DEVELOPMENT: GENETIC AND DIETARY INFLUENCES. Y.M. Vega*, A.A. Puchal*, and R.K. Buddington. Biological Sciences, Mississippi State University, Mississippi State, MS 39762.

Genetic and dietary factors have been identified as signals regulating development of the intestine, however, the relative roles of each remain unclear. Hence, we examined the well-known reciprocal changes in sucrase and lactase activity using litters of Yorkshire piglets removed from the sow 24-35 hours after birth and divided into one group fed a milk replacer containing lactose (LAC) and a second group fed an identical milk replacer, except the lactose was replaced by a 60:40 mixture of maltodextrin:sucrose (MDS). We assayed for lactase and sucrase using brush-border membrane vesicles prepared from the proximal, mid, and distal small intestine of piglets from each group just prior to being fed the two milk replacers and at 5, 10, 15, and 20 days of age. During the first 10 days of postnatal development piglets from both groups were similar in having low sucrase activity and high lactase activity per mg protein when averaged over the three regions. Between 10 and 15 days sucrase activity increased whereas lactase activity declined in both groups, implying the reciprocal shifts are triggered by signals that are independent of dietary inputs. Despite declining lactase activity per mg protein during suckling, total lactase activity (calculated as the product of lactase activity per mg protein in each region times the total quantity of brush-border protein in each region and summed over the entire intestine) increased in both groups due to intestinal growth with the greatest increases in the LAC piglets. Therefore genetic programming is responsible for (1) maintaining low sucrase and high lactase activities during the first 10 days after birth and (2) triggering the reciprocal shifts in activities between 10 and 15 days. However, the magnitude of the reciprocal shifts are influenced by dietary composition. Supported by the Carnation Company.

83.2

INCREASED MERCURY RESISTANCE IN MONKEY GINGIVAL AND INTESTINAL BACTERIAL FLORA AFTER PLACEMENT OF DENTAL "SILVER" FILLINGS A.O. Summers* and J. Wireman*. Microbiology Dept., Univ. of Georgia, Athens, GA; M.J. Vimy* and F.L. Lorscheider. Depts. of Medicine and Physiology, Univ. of Calgary, Alberta, Can.

Mercury (Hg) vapor is continuously released from silver amalgam fillings in humans. However, the bioavailability and toxicological relevance of this Hg exposure is uncertain. Since an increase in Hg resistant bacteria in response to Hg contamination of soil or water is an indication of bioavailability of Hg in the environment, we examined whether the incidence of such bacteria in the gingival and fecal flora is altered following placement of amalgam tooth fillings. Occlusal fillings (16, total Hg 1500 mg) were inserted into two adult male cynomolgus monkeys under general anesthesia, using standard dental procedures. Duplicate samples (12) of fecal and gingival microbial flora were taken from each monkey during 10 days prior and 30 days after amalgam placement. Samples were cultured for Gram positive facultative oral bacteria and both Gram negative and Gram positive facultative fecal bacteria. Primary isolates were screened to determine the proportion resistant to Hg and to arsenate (As) and tetracycline (Tc), agents to which bacterial resistance is found in nature. While As and Tc resistance were detected continuously in all cultures, Hg resistance was undetectable until the 10th day after amalgam placement. Thereafter, levels of Hg resistance in gingival and fecal flora ranged from 1 to 100%, averaging 30% in both monkeys until termination. From the 3rd-30th day total fecal Hg excretion averaged 300µg/animal/day. Thus, ingested Hg is sufficiently bioavailable to select for a substantial increase in the proportion of Hg resistant bacteria in both the oral cavity and the intestine. Since Hg resistant bacteria convert Hg(II) or methyl-Hg(I) to volatile, lipid soluble Hg(0) (Summers, Ann Rev Microbiol 40:607-34, 1986), the increased incidence of such bacteria in flora may influence the pharmacodynamics and toxicity of ingested Hg from dental amalgam.

83.3

NEUROIMMUNE MODULATION OF COLONIC ION TRANSPORT IN A HIBERNATOR. H.V. Carey and K. Bielefeldt*. University of Wisconsin School of Veterinary Medicine, Madison, WI 53706.

Hibernating (HIB) and active (ACT) ground squirrels were used to examine seasonal changes in colonic mucosal structure and mast cell number, and the effects of neuroimmune mediators on ion transport. Sheets of distal colon were mounted in flux chambers and bathed with 37°C buffer. Basal short-circuit current (Isc), which reflects active ion transport, was (in $\mu A/cm^2$) 27±4 in HIB and 10±13 in ACT tissues. Mean tissue conductance (in mS/cm^2) was 13±2 in HIB and 18±1 in ACT. Electrical stimulation of enteric neurons increased basal Isc by 123±6 $\mu A/cm^2$ in ACT and 73±6 $\mu A/cm^2$ in HIB. Substance P (0.1μM), which stimulates mast cell degranulation, increased Isc in HIB by 19±6 $\mu A/cm^2$ and in ACT by 33±7 $\mu A/cm^2$. The mast cell mediators 5-HT (10μM) and histamine (10μM) increased Isc in HIB by 53±14 and 89±26 $\mu A/cm^2$, respectively. 5-HT increased Isc in ACT by 153±16 $\mu A/cm^2$. Mucosal mast cell number/mm^2 was 12 and 53 in HIB and ACT, respectively. Crypt depth, crypt width, and # crypts/mm were similar in HIB and ACT. Thus, despite extended food and water deprivation, colonic mucosa in HIB retains gross structure and ion transport capacity, and is responsive to neuroimmune mediators. However, mast cell number is reduced during hibernation, which may reflect altered nutritional status and/or an endogenous rhythm in immune competence.

83.4

THE EFFECT OF SODIUM CONCENTRATION IN A CARBOHYDRATE-ELECTROLYTE SOLUTION ON INTESTINAL ABSORPTION. C.V. Gisolfi, R.D. Summers, H.P. Schedl, and T.L. Bleiler. University of Iowa, Iowa City, IA 52242

Intestinal absorption during infusion (15 ml/min) of water or a 6% carbohydrate (2% glucose, 4% sucrose) soln containing either 0, 25 or 50 mEq/l Na^+ was measured by segmental perfusion with a triple lumen catheter in males (age 24.3±1.6) at rest. A 45-min equilibration period preceded a 75-min test session. Water and solute fluxs were determined from differences in concentration of polyethylene glycol and solute across a 40-cm intestinal segment of the duodenojejunum. A 2-factor repeated ANOVA indicated no differences (P>0.1) over time for water, Na^+, K^+ or glucose flux for all solns.

Solution	N	Water $ml\,hr^{-1}cm^{-1}$	Na^+ $mEq\,hr^{-1}cm^{-1}$	K^+ $mEq\,hr^{-1}cm^{-1}$	Glucose $mEq\,hr^{-1}cm^{-1}$
Water	10	-9.16±1.39	-0.157±0.10	0.0003±0.004	0.00±0.00
0 mEq/l Na^+	5	-13.16±1.15*	-0.328±0.17	-0.013±0.014	-1.31±0.03*
25 mEq/l Na^+	7	-14.22±1.00*	-0.512±0.11*	-0.041±0.010*†	-1.23±0.09*
50 mEq/l Na^+	7	-12.53±1.30	-0.575±0.13*	-0.024±0.008*	-1.33±0.07*

*P<0.05 from water †P<0.05 from 0 Na^+

Compared with plain water, (a) 25 mEq Na^+ enhanced (P<0.05) water, Na^+, K^+ and glucose absorption; (b) carbohydrate without Na^+ increased (P<0.05) water and glucose absorption, and (c) 50 mEq Na^+ increased (P<0.05) Na^+, K^+ and glucose absorption. Plasma volume increased (P<0.01) ≈ 5% over time with no difference between solns. We conclude that 0, 25 or 50 mEq/l of Na^+ in a 6% CE soln have similar effects on water, Na^+, K^+ and glucose absorption. Low concentrations of Na^+ with glucose enhance net water absorption. Glucose is the more important factor enhancing intestinal water absorption compared with plain water because glucose alone (0 mEq Na^+) is as effective as glucose plus Na^+ (25 mEq Na^+). In the absence of added electrolytes, electrolyte absorption is impaired as compared with low electrolyte concentration. A mechanism is suggested giving glucose an essential role in the initiation of bulk soln flow through the paracellular pathway. Supported by the Quaker Oats Company.

ONTOGENY OF GASTROINTESTINAL SECRETORY FUNCTIONS

84.1

ONTOGENY OF INTESTINAL SOLUTE TRANSPORT IN THE PIGLET. A.A. Puchal*, Y.M. Vega*, and R.K. Buddington. Biological Sciences, Mississippi State University, Mississippi State, MS 39762.

Age-related changes in intestinal transport are known to occur for several species and different solutes. However, the patterns of change and the mechanisms responsible for the changes are not clearly understood. Thus we used an in vitro method to measure rates of brush-border transport as functions of concentration for three sugars (glucose, galactose, fructose) and four amino acids (aspartate, leucine, lysine, proline) in the proximal small intestine, and taurocholate in the distal small intestine of piglets at birth, during suckling (10 days), and after weaning (30 days). Our kinetic analyses yield four conclusions. First, the number of sugar and amino acid transporters per unit tissue decline after birth. Second, of the sugar transporters the aldohexose transporters undergo the greatest postnatal declines, particularly the transporter(s) which principally carry galactose. In contrast, fructose transport exhibits the least decline. The changes in sugar transport coincide with the removal of galactose from the diet and the addition of fructose at the time of weaning. Third, higher rates of nutrient absorption during early development are partly due to greater passive permeability. Despite the age-related declines in the densities of sugar and amino acid transporters and passive permeability, because of intestinal growth total nutrient absorptive capacities (product of absorption per cm^2 intestine multiplied by the total intestinal surface area) remain matched to, or exceed, the expected increases in metabolic requirements of the growing piglets. Fourth, unlike the nutrients, Na^+-dependent transport of taurocholate is low at birth and during suckling and increases at the time of weaning. Supported by CIRIT, 1989.

84.2

ARE SURGES OF PLASMA CCK AND SECRETIN RESPONSIBLE FOR PANCREATIC DEVELOPMENT IN NEONATAL GUINEA PIGS? Corey S. Joekel, Margery K. Herrington, Jon A. Vanderhoof, Thomas E. Adrian. Creighton University School of Medicine, Dept's of Physiology and Pediatrics, Omaha, NE

Following initiation of enteral feeding, surges in circulating cholecystokinin (CCK) and secretin occur which may affect neonatal pancreatic growth and function. We evaluated levels of CCK and secretin in plasma, in relation to stimulated pancreatic amylase release and pancreatic weight in neonatal guinea pigs. Plasma CCK was low at birth (3.1 ± 0.8 pmol/l) but rose markedly at day 15 (10.9 ± 0.8 pmol/l, $p<0.001$). Plasma secretin was also low at birth (3.8 ± 0.8 pmol/l) but peaked on day 4 (16.5 ± 1.4 $p < 0.001$) and remained elevated through day 15. Adult plasma CCK and secretin levels were 12.3 ± 0.8 and 8.9 ± 1.5 pmol/l respectively. Stimulated amylase secretion from dispersed acini by CCK-8, carbachol and phorbol ester was present at birth. Dose responses at days 4, 8 and 15 were similar to those at birth with identical ED_{50}'s for CCK (3 x 10^{-11}M), carbachol (3 x 10^{-6}M), and phorbol ester (10^{-7}M). Pancreatic weight more than doubled during the first week of life, with the greatest increase during the first 4 days (153 ± 4 to 250 ± 8 mg/100g body wt., $p<0.001$), at which time plasma CCK was not significantly changed. Pancreatic weight (per 100g of body weight) did not significantly increase during the second week. Chronic infusions with a specific CCK receptor antagonist (MK329, 25 nmol/kg/hr) did not alter plasma CCK levels or pancreatic weights in neonates, but did enhance subsequent secretory responses in dispersed acini. In summary, stimulated pancreatic amylase release is fully developed at birth in guinea pigs, and is independent of surges in circulating CCK and secretin. It is unlikely that CCK plays a major role in neonatal guinea pig pancreatic development. Most pancreatic growth precedes plasma surges of CCK, and chronic CCK receptor blockade with MK329 does not inhibit pancreatic growth or subsequent secretagogue responsiveness, or have an effect on plasma CCK levels.

NEURAL REGULATION OF GASTROINTESTINAL SECRETION

85.1

AN EXPLANATION FOR THE GASTRIC HYPERSECRETION FOUND IN THE PYLORUS LIGATED RAT. Zalmon Pober, Massachusetts College of Pharmacy and Allied Health Sciences, Springfield, MA 01119.

It has been demonstrated that the pylorus ligated rat hypersecretes gastric acid. While this hypersecretion has been shown to be of vagal origin, little has been done to identify its stimulus. A series of experiments were performed in Sprague Dawley derived rats, surgically prepared under ether anesthesia. The pyloric sphincter was ligated along with various other surgical manipulations. Both intestinal obstruction by ligation approximately 20 cm aboral to the pyloric sphincter and diversion of intestinal contents to the cecum reduced unstimulated gastric secretion in the pylorus ligated rat. However, perfusion of the lower small intestine with bicarbonate (143 mEq/L) stimulated secretion. Perfusion with either saline or deoxycholic acid (0.05 mg/L) did not alter secretion. This supports the role of bicarbonate in the hypersecretion of gastric acid in the pyloric ligated rat. The reflex appears to involve the myenteric plexus, since section of the pylorus appeared to block gastric secretion. Blood plasma, from animals with either pyloric ligation alone or with intestinal ligation, administered to pylorus ligated rats equally inhibited gastric secretion. This suggests that while some factor inhibiting gastric secretion may be present, it appears that it is unrelated to pyloric ligation.

85.2

SYMPATHETIC INHIBITION OF PARASYMPATHETIC INDUCED SUBMANDIBULAR SALIVARY FLOW. Mary A. Lung. Department of Physiology, University of Hong Kong, Hong Kong.

The study was undertaken to investigate if sympathetic inhibition of parasympathetic induced salivary flow is related to a change in blood flow caused by vasoconstriction. In pentobarbitone anaesthetized dogs, submandibular arterial inflow and salivary flow were measured with electro-magnetic flow sensors (J. Physiol. 422, 80P, 1990). Controlled vascular perfusion of the gland was also performed. Parasympathetic nerve stimulation (5V, 1ms and 8Hz) induced copious secretion (2±0.1ml/min, n=5). Additional sympathetic stimulation (20V, 1ms and 16Hz) significantly diminished the para-sympathetic salivary flow whether the gland was with spontaneous blood flow or controlled vascular perfusion. Hence, inhibition of parasympathetic salivary flow by a superimposed sympathetic nerve stimulation is not due to a reduction of blood flow caused by vasoconstriction.
(supported by HKU Research Funds 337/034/0011 and Lee Wing Tat Medical Research Fund 377/030/7840).

86.1

MACROCYCLIC POLYETHERS AS MYOCARDIAL INOTROPIC AGENTS: SITE OF ACTION. [1]Cindy La Neave, [1]Keith Pannell*, [2]Shawnee Sloop, [2]Tom Nosek, [2]Ralph Kolbeck. [1]University of Texas at El Paso, El Paso, Texas 79968-0513,[2] Medical College of Georgia, Augusta, Georgia, 30912.

Macrocyclic polyethers exert a variety of positive and negative inotropic responses in the myocardium (R. C. Kolbeck, et al, Experientia 40:727, 1984). Recently, we found that the polyethers were capable of altering the transmembrane movement of sodium, potassium, and calcium, a finding which may be related to their inotropic properties. The present study was undertaken to determine if the "Crown Ethers" could also exert a direct influence on the ability of the myocardial contractile proteins to develop tension. Small muscle bundles (<200 μm in diameter) were isolated from rat papillary muscles. These fibers were then exposed to saponin for 30 min in order to permeabilize the sarcolemma but leave the sarcoplasmic reticulum membrane intact. The contractile response of the incubated "skinned " fibers to various polyethers (10^{-4}M) was then determined by means of an optoelectric force transducer. 2,3,8-trioxanonyl-15-Crown-5 and dibenzo-18-Crown-6 (two positive inotropic agents), benzyloxymethyl-15-Crown-5 (a negative inotropic agent), and dibenzo-30-Crown-10 (a biphasic inotropic agent had no effect on the ability of the skinned fibers to develop tension. These findings suggest that the inotropic effects of the macrocyclic polyethers are almost certainly due to alterations in membrane physiology, with the agents either functioning as ionophores or membrane pores. Supported by NIH: Area R15 HL35735, MBRS RR08012, MARC GM 08048.

86.2

PERFORMANCE OF REPERFUSED ISCHEMIC AND HYPOXIC ISOLATED RAT HEARTS. R.Motterlini, M.Tarantola, M.Beretta, M.Samaja, A.Corno, F.Santoro, A.Grossi (SPON:C.Marconi). Istituto Scientifico San Raffaele and Università di Milano, Italy.

The O_2 supply to tissues is characterized by the product (blood flow) x (blood O_2 content) and can thus be theoretically shortened decreasing either the flow (low-flow ischemia) or the PO_2 (hypoxia), but the two conditions are only apparently equivalent. To test this hypothesis, we have exposed isolated perfused rat hearts to 20 min O_2 shortage (10% of the initial value) by either way followed by 20 min reperfusion or reoxygenation. Then, we have compared the heart performance under comparable O_2 shortage conditions and during the recovery. Results: 1) The heart contractility (developed pressure and maximal rate of pressure development and relaxation) was similarly depressed in both groups during the O_2 shortage, but recovered better in the low-flow ischemia group; 2) The vascular bed was nearly unaffected in the low-flow ischemia group but was irreversibly injured in the hypoxia group as it appeared from the significant ($p<0.05$) increase of the end-diastolic and coronary pressures; 3) The O_2 uptake and lactate production were the same in the two groups during the O_2 shortage but the depression was irreversible in the hypoxia group only. We conclude that the same degree of O_2 shortage is more deleterious for the myocardial function and metabolism at high coronary flow perhaps because of the enhanced removal of membrane diffusible substrates potentially useful during reperfusion or reoxygenation. Supported by grants from the Istituto Scientifico San Raffaele, Milano, and the Target Project Biotechnology and Bioinstrumentation, Italy.

86.3

POST-ISCHEMIC RECOVERY OF ISOLATED RAT HEARTS AND THE RED CELL OXYGEN AFFINITY. M.Samaja, R. Motterlini, M. Tarantola, M.Beretta, F.Rossi, L.Sabbioneda, and A.Zanella (SPON:C.Marconi) Università di Milano, Istituto Scientifico San Raffaele, and Policlinico of Milano, Italy.

We have tested the hypothesis that a low red cell affinity for O_2 is advantageous for the myocardial oxygenation and function under various conditions of O_2 supply. Non-working isolated rat hearts were perfused at 37°C with the following perfusates in sequence: 1) Krebs-Henseleit buffer at high coronary flow (15 ml/min); 2) Red cells with high or low O_2 affinity at the same flow; 3) Red cells at flow reduced stepwise to 2 ml/min; 4) Buffer at high flow (15 ml/min). The acid/base properties of the perfusate (PaO_2>600 Torr, $PaCO_2$=42 Torr, pH=7.4) and the hematocrit (10%) were constant throughout, the only variable being the red cell O_2 affinity (P_{50}=18 and 30 Torr) that was changed using stored blood and red cells incubated with inosine, pyruvate and phosphate, respectively. The myocardial functional parameters and the O_2 uptake were related to the red cell O_2 affinity indicating that: 1) A low red cell O_2 affinity was advantageous for myocardial function at high coronary flow; 2) There were no detectable differences between the two O_2 affinities in low-flow ischemia; 3) The recovery of the hearts from ischemia was improved in those hearts that were made ischemic with low O_2 affinity red cells; 4) The myocardial performance was weakly correlated to the O_2 uptake, suggesting that other factors are involved in the mechanism of the O_2 unloading to tissues. Supported by grants from the Istituto Scientifico San Raffaele, Milano, and the Target Project Biotechnology and Bioinstrumentation, Italy.

86.4

EFFECT OF SARCOLEMMAL Na^+-K^+-ATPase INHIBITION ON TENSION PROLONGATION OF REOXYGENATED HYPOXIC CARDIAC MUSCLE. Brian P. McGlinch, Monte Norgaard, Dennis Lura, Jorge A. Estrin*. Univ of Minneosta, Minneapolis, MN 55455

To examine the effects of a reduction in sarcomere Na^+ efflux from inhibition of the Na^+-K^+-ATPase pump on tension prolongation (TP) following reoxygenation of hypoxic cardiac muscle, we determined the rate of relaxation (RR, $mN{\cdot}mm^{-2}{\cdot}sec^{-1}$) and time to 50% relaxation ($T_{50}R$, msec) of isometrically contracting, ferret papillary muscles subjected to 30 minutes of hypoxia (H) (N_2 95%, CO_2 5%) and 2 hours of reoxygenation (R) (O_2 95%, CO_2 5%) [CSA = 0.44 ± 0.1 mm^2 (mean ± SEM), temp 30° C, rate 12 bpm, K-H media ($[Na^+]_o$ = 135 mM, $[Ca^{2+}]_o$ = 2 mM, O_2 95%, CO_2 5%)] after stablization for 1 hour in the absence (Group I: controls, n = 13) and presence of ouabain [(Group II: n = 7, 1 x 10^{-8} M, increase in AT = 2 ± 12%, p = NS, paired t-test) and (Group III: n = 13, 1 x 10^{-6} M, increase in AT = 44 ± 12%, $p < 0.002$)]. During normoxia, ouabain increased RR [38 ± 7% from 369 ± 48, ($p < .0001$)] only in Group III without causing changes in $T_{50}R$ max in any group. In Group III at 1 min of R, $T_{50}R$ max increased, a measure of TP, by 63 ± 12% from control (122 ± 7, $p < .0009$) at end of stabilization. The increase in $T_{50}R$ max in Group III was greater ($p < .03$, unpaired t-test) than that of Groups I (35 ± 2% from 114 ± 6) and II (36 ± 18% from 135 ± 14). Upon R, RR decreased ($p < .0001$) in all groups (I: -90 ± 4%, II: -88 ± 4%, III: -86 ± 3% from controls 250 ± 34, 219 ± 21, 370 ± 48, Groups I, II, and III, respectively). Thus, during reoxygenation of hypoxic cardiac muscle, inhibition of the Na^+-K^+-ATPase pump worsens TP.

86.5

EFFECTS OF CALCIUM CALMODULIN INHIBITION ON TENSION PROLONGATION FOLLOWING REOXYGENATION OF HYPOXIC CARDIAC MUSCLE. Ann Kanabe, Dennis Lura, Brian P. McGlinch, Monte Norgaard, Jorge A. Estrin*. Univ. of Minnesota, Minneapolis, MN 55455

To determine the role of Ca^{2+}-Calmodulin (Ca^{2+}Cal) regulated cytosol protease activity on tension prolongation (TP) following reoxygenation of hypoxic cardiac muscle, active tension (AT, $mN{\cdot}mm^{-2}$), rate of relaxation (RR, $mN{\cdot}mm^{-2}{\cdot}sec^{-1}$) and time to 50% relaxation ($T_{50}R$, msec) of isometrically contracting kitten papillary muscles[CSA 0.76 ± 0.06 mm^2, (mean ± SEM), Temp 30° C, rate 12 bpm, K-H media ($[Na^+]_o$ = 135 mM, $[Ca^{2+}]_o$ = 2 mM, O_2 95%, CO_2 5%] stabilized in the presence of increasing concentrations of N-(6-aminohexyl)-5-chloro-1-naphthalenesulfonamide HCl (W7), a known Ca^{2+}Cal inhibitor, (Group II: n = 5, W7: 1 x 10^{-7} M; Group III: n = 5, W7: 1 x 10^{-6} M; Group IV: n = 5, W7: 1 x 10^{-5} M), were subjected to 30 minutes of hypoxia (H) (N_2 95%, CO_2 5%) and 2 hours of reoxygenation (R) (O_2 95%, CO_2 5%), and were compared to those of control muscles (Group I, n = 14) not exposed to W7. W7 had no significant effects on AT, RR and $T_{50}R$ during normoxia or hypoxia. During R, $T_{50}R$ max of Groups I, II, III and IV rose [I: 142 ± 13%, ($p < .0001$, two-tailed paired t-test); II: 73 ± 16% ($p < .02$); III: 120 ± 19% ($p < .009$), IV: 77 ± 10% ($p < .002$)] from their respective controls at the end of stabilization (I: 227 ± 11, II: 226 ± 11, III: 188 ± 18, IV: 245 ± 17). The % rise in $T_{50}R$ of Groups II and IV was significantly less ($p < .01$, unpaired t-test) than that of control muscles. Thus, a Ca^{2+}Cal protease, probably linked to the production of xanthine oxidase, participates in the causation of TP.

86.6

EVIDENCE THAT BINDING OF INDO-1 TO CARDIAC MYOCYTE PROTEINS DOES NOT MARKEDLY CHANGE Kd FOR Ca^{2+}. H. Ikenouchi* and W.H. Barry. University of Utah Medical Center, Salt Lake City, Utah 84132.

Quantitative measurement of $[Ca^{2+}]_i$ with indo-1 is complicated by the possibility that the value of the dissociation constant (Kd) may be influenced by binding of indo-1 to intracellular proteins. We investigated this question in cultured chick ventricular myocytes by use of two different calibration methods. First, the indo-1 fluorescence ratio (R) (400/500nm) was measured in beating myocytes loaded by exposure to indo-1 AM. Then, cells were exposed to the Ca^{2+} ionophore BrA-23187 and R was measured in the presence of 500nM Ca^{2+} (EGTA-Ca^{2+} buffer). After that cells were permeabilized to Ca^{2+} by a 1 minute exposure to 25μM digitonin in the presence of "zero" Ca^{2+} (10mM EGTA) and saturating 1mM Ca^{2+} to obtain Rmin and Rmax. We then calculated $[Ca^{2+}]_i$ from the formula $[Ca^{2+}]_i$ = Kd (R-Rmin/Rmax-R)β. With Kd= 250nM, calculated peak systolic $[Ca^{2+}]_i$ was 750+44nM, and end diastolic was 269+19nM (mean+SEM, n=16). The R's corresponding to a Ca^{2+}=500nM measured with both calibration methods were very similar (digitonin, 0.67+0.03; BrA-23187, 0.66+0.03, ns). As the BrA-23187 method is independent of the value chosen for Kd, we conclude that the Kd of 250nM for indo-1 measured in free solutions closely approximates the Kd for intracellular indo-1 in these cells; and that therefore the Kd of indo-1 for Ca^{2+} does not appear to be markedly affected by binding to proteins.

87.1

THAPSIGARGIN INHIBITS REPLETION OF INTRACELLULAR CALCIUM STORE IN VASCULAR SMOOTH MUSCLES A.M. Low*, V. Gaspar*, C.Y. Kwan*, E.E. Daniel, O. Thastrup*@ Dept. Biomed. Sci., McMaster Univ. Hamilton, L8N 3Z5, Canada and @Dept. Clin. Chem., Rigshospitalet, DK 2100 Copenhagen, Denmark.

We have examined the functional effects of thapsigargin (TSG), a putative inhibitor of the endoplasmic reticulum (ER) Ca^{2+}-pump and ATPase on vascular smooth muscles. Isometric contractions of rings of rat aorta (RA) and dog mesenteric artery (DMA) were recorded using strain gauges. TSG (1μM) caused a concentration-dependent slow tension increase in rings of RA and some (6/25) DMA rings in normal Krebs (Ca^{2+}=2.5mM) which was blocked by nifedipine or Mn^{2+}. After incubation in Ca^{2+}-free Krebs, restoration of Ca^{2+} caused a larger (26.2±2.7% vs 7.6±1.0%, n=15; phenylephrine (PE) max contraction=100%) transient contraction after TSG treatment. Similar responses were obtained in DMA cells after collagenase dispersal. In TSG-treated rings, repletion of PE-sensitive intracellular Ca^{2+} store was significantly inhibited (70%) in both RA and DMA. A leftward shift of the concentration-response curves for PE and K^+ in RA and DMA was also observed with TSG. *Conclusion*: TSG was effective in inhibiting repletion of PE-sensitive intracellular store, possibly by selective inhibition of ER Ca^{2+}-pump activity. The different effectiveness of Ca^{2+} extrusion mechanisms may account for the sustained basal tension in RA and transient, in DMA.

87.2

ROLE OF ENDOTHELIUM IN SEX DIFFERENCES IN VASOPRESSIN (VP)-INDUCED CONTRACTION OF RAT AORTA. J.N. Stallone and M.G. Howard*. Dept. of Physiol., Northeastern Ohio Universities College of Medicine, Rootstown, OH 44272

Previously, we reported that in the rat, vascular reactivity to VP is higher in females than in males, both in the aorta and mesenteric vasculature. To explore possible mechanism(s) responsible for this sexually dimorphic response to VP, vascular reactivity to VP was examined in male (M) and female (F) rat thoracic aortae with endothelium intact (ENDO+) or deleted (ENDO-), and in the presence or absence of N^G-monomethyl-l-arginine (NMLA, 100 μM), or indomethacin (INDO, 10 μM). ENDO(+) and ENDO(-) aortic rings were prepared from age-matched (9-12 wks) male and female Sprague-Dawley rats and mounted for isometric tension recording (in Krebs-Henseleit-bicarbonate, 37°C, 2.50 g passive tension). After equilibration (2 hr), a cumulative dose-response curve to arginine VP (10^{-11}-10^{-6} M) was obtained. Data presented are means±SE, n = 3-4 animals per experimental group. Maximum response of ENDO(+) aortae to VP was markedly higher in F (3,325±688 mg) than in M (1,000±110 mg). In ENDO(-) aortae, maximum response to VP was similar in M (3,788±480 mg) and F (3,838±288 mg). Pretreatment of aortae with NMLA markedly increased maximum response to VP in ENDO(+) M (3,317±246 mg), but had little or no effect in ENDO(+) F (4,188±753 mg). Pretreatment of aortae with INDO had no effect on maximum response of F ENDO(+) (3,300±458 mg) or F ENDO(-) (3,867±290 mg) aortae or M ENDO(+) (1,062±228) aortae; however, maximum response of M ENDO(-) aortae (1,519±406 mg) was markedly reduced. These data suggest that endothelium-derived relaxing factor and metabolites of arachidonic acid are responsible for the marked sex differences in VP-induced contraction of the rat aorta. (Supported by Amer. Heart Assoc.-Ohio Affiliate)

87.3

EFFECT OF ATP ON CALCIUM CHANNELS IN RAT AORTA. A.F. Dominiczak* and D.F. Bohr. Univ. of Michigan, Ann Arbor, MI 48109

ATP is known to have a biphasic effect on vascular smooth muscle(VSM). Its contractile effect is caused by the direct action of ATP on the VSM and its relaxant effect is thought to be secondary to the release of EDRF by the endothelium. The current study indicates that ATP may cause VSM relaxation by an additional mechanism. Control contractions of rings from rat aortae were recorded in response to KCl(30mM), norepinephrine(10^{-8}M) and ATP($3x10^{-3}$M). In the presence of calcium these responses were approximately equal. In the absence of calcium(plus EGTA 1mM), after transient contractions had returned to baseline, addition of calcium(3mM) to the bath caused the following contractions expressed as percent of control responses in complete physiological salt solution: KCl 99±3%, NE 96±3% and ATP 34±5%. In a second study we observed that ATP produced the following inhibitions of a KCl response in the presence of endothelium: ATP 10^{-4}, 25%; 10^{-3}, 47%; $2x10^{-3}$, 47%; $3x10^{-3}$, 56%. When the endothelium was mechanically removed these inhibitions were: 0%, 19%, 26%, 35%, respectively. The inbition of KCl response was also present following pre-treatment of VSM with NG-monomethyl L-arginine ($3x10^{-2}$M, a specific inhibitor of endothelium-derived nitric oxide synthesis): 49±3% for ATP $3x10^{-3}$M. We conclude that in addition to the release of EDRF, ATP causes relaxation by inactivation of voltage dependent calcium channels.

87.4

PHORBOL ESTER- AND AGONIST-STIMULATED TRANSLOCATION OF PROTEIN KINASE C IN ARTERIAL SMOOTH MUSCLE. Harold A. Singer*, Jess Oren*, and Charla Sweeley* (SPON: K.M. Baker). Weis Center for Research, Geisinger Clinic, Danville, PA 17822

Activation of protein kinase C (PKC) in vascular smooth muscle has been proposed to result in tonic force development by mechanisms independent of myosin light chain kinase and phosphorylation of the 20 kilodalton regulatory light chain of myosin. In the present study, particulate and cytosolic fractions from intact carotid arterial smooth muscle were isolated in the absence of Ca^{2+}. Phorbol 12,13 dibutyrate (PDB) stimulated the translocation of PKC activity to the particulate fraction (increased 1.69-fold compared to control) with a time course which paralleled force development. Ca^{2+} depletion of the tissue reduced, but did not eliminate, the force and increase in PKC activity in the particulate fraction. Stimulation with histamine (10^{-5} M) resulted in rapid and sustained increases in both force and membrane-associated protein kinase C activity (0.8 fold). KCl-depolarization evoked a rapid and sustained contractile response, but only a slow increase (1.24 fold) in membrane-associated PKC activity by 45 min which was not blocked by prazosin. BAY K8644 (10^{-7} M) evoked a 0.69-fold increase in particulate activity after 30 min. We have interpreted the increased activity of PKC in the particulate fraction as an index of its activation in situ, directly in the case of PDB or by stimulating diacylglycerol accumulation in the cases of histamine, KCl-depolarization, or BAY K8644.

87.5

RELAXATION OF PORCINE TRACHEAL SMOOTH MUSCLE (TSM) BY NEURAL AND NON-NEURAL MECHANISMS: POSSIBLE ROLE OF NEUROENDOCRINE CELLS. M.S. Kannan*, G. Smith*, P. Lackner* and D.E. Johnson* (SPON: S.M. O'Grady). Departments of Veterinary Biology and Pediatrics, University of Minnesota, St. Paul, MN 55108

In strips of TSM in vitro from 6-12 week old pigs, we investigated the mechanisms of neural and non-neural relaxations With tone induced by carbachol, electrical field stimulation (EFS, at 0.5 ms, 70 V, 5 sec) resulted in frequency-dependent relaxations, blocked by tetrodotoxin (TTX, 3 uM), partially by ω-conotoxin (100 nM), but were insensitive to propranolol or atropine (3 uM each, n=4-6). Addition of dimethylphenylpiperazinium chloride (DMPP, 10-200 uM range) resulted in TTX-and ω-conotoxin-insensitive rapid relaxation, which quickly desensitized, with no significant relaxations after the 3rd exposure to this agent (n=4). Similar results were obtained with VIP (0.1 uM) (n=4). However, desensitization of DMPP or VIP responses did not affect the relaxations to EFS. The results suggest: a) EFS results in neural release of a non-adrenergic, non-cholinergic neurotransmitter that is unlikely to be VIP; and b) DMPP-induced relaxations arise from release of an inhibitory agent from non-neural, possibly neuroendocrine cells, since they were insensitive to TTX and ω-conotoxin. Supported by USDA formula funds and BRSG funds.

87.6

Potentiation of the Ach Induced Contraction by NPY in "in vitro" rat tracheal smooth muscle. Guido E. Santacana and Reinaldo Aponte, Dept. of Physiology. Univ. Central del Caribe, School of Medicine, Cayey, P.R.

The vasoactive peptide neuropeptide Y (NPY) has been shown to cause vasoconstriction of isolated cat cerebral arteries. NPY is released together with norepinephrine from sympathetic nerve fibers in blood vessels. Other peripheral areas were the constricting effect of NPY are observed include skeletal muscle arteries, rabbit ear artery and hepatic arterial and portal vascular beds.

Although regulatory effects of NPY have been observed in sphincter of Oddi and Gallbladder smooth muscle, its effect at the level of visceral smooth muscle has not been elucidated in other organ systems. Our study indicates that NPY (5×10^{-7}M to 5×10^{-6}M) excerts a small but significant relaxing effect on isolated "in vitro" rat tracheal smooth muscle. The relaxing effect is transient and disappears after one minute of exposure to NPY. In addition, NPY (5×10^{-6}M) potentiates the acetylcholine (Ach) induced contraction of rat tracheal smooth muscle by 33% after the tissue is incubated for 10 minutes in the presence of the neuropeptide.

Our observations regarding the effects of NPY in rat tracheal smooth muscle adds additional information concerning the actions of this neuropeptide in smooth muscle other than that pertaining to the circulatory system.

87.7

INHIBITION OF ACETYLCHOLINESTERASE ACTIVITY IN TRACHEAL SMOOTH MUSCLE HOMOGENATES CAUSED BY IMMUNE SENSITIZATION. R.W. Mitchell and A.R. Leff. Sect. of Pulm. and Crit. Care Med., Div. of Biol. Sci., U. of Chicago, Chicago, IL 60637

We measured acetylcholinesterase (AChase) activity in tracheal smooth muscle (TSM) homogenates obtained from dogs sensitized in vivo to ragweed pollen extract [ragweed sensitized (RWS); n = 6] and sham sensitized littermate controls (LMC; n = 6). The TSM from excised tracheas was homogenized at 4°C; AChase activity [Absorbance Units (AU)/min/mg homogenate protein] was measured spectrophotometrically. The AChase from TSM homogenates of both RWS and LMC saturated at 3.12 mM substrate (acetylthiocholine). However, maximal AChase activity in RWS homogenates was significantly less (0.811 ± 0.092 AU/min/mg) compared to LMC homogenates (1.592 ± 0.184 AU/min/mg; $P < 0.01$). Kinetic analysis (Eadie-Hofstee) indicated similar Michaelis constants (K_M) for AChase from RWS (0.337 ± 0.076) and LMC (0.289 ± 0.093) homogenates (P = NS). The concentration of physostigmine (PS) eliciting half-maximal inhibition (K_i) of AChase activity also was similar for TSM homogenates from RWS (-7.93 ± 0.035 log M) and LMC (-7.87 ± 0.012 log M; P = NS). Select mediators of anaphylaxis (10^{-4}M histamine, 10^{-6}M serotonin, 10^{-5}M prostaglandin E_2, 10^{-6}M prostaglandin $F_{2\alpha}$, and 10^{-7}M leukotriene D_4) did not affect AChase activity. These data demonstate reduced AChase activity in homogenates of canine TSM from an actively sensitized ragweed model of allergic bronchospasm. Kinetic analysis indicated similar K_M and K_i values for TSM AChase from RWS and LMC dogs, and AChase activity was unaffected by mediators of anaphylaxis. Our data demonstrate that functional expression of AChase in TSM is inhibited by active immune-sensitization. (Supported by NHLBI HL42758, HL35718, and HL32495.)

87.8

ACTIONS OF ACETYLCHOLINE ON ELECTROGENIC SODIUM PUMPING IN MOLLUSCAN BUCCAL MUSCLE. Robert B. Hill. University of Rhode Island, Kingston, R.I. 02881

Acetylcholine (ACh) has frequently been shown to act as an excitatory neurotransmitter in control of molluscan buccal muscle. Applied ACh has a relatively simple set of effects on the radular protractor muscle (RPM) of Busycon canaliculatum. Short-term treatment with high concentrations induces a Na-dependent depolarization, accompanied by Ca-dependent force. Co-treatment with serotonin (5HT) enhances the appearance of several types of rhythmicity in the response to ACh. Ca-block eliminates the rhythmicity induced by co-treatment with 5HT but not repolarization by 5HT. ACh has a Na-dependent action on the response of the RPM to K-free external medium. At 10^{-7}M, ACh increases the rate of the depolarizing phase while decreasing the amplitude of the hyperpolarizing phase. This may be attributed to induced Na-entry, with the Na-pump stopped. Depolarization by zero-K is enhanced progressively as ACh treatment is increased from 10^{-7}M to 10^{-5}M. Superimposed rhythmicity begins to appear at 10^{-6}M and is marked at 10^{-3}M. This may be evidence for voltage-gated Ca-channels. The ACh-induced depolarizing response to zero-K is abolished in Na-free solution or by strophanthidin.

87.9

NON-SPECIFIC AUGMENTATION OF CANINE TRACHEAL SMOOTH MUSCLE CONTRACTION BY INDOMETHACIN. J. Tallet*, K.J. Popovich, A.R. Leff and R.M. Mitchell. U. of Chicago, Chicago, IL 60637

We compared the effect of the cyclooxygenase inhibitor indomethacin (INDO) with the effect of the inhibitor of cyclooxygenase and 5-lipoxgenase nordihydroguaiaretic acid (NDGA) on contraction elicited by acetylcholine (ACh) in epithelium-free tracheal smooth muscle (TSM) from 7 dogs in vitro. Concentration-response curves were generated with 10^{-9} M to 10^{-3} M ACh in four groups of TSM: treated with 10^{-6} M INDO; treated with 10^{-5} M NDGA; treated with 10^{-6} M INDO plus 10^{-5} M NDGA; and a non-treated control group. The pD2 (negative log EC50, *effective concentration 50%*) and maximum active tension developed by TSM (AT_{max}) were determined for each concentration-response curve. The pD2 of TSM treated with INDO (7.07 ± 0.22) was significantly less than control (6.28 ± 0.09; P = 0.013, Scheffe analysis after ANOVA) and NDGA-treated TSM (6.47 ± 0.15; P = 0.311 vs control; P = 0.015 vs INDO-treated; Scheffe) but not different from INDO+NDGA-treated TSM (7.10 ± 0.40; P = 0.212, Scheffe). The AT_{max} values were not different among groups (P = 0.256, ANOVA) but followed the trend demonstrated by the pD2 values: NDGA ≈ Control < INDO ≈ INDO+NDGA. Analysis of bath medium surrounding TSM from 3 dogs by high pressure liquid chromatography demonstrated prostaglandin E_2 (PGE_2). Production of PGE_2 was decreased equivalently by INDO and NDGA when compared to control. Production of PGE_2 was not inhibited further in TSM treated with INDO+NDGA. We demonstrate equivalent inhibition of prostaglandin production by INDO and NDGA. We also demonstrate increased sensitivity of canine TSM to ACh in the presence of INDO that cannot be accounted for by the inhibition of cyclooxygenase. (Supported by NHLBI HL42578, HL35718 and HL32495.)

SKELETAL MUSCLE PHYSIOLOGY AND CYTOSKELETON

88.1

Toward a homeomorphic model of intracellular calcium transients during muscle activation. Y. Laouris*, A. Shambayaty* and D.G. Stuart. Department of Physiology, College of Medicine, University of Arizona, Tucson, AZ, 85724.

The calcium (Ca) transient following muscle activation has traditionally been modelled as a first-order system (cf. Stein et al., J. Biophys. 54:705-717, 1988). While this approach has been sufficient for some purposes, it fails to account for the fact that the Ca response to subsequent pulses has temporal dependencies. The traditional model also lacks homeomorphism with its real counterpart, in which at least three systems are interacting: Ca release, binding to proteins, and reuptake. We have developed a *near-homeomorphic* Ca model which, in its current version, consists of two modules, one for Ca release and the other for reuptake. To account for changes in the gain of the release mechanism in response to repetitive stimulation, a modification of the Hodgkin Huxley model was used. The reuptake pump has been modelled as a first-order lag, with a pure time delay. With this approach, in contrast to a simple first-order lag model, it has been possible to account for experimental observations (cf. Miledi et al., J. Physiol. 333:655-679, 1982), including: 1) the latency between muscle fiber action potential and onset of Ca response; 2) temporal nonlinearities; 3) a progressive decrease in Ca response amplitude and a slowing in its decay during repetitive stimulation; and 4) the saturation in Ca dynamics, also during repetitive stimulation. Future plans include incorporation of this model into a comprehensive model of muscle fatigue which will include intracellular Ca binding and kinetics, and fatigue-induced changes in pH and force production. Supported by USPHS grants NS 07309, HL 07249, NS 25077, RR 05675.

88.2

SARCOMERE LENGTH, HIP JOINT MOMENT ARM AND MUSCLE FORCE USED AS TORQUE PREDICTORS IN THE FROG HINDLIMB. R.L. Lieber, S.D. Shoemaker* and A.M. Green*. University of California and Veterans Administration Medical Center, San Diego, CA 92161.

INTRODUCTION AND METHODS: We measured sarcomere length (*sl*), hip joint moment arm (R_H), and resultant isometric torque (τ_{obs}) in the frog semitendinosus (Rana pipiens) at 10° intervals over the range 30° to 140° of hip flexion. We then excised the muscle from the bone-muscle complex and measured maximum tetanic tension (P_o). Based on the *sl*-tension relationship (LT(*sl*), Gordon *et al.* 1966), and measured values for P_o, *sl*, and R_H, we then predicted torque (τ_{pred}) over the same range of joint angles, using the relationship: $\tau_{pred} = P_o \cdot LT(sl) \cdot R_H$.

RESULTS AND DISCUSSION: Over the entire hip joint range, τ_{pred} was approximately 10% less than τ_{obs}. When normalized to maximum isometric torque, τ_{pred} closely matched τ_{obs}. In this system, R_H dominated the shape and magnitude of the torque curve (based on the observation that peak muscle force occurred at 40° of flexion, peak R_H occurred at 80° of flexion, and peak τ_{obs} occurred at 70° of flexion). Relatively small variations in *sl* (less than about 0.3 μm) had virtually no effect on the shape of the torque curve. Thus, in the case where sarcomere length change is relatively small during joint rotation (approximately 0.1 μm/°, due to a relatively long fiber length and small moment arm), isometric joint torque was determined primarily by the magnitude of the moment arm. Supported by the VA and NIH AR35192.

88.3

STIMULATION OF SKELETAL MUSCLE GROWTH BY ANABOLIC HORMONES. H.S. Pitkow, F. Rothberg*, and D. Robertson.* Penna. Col. of Podiatric Medicine, Phila., PA. 19107

In order to ascertain the effects of various anabolic steroids on the growth of five lower extremity muscle groups, adult male Sprague-Dawley rats (150-175 gm; 12 animals/group) were castrated and given 500 µg of either isoandrosterone (IS), 19-nor-testosterone (NT), testosterone propionate (TP), or ethynl testosterone (ET) in sesame oil subcutaneously daily for 30 days. A castrate control (CC) and normal control (NC) group were given sesame oil only during this period. At autopsy the nucleic acid contents, protein, and dry weights were determined in these muscle groups. We observed that the four anabolic steroids had their greatest effect on RNA content for estimating cellular synthetic competence. IS, a weak steroid with no androgen effects, had the greatest anabolic effect on the five muscle groups. Since the anterior thigh (ATM) and anterior-lateral leg muscle (A,LLM) groups were the most sensitive to anabolic steroid action, this indicated that these two muscle groups would be more responsive to IS in muscle growth and healing following a surgical operation.

88.4

Effects of Age and Diet on Viscoelastic Properties of Skeletal Muscle. N. G. Kelly and R. J. McCarter. U.T. Health Science Center, Physiology Dept., San Antonio, Tx., 78284

Viscoelastic properties of skeletal muscle of male Fischer 344 rats were investigated in order to establish changes in passive properties of muscles with age. Muscle strips of respresentative fast twitch (lateral omohyoideus, LOMO) and slow twitch (soleus, SOL) muscles were dissected from ad libitum-fed rats of 2, 6, and 24 months of age. Additionally, muscle strips were excised from 24 month-old rats fed 60% of ad libitum food intake from 6 weeks to 24 months of age. Results indicate that SOL muscles become more compliant between 2 and 6 months of age but then decrease in compliance between 6 and 24 months of age. There was no age-related change in compliance of LOMO muscles. LOMO muscles were much more compliant than SOL at all ages. For example at 6 months of age and at 130% original length (Lo), average compliance of LOMO muscles and SOL muscles was 0.022 kPa^{-1} and 0.002 kPa^{-1} respectively. Yield stress of both muscles increased with advanced age. Average yield stress of LOMO was 444 kPa versus 949 kPa for SOL muscles in 24 month-old rats. Yield strain decreased with advanced age. Average yield strain in 24 month-old rats was: LOMO 170% Lo; SOL 153% Lo. Our results show that skeletal muscle becomes less compliant with advanced age and that chronic dietary restriction does not modulate this change in distensibility.

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88.5

MUSCLE ATROPHY DURING IMMOBILIZATION IN PLANTAR FLEXION IS NOT REVERSED BY RETURN TO JOINT NEUTRAL. Maxwell, L.C. and Enwemeka, C.S. Dept. Physiology, Univ. Texas Health Science Center at San Antonio, TX 78284 and Univ. Miami School of Medicine, Miami, FL 33146.

In clinical practice, repaired Achilles tendon ruptures are often protected by immobilization casts for four weeks in the fully plantar flexed position and another four to six weeks after returning the ankle to joint neutral. Moderate to severe muscle atrophy occurs within four weeks of immobilization in plantar flexion. We tested the hypothesis that the extent of atrophy could be minimized by return of the ankle to joint neutral after four weeks. Eighteen rabbits were anesthetized, and their right hindlimbs casted with the knee flexed 90° and the ankle fully plantar flexed. Three animals each were studied after 3, 4, 6, or 8 weeks of immobilization. After 4 weeks of immobilization, the immobilization casts of the remaining 6 rabbits were modified to return the ankle to joint neutral for another 2 or 4 weeks. For muscle studies, the animals were anesthetized, and the soleus (SOL), plantaris (PLN) and gastrocnemius (GST) muscles were removed and weighed; the SOL and PLN were quick-frozen and processed for histochemical fiber typing and fiber cross-sectional area measurement. All three muscles showed significantly reduced muscle weight to body weight ratios after three weeks of immobilization. SOL was the most affected and GST was least affected. There was no significant further atrophy through 8 weeks of immobilization. The atrophy correlated with a significant reduction of mean fiber cross-sectional area (MFA) for Types I, IIo, and IIc fibers in SOL and PLN. In PLN, Type IIg fiber area was not significantly reduced. MFA of muscle fibers of SOL and PLN muscles from limbs returned to ankle joint neutral for 2 or 4 weeks were not different from those of limbs kept at plantar flexion for 6 or 8 weeks. These data indicate that atrophy had reached a near-maximal extent within 4 weeks, and that subsequent return of the ankle to joint neutral did not reverse the atrophy.

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88.6

DISUSE ATROPHY IN A HIBERNATOR, THE GOLDEN MANTLED GROUND SQUIRREL (***SPERMOPHILUS LATERALIS***). Frank van Breukelen*, Steven J. Wickler, and Donald F. Hoyt. Calif. State Polytechnic Univ., Pomona, CA 91768

Decreased physical activity, whether from prolonged bed rest, immobilization or cessation of training for sports, leads to a loss of muscle mass (atrophy) and a decreased mass specific activity of enzymes involved in aerobic metabolism in skeletal muscle. Hibernation imposes periods of decreased activity but has received little attention in regards to muscle function. The present study was initiated to assess the effect of a 6 month hibernation on skeletal muscle Muscles (gastrocnemius and semitendinosus) were sampled from three groups of golden mantled ground squirrels: animals freshly caught in the fall (FF, n=7), animals freshly caught in the field within 1-2 weeks of their emergence (FS, n=7); and animals hibernated in the laboratory at 13 C .and sampled in the spring (HS, n=8). Mass specific enzyme activity was measured in all muscles using citrate synthase (CS) as an indicator of aerobic metabolism. To reduce errors associated with subcutaneous adipose and viscera masses, muscle masses were expressed per carcass mass (CM). Skeletal muscles were significantly ($P<0.05$) atrophied in both groups sampled in the spring when compared to fall animals [semitendinosus: FF=1.235±.061 mg/kg CM vs FS=.500±.066 and HS=0.703±.057 mg/kg CM; gastrocnemius: FF=10.3±.3 mg/kg vs FS=9.2±.3 and HS=8.8±.3 mg/kg CM]. Despite this atrophy , mass specific activities of CS were increased in animals sampled in the spring [25.3+1.9 < 32.9+2.1 < 41.7+1.9 µmoles/g•min for FF,FS, and HS groups, respectively]. As in other models of disuse atrophy, hibernation produces significant muscle atrophy. However in contradistinction, mass specific activities of an enzyme in aerobic metabolism were elevated in hibernators. This increase may reflect the importance of the thermogenic component of skeletal muscle in hibernators. The mechanisms by which these changes are induced warrant further investigation. [Supported by a CSU program for Research, Scholarship and Creative Activities to SJW and DFH].

88.7

DISUSE ATROPHY IN RODENTS: A HIBERNATOR RESPONDS ATYPICALLY. Steven J. Wickler, and Donald F. Hoyt. Calif. State Polytechnic University, Pomona, CA 91768.

Data on hibernating hamsters and Golden-mantled Ground Squirrels indicate that, as a result of hibernation, there is muscle atrophy but the mass-specific activities of mitochondrial enzymes increase. This is different from the classical response to inactivity in which these enzyme activities decrease. The present study was under taken to test the hypothesis that hibernators have evolved an unusual physiological capacity to resist detraining and will also respond differently to decreased activity when not hibernating. Seven Golden-mantled Ground Squirrels (Spermophilus lateralis bernardinus) were sacrificed two days after capture. The gastrocnemius muscle was removed, trimmed of fascia, weighed immediately, frozen and stored at -70 °C until homogenized. The remaining nine animals were held at 20°C (LD 12:12) in standard rat cages (24 cm x 18 cm x 13 cm) with ad lib. rat chow and observed daily. None of them exhibited torpor. Thirty days after capture they were sacrificed and tissue samples collected and treated as before. When muscle masses were expressed as a percent of carcass mass and compared using two-way ANOVA (grouped by sex and treatment), the muscle demonstrated significant atrophy ($p<.001$), decreasing by 16%. The response was not different for the two sexes. We measured mass-specific activities of citrate synthase (CS), an indicator of aerobic metabolism, and B-hydroxyacyl-CoA dehydrogenase (HOAD), an indicator of beta oxidation. Mass-specific activities of both enzymes were significantly increased ($p<.05$) after one month of inactivity. The activity of CS increased 31% from a mean value of 26.2 ± 3.1 to 34.3 ± 3.1 micromoles/min•gram muscle tissue. HOAD activity increased 24% from 18.3 ± 3.1 to 22.8 ± 2.6 micromoles/min•gram. Thus, during normothermic detraining, Golden-mantled Ground Squirrels exhibit the same kinds of changes as they do when hibernating and the opposite of that shown by all other species of animals that have been studied to date. Further study of this unusual adaptation should be very helpful in elucidating the cellular mechanisms responsible for disuse atrophy in all species.

88.8

EFFECTS OF PROLONGED EXERCISE ON CA^{2+} RELEASE FROM SARCOPLASMIC RETICULUM

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Disruption of the normal regulation of intracellular Ca2+ has been hypothesized as one possible cause of fatigue during an acute bout of prolonged exercise. Support for this suggestion comes from previous work from this laboratory demonstrating that exercise reduces Ca2+-stimulated ATPase activity and Ca2+ uptake in isolated sarcoplasmic reticulum (SR). Despite these findings, no data exist on the effects of this type of exercise on Ca2+ release from SR. SR vesicles were isolated from the red portion of rat gastrocnemius muscles following a single bout of treadmill running (duration> 1.5 hr). Measurements of Ca2+ uptake and release were performed in a temperature controlled reaction vessel (37°C) using a Ca2+ selective mini-electrode. Ca2+ uptake in the absence of a precipitating anion commenced upon the addition SR protein to a final concentration of 0.1 mg/ml. Once maximal uptake was achieved, release was initiated by adding $AgCl_2$, a compound which has been reported to function by oxidizing critical sulfhydryl groups associated with the Ca2+ release channel. Exercise depressed the initial rate of Ca2+ uptake as well the maximum capacity by approximately 30%. Despite this attenuation in uptake parameters, the magnitude of release was unaffected. These results may be explained by a direct exercise-induced modification of the Ca2+ ATPase which is independent of any effect on the release channel.

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88.9

MYOSIN ATPase ACTIVITY OF MUSCLE FIBERS THAT EXPRESS SLOW AND FAST MYOSIN. R.R. Roy, B.Jiang*, J.F. Marini* and V.R. Edgerton. Brain Research Institute and Kinesiology Department, UCLA, LA, CA 90024-1568.

The interrelationships among myosin ATPase activity, the presence of slow and fast monoclonal myosin heavy chains (MHC) and the staining patterns for qualitative myosin ATPase at an alkaline and an acid preincubation, were determined in soleus and medial gastrocnemius (MG) fibers of adult normal and spinal transected (at vertebral level T12-T13) cats. In both muscles of the two groups, the mean ATPase activity of fibers that reacted only with the fast antibody was ~twice that of the fibers that reacted only with the slow antibody. Fibers that expressed both MHCs in either muscle had intermediate ATPase activities. Two distinct populations of fibers were observed in control soleus. Fibers that reacted with only slow MHC had low ATPase activity, stained lightly for alkaline and darkly for acid ATPase. The reverse pattern was observed in fibers that reacted only with the fast MHC antibody. In the MG, the fibers were not separated in as distinct of subgroups as observed in the soleus. Some fibers had intermediate values for each of the reactions and the fibers expressing only the fast MHC had a much wider range of ATPase activities than the same fiber type in the soleus. In addition, a linear relationship between the optical density after acid preincubation and ATPase activity in fibers expressing only fast MHC existed in the normal MG and persisted after spinalization. In summary, each ATPase reaction could be used to distinguish between fibers that expressed slow and fast MHCs. However, the degree of accuracy of each reaction appeared to be muscle specific. The order was ATPase activity, acid ATPase and alkaline ATPase for the soleus and ATPase activity, alkaline ATPase and acid ATPase for the MG. These results suggest that ATPase activity is highly correlated with the type of MHC expressed in fibers of the cat soleus and MG, but that this relationship can be influenced by a number of factors such as pH sensitivity, the intrinsic properties of the muscle and experimental manipulations. Supported by NIH Grant NS16333.

88.10

A SINGLE LENGTHENING CONTRACTION CAN INDUCE INJURY TO SKELETAL MUSCLE FIBERS. Eileen Zerba and John A. Faulkner. Department of Physiology, University of Michigan, Ann Arbor, MI, 48109.

Functional deficits and histological evidence of injury to skeletal muscle fibers of mice have been observed following a series of repeated lengthening contractions at a train rate of 0.25 Hz. Although reports of pain and soreness in human beings support the occurence of contraction-induced injury after single contractions no documentation exists of the initiating circumstances or the magnitude of the injury. We hypothesize that: 1) a significant deficit in force can be produced by a single lengthening contraction, and 2) the velocity and extent of lengthening are associated with the magnitude of injury immediately and at 3 days following a single lengthening contraction. Mouse extensor digitorum longus muscles were exposed to single lengthening contractions in situ. After isometric force plateaued, the contracting muscle was stretched once through a displacement of 35%, 55%, and 75% of fiber length (L_f). The displacement was from 5% below L_f to either 30%, 50% or 70% above L_f at isovelocities of 0.5, 1.0 and 2 L_f/s. The amount of injury to muscles was determined immediately and 3 days after the protocol by measurement of maximum isometric force (P_o) and by damage to morphology of fibers. Immediately following a single lengthening contraction at 2 L_f/s, muscles lengthened 35%, 55% and 75% of L_f produced forces that were 100%, 84%, and 42% of their initial isometric force, respectively. At 3 days, the forces produced by muscles lengthened 35% and 55% of L_f did not differ from values for pre-injured P_o, whereas muscles lengthened 75% of L_f produced forces that were 35% of control values for P_o. Histological evidence of injury closely paralleled deficits in force associated with the injury protocols. We conclude that a single lengthening contraction can induce injury when a muscle is lengthened $\geq$55% of L_f and at velocities $\geq$2 L_f/s. Supported by AG 06157.

88.11

COORDINATED OPTICAL AND MAGNETIC RESONANCE IMAGING/SPECTROSCOPY OF Hb AND Mb DEOXYGENATION IN EXERCISING MUSCLE. B. Chance, S. Nioka, D.-J. Wang, M. Hogan and W.Bruchue. Univ. of Pennsylvania Medical School, Phila., PA, 19104

The recent developments of phase modulated spectroscopy (PMS) affording quantifiable measurements of hemoglobin (Hb) and myoglobin (Mb) deoxygenation in exercising muscle (1), and of proton spectroscopy of the proximal histidine of Mb (exclusive of Hb) (2,3) permit a quantification of muscle hypoxia during exercise. Fiber optic coupling of PMS to the vastus lateralis of a middle aged expert rower shows the progressive deoxygenation of Hb and Mb in bicycle ergometry with 50% maximal effect observed at 250 W. Cuff ischemia causes no further deoxygenation response; both Hb and Mb appeared deoxygenated. In order to ensure that PMS measures Mb we used ^{1}H NMR to evaluate Mb deoxygenation in a dog model. The elliptical surface coil is fitted to the gastrocnemius of a large anesthetized mongrel dog and attachment of the optical fibers within the coil allowed simultaneous monitoring by optical and NMR spectroscopy. EMS at 5Hz gives progressive deoxygenation to 70% full scale deoxygenation by PMS. No deoxygenation of Mb was detected by NMR. N_2 breathing then induced complete Mb deoxygenation and a further 30% change of PMS signal. We conclude: 1) The optical method measures both Hb and Mb deoxygenation and 2) by applying the dog data to this particular subject, we calculate Mb deoxygenation begins at 200 W and is complete at 360 W.

(1) Chance B, et al (1990) Biophys. J. 57:189. 2) Jue T & Anderson S (1990) Mag.Reson.Med. 13:524; 3) Wang, D.-J, et al Soc. Mag.Reson. Med. 9th Ann. Mtg. submitted Support in part HL 31934; HL 44125, GM 42322 and HL 18708.

88.12

ACUTE EFFECTS OF RESISTANCE EXERCISE ON MRI OF SKELETAL MUSCLE: CONCENTRIC VS ECCENTRIC CONTRACTIONS. F. Shellock, T. Fukunaga*, J.Mink*, V.R. Edgerton*. Cedars-Sinai Medical Center and Dept. of Kinesiology, UCLA, Los Angeles, CA 90048

Exercise produces alterations in the amount and distribution of water in skeletal muscle that is clearly demonstrated by magnetic resonance imaging (MRI). In this study, the acute effects of eccentric vs concentric resistance exercise on MRI of skeletal muscle was evaluated. Axial plane, T2-weighted images were obtained from the mid-forearm to the humeral head areas in five untrained subjects immediately before and after eccentric and concentric contractions performed to "subjective failure" by doing biceps curl resistance exercise. Concentric contractions produced a significant increase in signal intensity localized to the exercising muscles (i.e., biceps and brachialis) immediately after exercise. There were little or no signal intensity changes observed for the muscles performing eccentric contractions. This data suggests that concentric contractions are more likely to produce increases in extracellular water compared to eccentric contractions.

88.13

GLYCONEOGENIC ENZYME ACTIVITIES IN NORMAL AND PSEUDOMYOTONIC MUSCLES. R.J. Talmadge* and H. Silverman* (SPON: T.H. Dietz). Louisiana State University, Baton Rouge, LA 70803

The superficial region of the pseudomyotonic gastrocnemius muscle of the C57Bl6J dy^{2J}/dy^{2J} mouse contains elevated lactate and glycogen. Autoradiography indicates an increased lactate uptake by muscle fibers that store high amounts of glycogen. In this study activities of glyconeogenic enzymes and glycogen synthetase were evaluated in order to determine if any enzymatic adaptations in the lactate to glycogen pathway had occurred. Total glycogen synthetase activity was increased in the pseudomyotonic gastrocnemius by 23%. The percentage of glycogen synthetase found in the active form was elevated by 17%. The total amount in the active (I) form was increased by 44%. Histochemistry demonstrates that this increase in glycogen synthetase activity was found primarily in high glycogen containing fibers in the dy^{2J} gastrocnemius. In normal muscle glycogen synthetase activity was slightly greater in FOG fibers than FG fibers. FOG fibers also contain greater amounts of glycogen as determined by PAS staining. Phosphoenolpyruvate carboxykinase and malic enzyme were elevated by 58% and 51% respectively. Malic enzyme activity was preferentially elevated in the high glycogen fibers. Malate dehydrogenase (MDH) was elevated by 66%. The fiber type distribution of MDH followed that of succinate dehydrogenase and did not correspond to high glycogen fibers. The activity of fructose 1,6 bisphosphatase was decreased.

88.14

CONTRACTILE PERFORMANCE, GLYCOGEN STORES, AND LACTATE PRODUCTION OF FROG MUSCLE: IS THERE A CORRELATION WITH LIFESTYLE? Jeremy W. Patterson*, Univ. of Zimbabwe, Box MP 167, Harare, ZIMBABWE.

Endurance, speed of contraction, maximum twitch tension, and glycogen and lactate concentrations were studied in isolated preparations of the gastrocnemius muscle of three species of Anura. Muscle of Bufo gutturalis (the species with the greatest capacity for sustained activity) had the greatest endurance and the largest store of glycogen. Muscle of Rana angolensis (the species capable of the most rapid movement) produced the greatest twitch tension. Muscle of Phrynomerus bifasciatus (a species which walks rather than jumps and which is capable of only slow movement) had the slowest speed of contraction and the lowest maximum twitch tension. Neither glycogen depletion nor lactate build up during exercise provided an adequate explanation of the biochemical basis of exhaustion in muscle. In general, there was a good correlation between muscle characteristics and lifestyle in these frogs, although lactate concentration did not correlate with lifestyle. This work was supported by the Research Board of the University of Zimbabwe.

88.15

THERMAL ACCLIMATION MODIFIES GLYCOLYTIC ENZYME BINDING IN RED AND WHITE MUSCLE OF GOLDFISH, *Carassius auratus*. Maria Huber* and Helga Guderley, Université Laval, Québec, P.Q. G1K 7P4

Thermal acclimation changes protein isoforms, enzyme levels and mitochondrial abundance in goldfish muscle. As glycolytic enzyme binding varies with the physiological status and is a potentially important regulatory mechanism, it may vary with thermal acclimation. Goldfish were acclimated to 8 and 25°C for six weeks before examining the dynamics of glycolytic enzyme binding during the transition from rest to exhaustion. At 25°C, exhausting exercise markedly increased phosphofructokinase (PFK) binding in red and white muscle, while at 8°C exercise did not modify PFK binding. White muscle consistently shows greater binding of the glycolytic enzymes, particularly PFK. Warm acclimation increased the binding of the glycolytic enzymes, particularly PFK, in both rested and exhausted red muscle, while it only altered binding in exhausted white muscle. Fatigue leads to opposite changes in the binding of PFK and the other glycolytic enzymes, probably due to a decrease in pH. This response may reflect the disruption of a glycolytic complex.

88.16

THE EFFECT OF HYDROGEN PREROXIDE AND DITHIOTHREITOL ON LENS ACTIN. Mary Li and P.N. Farnsworth. UMDNJ, Dept. of Physiology and Ophthamology, Newark, NJ 07103-2714

The importance of actin and its role in the cortical lens fiber cell matrix is well established. Both in vitro and in vivo studies have shown that oxidative insult to the lens produces an abnormal matrix. The ratios of nuclear to cortical G actin/g protein in two year old cow and six month calf lenses are 0.80 and 0.27, respectively, (DNAse I inhibition assay). The incubation of lens homogenates with H_2O_2 for 30 minutes resulted in an increased concentration of G actin, and after 30 minutes in a progressive decrease in the concentration of G actin. Its oxidative modification was dependent on the concentration of H_2O_2 and length of incubation. The oxidized actin was compared with normal actin before and after dithiothreitol treatment by immunoblotting using anti-actin antiserum. Oxidation of lens actin produced, in addition to the control band, evidence for high molecular weight aggregates and one band which approximated the molecular weight of actin trimers. Following dithiothreitol treatment the actin trimers disappeared and the monomeric G actin increased. These data show that oxidative insult can not only depolymerize F actin to G actin but also induce G actin aggregation and subsequent degradation. The aggregation of actin molecules is reversed by dithiothreitol and mercaptoethanol. Supported by NIH Grant EY05787.

PULMONARY VENTILATION

89.1

VENTILATION-PERFUSION RELATIONSHIPS DURING HEAD-OUT WATER IMMERSION (HOI). T. Derion*, H.J.B. Guy*, K. Tsukimoto*, W. Schaffartzik*, R. Prediletto*, D.R. Knight, and P.D. Wagner. Dept. of Medicine, Univ. of Calif., San Diego, La Jolla, CA 92093.

In HOI, airway closure during tidal breathing can occur, may result in low $\dot{V}_A/\dot{Q}$ areas, shunt, and may cause hypoxemia. We measured the distribution of $\dot{V}_A/\dot{Q}$ ratios in 4 nonsmoking males (46 ± 3 yr) whose closing volume (CV) > expiratory reserve volume (ERV) during HOI ($p<0.05$). Arterial and expired inert gas concentrations, and dye-dilution cardiac output ($\dot{Q}$) were measured before and at 2, 5, 10, 15, and 20 min of HOI in 35°C water. CV was determined with a single-breath He test; ERV was measured by spirometry.

	dry	2	5	10	15	20 min
$\dot{V}_E$ (L/min)	9.8	12.9	10.4	9.2	10.9	8.7
$\dot{Q}$ (L/min)	5.9	7.1	7.7*	6.9	7.3	6.9
$\dot{V}O_2$ (L/min)	0.31	0.39	0.30	0.26	0.32	0.28
CV (L)	0.92					1.13
ERV (L)	2.06					0.63
PaO_2 (torr)	93	90	92	92	95	91
$PaCO_2$ (torr)	37	38*	37*	37	37	38
%shunt	0.6	2.3*	2.4*	1.5	1.2	1.2
%Q in $\dot{V}_A/\dot{Q}$ < 0.1	2.2	5.3	7.2	5.0	3.4	4.2
$logSD_Q$	0.73	0.79	0.86	0.78	0.77	0.80

*greater than control (dry) value, $p<0.05$.

Except for an increase in true shunt, $\dot{V}_A/\dot{Q}$ relationships did not significantly worsen during HOI despite a tendency to do so ($logSD_Q$). Surprisingly, hypoxemia did not occur although CV>ERV. We explain this by the offsetting effects of increased $\dot{Q}$ and increased $\dot{V}_A/\dot{Q}$ inequality/shunt and the minor amount of change in each. (Supported by NIH HL07212, HL17731; NASA NAGW-897; ALAC.)

89.2

CHEST WALL CONTRIBUTION TO V_A/Q HETEROGENEITY. ME Middaugh* and MP Hlastala. Univ of Wash, Seattle, WA 98195

The shape of the unconfined lungs is similar, but not identical to the shape of the chest cavity. During inflation, distortion results in a nonuniform distribution of ventilation and a consequent heterogeneous V_A/Q distribution. This study tested the hypothesis that opening the chest wall improves V_A/Q distribution. Supine, pentobarbital anesthetized and mechanically ventilated dogs were studied with the multiple inert gas elimination technique (MIGET). The V_A/Q distributions were determined in: 1) closed chest, 0 cmH_2O PEEP, [Cl-0]; 2) open chest, via a sternal thoracotomy, 5 cmH_2O PEEP, [Op-5].

	SD_Q	SD_V	V_{DIG}/V_T	Q_S/Q_T	Aa_{area}	E_{area}	R_{area}
Cl-0	0.798	1.821*	0.332*	0.030	0.657*	0.425*	0.232*
vs	±.151	±.252	±.076	±.030	±.112	±.088	±.036
Op-5	0.736	1.323	0.399	0.007	0.400	0.243	0.156
	±.122	±.361	±.056	±.007	±.110	±.083	±.035

(Mean ±SD) *$p<0.05$ Aa_{area}= Alveolar-arterial area, E_{area}= Excretion area, R_{area}= Retention area. Opening the chest improves gas exchange (↓Aa area). The effect is likely due to an improvement in V_A distribution (ΔSD_V is significant; ΔSD_Q is not) although the possibility of an improvement in Q distribution cannot be excluded. We conclude that the chest wall contributes to V_A/Q heterogeneity via a distortion of the lung during inflation.

89.3

POSTURE AND GAS EXCHANGE IN THE PIG. G.G. Berdine, R. Rodriguez*, and J.L. Lehr*. Univ Texas Health Sciences Ctr and Audie Murphy VA Hospital, San Antonio, TX 78284 and Harvard School Public Health, Boston, MA 02115.

Recent studies have demonstrated V/Q mismatching in supine dogs. We reasoned that this might be related to the effect of the abdominal contents on FRC. Six juvenile (12 wks) pigs were anesthetized with pentobarbital, ventilated through a tracheostomy, paralyzed with pancuronium, and suspended in the prone position. Tidal volume was 15 ml/kg and rate was adjusted for a normal P_aCO_2. The pigs were then placed in the supine position. Finally, a laparotomy was performed and the stomach and intestines were draped over the groin. FRC was measured by He dilution.

	P_aO_2 (torr)	P_aCO_2 (torr)	FRC (ml)
PRONE	112 ± 7	37 ± 2	514 ± 91
SUPINE	87 ± 15	43 ± 5	367 ± 48
EVISCERATED	94 ± 9	40 ± 3	454 ± 57

Posture affected P_aO_2 ($p < 0.0001$), P_aCO_2 ($p < 0.02$), and FRC ($p < 0.0002$). Evisceration recovered a greater ($p < 0.02$) fraction of FRC (67%) compared to P_aO_2 (19%). Measurement of CO_2 production in two pigs suggested that the effect on P_aCO_2 was due to a change in dead space. We conclude that the supine posture can increase dead space as well as V/Q mismatching, and that the effect of the abdominal contents on FRC is at most a minor factor in this phenomena. Supported by NIH HL32674 and HL33009.

89.4

LUNG VOLUME MAINTENANCE DURING HIGH FREQUENCY JET VENTILATION (HFJV) IMPROVES PHYSIOLOGICAL AND BIOCHEMICAL OUTCOME OF LAVAGED RABBIT LUNG. M Sugiura*, H Nakabayashi*, S Vaclavik*, AB Froese. Queen's University, Kingston ON K7L 3N6.

Lung volume maintenance improves outcome in early treatment of Respiratory Distress Syndrome (RDS) with High Frequency Oscillation (HFO). In this study we assessed HFJV (Bunnell Life Pulse) used at a low or high mean lung volume, with and without intermittent mandatory ventilation (IMV) breaths, in an RDS model. 30 New Zealand White rabbits (2.92±0.20kg) were lavaged with normal saline and randomized to receive HFJV/LO, HFJV+IMV/LO, HFJV/HI, HFJV+IMV/HI or HFO/HI. In low volume groups, $Pa0_2$ was 80-100mmHg; in high volume groups $Pa0_2$ was kept >350mmHg. After 4h ventilation, lung compliance and lamellar body (LB) and lung lavage phospholipid (PPL) contents were significantly lower in low volume than high volume groups. (Vmax=volume at 30cmH_2O)

	HFJV/LO	HFJV+IMV/LO	HFJV/HI	HFJV+IMV/HI	HFO/HI
Vmax	18.3	18.3	27.0	25.9	26.6
(ml/kg)	±2.1	±1.2	±1.1	±1.2	±1.6
Lavage PPL	462	463	848	1259	1217
(nmol Pi/kg)	±40	±13	±53	± 63	± 87
LB PPL	859	810	2196	2625	3025
(nmol Pi/kg)	±34	±38	± 69	±132	±169

We conclude that a high volume strategy of HFJV minimizes lung injury in primary treatment of this RDS model. No independent impact of IMV breaths was detected over 4h. Supported by MRC MA-10248

89.5

VENTILATOR PATTERN INFLUENCES EXOGENOUS SURFACTANT EFFECTIVENESS IN THE RABBIT. AB Froese, PR McCulloch,* S Vaclavik,* M Sugiura,* F Moller,* F Possmayer. Queen's University, Kingston, ON K7L 3N6.

Ventilator pattern influences surfactant balance in the atelectasis-prone lung (FASEB J 2: A1183, 1988). We evaluated 4 ventilator patterns following 80mg/kg exogenous bovine lipid extract surfactant in 24 anesthetized, paralysed saline-lavaged New Zealand White rabbits. Randomization occurred after surfactant treatment produced a PaO_2>350mmHg on FiO_2 of 1.0 with Paw of 7.6±0.8cm$H_2$0 during high frequency oscillatory ventilation (HFO) at 15Hz. Ventilator patterns were: HFO-HI, PaO_2>350mmHg; HFO-LO, P_aO_2 70-100mmHg; CMV-HI, PaO_2>350mmHg or pressures ≤39/9cm$H_2$0; CMV-LO, PaO_2 70-100mmHg. Target PaO_2 was sustained in all HFO-HI animals but only 1 of 6 in the CMV-HI group. Lung volume at 15cm$H_2$0 pressure (V_{15}) and phospholipids in lavage fluid (lav PPL) and lamellar body fractions (LB PPL) were assessed at 4h.

(mean±SE)	Control	LAVAGED	HFO-HI	HFO-LO	CMV-HI	CMV-LO
V_{15}	25.5	21.5	22.5	16.5	11.0	7.0
(ml/kg)	±1.3	±1.7	± .8	±2.0	±1.1	±.4
Lav PPL		787	1582	924	1365	682
(nMol Pi/kg)		± 88	± 81	±140	±295	±54
LB PPL	3325	2300	3062	1165	1739	1089
(nMol Pi/kg)	±144	±341	±266	± 83	±125	±107

We conclude that maintaining lung expansion enhances exogenous surfactant efficacy. Supported by MRC MA-10248.

89.6

DIRECT WASH-OUT - AN ESSENTIAL GAS TRANSPORT MECHANISM DURING HIGH-FREQUENCY OSCILLATION (HFO)

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CO2-elimination during HFO was investigated in 7 dogs (anatomical dead space: 70-120 ml) at oscillatory volumes, effectively delivered to the lungs (VDEL) of 60, 50, 40, and 30 ml. VDEL was measured on line with an ultrasonic airflow meter. The experiments were performed at 15 Hz, using an HFO-system without bias tube. The HFO-circuit related rebreathing volume, i.e. the volume of tubes, connecting the lungs with the surrounding (endotracheal tube and three port connector) was 35 ml.

Decreasing VDEL from 60 ml to 40 ml resulted in a moderate PaCO2 increase from 3.03±0.54 kPa to 4.60±0.89 kPa ($p < 0.025$, Wilcoxon test of two samples) and PaCO2 and VDEL were highly correlated in a reciprocal regression analysis in each individual dog (r2=0.95-1.00). These regression equations, however failed to predict PaCO2 at a VDEL of 30 ml: The actual PaCO2 of 8.26±1.77 kPa was significantly higher than the predicted value of 6.25±1.46 kPa ($p < 0.025$).

These findings confirm that CO2-elimination during HFO is possible with VDEL's considerably smaller than the anatomical dead space volume. Efficacy of CO2-elimination, however is limited if VDEL becomes smaller than the HFO-circuit related rebreathing volume. Hence, direct CO2 wash-out from central airways must be considered as an essential gas transport mechanism during HFO.

LUNG CELL

90.1

ATRIAL NATRIURETIC FACTOR (ANF) INHIBITS CILIARY MOTILITY IN CULTURED RABBIT TRACHEAL EPITHELIUM. K. Kobayashi,* J. Tamaoki, N. Sakai,* T. Kanemura, S. Horii,* K. Isono,* S. Takeuchi,* A. Chiyotani,* I. Yamawaki,* T. Takizawa* First Dept. of Med., Tokyo Women's Medical College, Tokyo 162, Japan.

To study the effect of ANF on airway ciliary motility, we measured ciliary beat frequency (CBF) by a photoelectric method in response to ANF in cultured tracheal epithelium from rabbits. ANF dose-dependently decreased CBF ; the maximal decrease from the baseline was 26.1 ± 1.5 % (mean ± SE, $P < 0.001$) and IC_{50} was 3×10^{-12} M. Pretreatment of tissues with the enkephalinase inhibitor phosphoramidon (10^{-6} M) potentiated the effect of ANF, so that the dose-response curve for ANF was shifted to lower concentrations by 0.5 log U ($P < 0.05$). The effect of ANF was not changed by indomethacin or nordihydroguaiaretic acid, but was abolished by methylene blue. The intracellular cyclic GMP levels were increased by ANF, an effect that was potentiated from 55.3 ± 3.4 to 87.5 ± 7.8 pmoles/mg protein ($P < 0.05$) by phosphoramidon. These results suggest that ANF inhibits ciliary motility through a guanylate cyclase-dependent regulatory pathway, and that enkepalinase may play a role in modulating the ANF effect on airway mucociliary transport function. (supported in part by a Grant No. 6877065 from the Ministry of Education, Japan)

90.2

INTRACELLULAR TAURINE CONTENT OF ALVEOLAR PNEUMOCYTES. V. Castranova, D.W. Porter*, W.G. Martin* and M.A. Banks.* Div. of Resp. Dis. Studies, NIOSH & Div. of Animal and Vet. Sci., West Virginia Univ., Morgantown, WV 26505, & Dept. of Food Sci. & Human Nut., Univ. of Fla., Gainesville, FL 32611.

Taurine is an amino acid which reportedly protects cellular membranes from damage. The purpose of the present study was to isolate three types of alveolar cells, i.e., macrophages (AM), type II cells (T_{II}), and type I cells (T_I), determine their taurine contents, and correlate them to cellular susceptibility to oxidants. AM were harvested by lavage (yield=7.2x10^6 cells/rat; purity=91%). AM characteristics were: cell volume=1456 μm^3, H_2O content=0.98 $\mu l/10^6$ cells, and taurine content=4.3 mM. T_{II} were isolated by enzymatic digestion and purified by centrifugal elutriation (yield=21.9x10^6 cells/rat; purity 90%). T_{II} characteristics were: cell volume=501 μm^3, H_2O content=0.21 $\mu l/10^6$ cells, and taurine content=14.4 mM. T_I were isolated by enzymatic digestion and purified by elutriation and specific surface absorption (yield=2.4x10^6 cells/rat; purity 79%). T_I characteristics were: cell volume=689 μm^3, H_2O content=0.48 $\mu l/10^6$ cells, and taurine content=0.14 mM. In conclusion, cellular taurine levels correlate well with the susceptibility of type I cells and the relative resistance of macrophages and type II cells to oxidant injury. Since plasma taurine=0.1 mM, mechanisms to accumulate taurine must exist in alveolar macrophages and type II cells.

90.3

THE IMPAIRMENT OF AIRWAY MUCOCILIARY TRANSPORT BY PSEUDOMONAS AERUGINOSA PRODUCTS INVOLVES OXYGEN RADICALS. ZS.V. Seybold,* W.M. Abraham and A. Wanner. Pulmonary Div., Univ. of Miami at Mt. Sinai Medical Ctr., Miami Beach, FL 33140.

We have previously shown that the cell free supernatant of a Pseudomonas aeruginosa (PA) culture and the PA products pyocyanin and 1-hydroxyphenazine inhibit tracheal ciliary activity via the generation of free oxygen radicals by phagocyte. In the present study, we wished to determine if tracheal mucociliary transport velocity (TMV) is also impaired by PA and if free oxygen radicals have a mediating role. In conscious sheep, TMV (measured with a radiographic method) was determined before and serially following aerosol challenge with cell free PA supernatant or unconditioned medium (control). TMV decreased from a mean baseline of 7±0.6 $mm.min^{-1}$ (±SE, n=5) by 34% at .5 and 24 hr post challenge ($p<.05$) and had returned to baseline 1 week later (-6%, p= NS). Unconditioned medium had no effect on TMV (+5%, p=NS). Aerosolized catalase prevented the effect of PA supernatant on TMV. In sheep tracheal tissues mounted in a chamber, PA supernatant decreased both surface liquid transport and ciliary beat frequency and tended to increase surface liquid depth. We conclude that 1) short term exposure to PA products decreases airway mucociliary clearance in vivo by a pathway involving free oxygen radicals, 2) the impairment is reversible within a week, and 3) cilioinhibition plays a role in the PA induced mucociliary dysfunction. (Supported by NIH grant ES03041).

90.4

SELECTIVE INDUCTION OF PULMONARY Mn-SUPEROXIDE DISMUTASE mRNA BY TUMOR NECROSIS FACTOR AND HYPEROXIA. Min-Fu Tsan*, Julie E. White*, Chris Treanor* and Jacquelin Shaffer* (SPON: A. Johnson). VA Medical Center and NYS Research Labs, Albany, NY 12208.

In a previous study, we have demonstrated that tracheal insufflation of recombinant human tumor necrosis factor-α (TNF) enhances pulmonary antioxidant enzyme activities and protects rats against oxygen toxicity. (J Appl Physiol 68: 1211-1219, 1990). To better understand the molecular basis for TNF-induced enhancement of pulmonary antioxidant enzyme activities, we measured pulmonary superoxide dismutase (SOD) mRNA (by northern blots) and specific proteins (by immunoblots). Tracheal insufflation of TNF (5 µg or 1.2 x 10^7 U) selectively induced pulmonary Mn-SOD mRNA in normoxia- or hyperoxia (100% O_2)-exposed rats, leading to increased amounts of Mn-SOD specific protein and enzyme activity. Tracheal insufflation of TNF had no effect on the levels of Cu, Zn-SOD mRNA or specific protein. Exposure of rats to hyperoxia for 55 hrs also selectively induced pulmonary Mn-SOD mRNA. However, the hyperoxia-induced increase in Mn-SOD mRNA was not associated with an increase in Mn-SOD specific protein or enzyme activity. These results suggest that the increased pulmonary Mn-SOD in TNF-insufflated rats may contribute to the TNF-induced protection against oxygen toxicity.

90.5

TUMOR NECROSIS FACTOR ENHANCES ENDOTHELIAL CELL SUSCEPTIBILITY TO OXYGEN TOXICITY: ROLE OF GLUTATHIONE. Zeineh Marcho*, Julie E. White*, Paul J. Higgins* and Min-Fu Tsan*
(SPON: A. Johnson). VA Medical Center, Albany, NY 12208

The effect of recombinant human tumor necrosis factor-α (TNF) on hyperoxia-induced endothelial cell injury in vitro was investigated. Tumor necrosis factor caused a time- and dose-dependent reduction in the number of viable calf pulmonary artery endothelial cells. The TNF-mediated endothelial cytotoxicity was much more pronounced under hyperoxia (95% O_2 and 5% CO_2) than under normaxia. Heat-inactivation of TNF completely abolished its cytotoxic effect to endothelial cells. Pretreatment of endothelial cells with TNF (0.01 µg/ml or 240 U/ml) for 18 hrs under normoxia reduced the intracellular concentration of glutathione (GSH) and rendered them more susceptible to hyperoxia- or H_2O_2-mediated cytotoxicity even in the absence of TNF. Tumor necrosis factor also induced changes in endothelial morphology and distribution of actin filaments. Exogenous GSH or L-2-oxothiazolidine-4-carboxylate, agents that enhance endothelial GSH concentrations, partially protected endothelial cells against TNF-mediated cytotoxicity, morphorlogical changes and actin filament redistribution, especially under the hyperoxic condition. These results demonstrated that TNF enhanced endothelial cell susceptibility to oxidant injury and suggested an important role of GSH in modulating endothelial response to TNF.

CARDIOVASCULAR ADRENERGIC SYSTEMS

91.1

LITHIUM CHLORIDE DECREASES VASOCONSTRICTION OF ARTERIOLES TO NOREPINEPHRINE AND ARGININE VASOPRESSIN IN VITRO. E.F. O'Connor*, J. Dunn* and J.E. Lawler.
Physiology Program and Department of Psychology, University of Tennessee, Knoxville, TN 37996.

Lithium chloride (LiCl) at 3 mM/l plasma reduces blood pressure in several rat strains. This is paradoxical in light of LiCl's stimulation of vasopressin (AVP) and norepinephrine (NE) release in vivo. One hypothesis is that LiCl releases pressor agents and reduces tissue responses. To test this, we exposed arterial strips from 4 borderline hypertensive rats (F1 cross of SHRxWKY) to NE and AVP in vitro. Strips were mounted in Ringers solution at 37°C and gassed with 95% O_2 and 5% CO_2. Tension (T) of the strip was adjusted to give a 75% response to 60 mM KCl. NE (10 nM - 5 uM) and AVP (1 nM - 10 nM) were added to the control (CONT) bath or to Ringers solution containing 3 mM/l LiCl. T was analyzed using LiCl and dose as factors. Responses to NE and AVP dose were decreased with LiCl ($p \ll 0.05$). The regression of T vs NE was reduced by LiCl, T=-3.0+15.8xNE (CONT) and T=-2.4+10.8xNE (LiCl). LiCl also reduced the T developed with AVP, T = 84.8 - 16.9 x AVP (CONT) and T=622.9-11.7xAVP (LiCl). These data suggest that LiCl must also act at the receptor level. (Supported by HL19680)

91.2

DECREASED MYOCARDIAL BETA-ADRENOCEPTOR DENSITY IN CANINES WITH CHRONIC HEART FAILURE. H.N. Sabbah, P.J. Gengo*[1], T. Kono*, P.D. Stein, J.K. Sharpe*[1], R.P. Steffen[1], and S. Goldstein*. Henry Ford Heart and Vascular Institute, Detroit, MI, 48202, and [1]Wellcome Research Laboratories, Research Triangle Park, NC, 27709

Myocardial beta-adrenergic receptor density (BD) was evaluated in 5 dogs with chronic heart failure produced by graded sequential intracoronary embolizations with microspheres. Dogs underwent 3 to 7 embolizations 1 to 3 weeks apart until LV ejection fraction was ≤ 30%. During the evolution of heart failure, LV ejection fraction decreased from 60±3% to 23±3% (P<.001) and plasma norepinephrine concentration (PNE) increased from 368±21 pg/ml to 561±71 pg/ml (P<.05). Three months after the last embolization, hearts were removed and prepared for radioligand binding. BD was measured by the method of Scatchard using [3H] dihydroalprenolol (DHA) with specific binding defined as that displaced by 1 uM propranolol. BD (Bmax) in cardiac microsomal membranes of heart failure dogs (323±18 fmol/mg of protein) was decreased compared to 5 matched control dogs (605±20 fmol/mg of protein) (P<.01). No change in the binding affinity (K_d) of DHA resulted after heart failure. The decrease in BD in this canine model of heart failure makes this preparation suitable for detailed examination of the role that beta-adrenoceptors have in the pathophysiology of chronic heart failure.

91.3

MECHANISM OF DESENSITIZATION INDUCED BY CHRONIC INFUSION OF ISOPROTERENOL. D.E. Vatner, N. Uemura*, J. Nejima*, C.J. Homcy, S.F. Vatner. Dept of Medicine and Pediatrics, Harvard Medical School, Children's Service, Massachusetts General Hospital, Boston, MA and New England Regional Primate Research Center, Southborough, MA 01772

To determine the mechanism of ß-adrenergic receptor desensitization with chronic infusion of isoproterenol (ISO), mini-osmotic pumps containing either saline or ISO were implanted subcutaneously for 3-4 weeks in dogs instrumented for measurements of left ventricular (LV) and arterial pressures. In conscious dogs an acute challenge to ISO (0.4 µg/kg/min), increased LV dP/dt by 6324±628 mmHg/sec and heart rate by 100±10 beats/min before ISO pumps and significantly less, p<0.01, for both LV dP/dt (2544±344 mmHg/sec), and heart rate (46±6 beats/min) after ISO pumps. In LV sarcolemmal membrane preparations from the dogs with ISO pumps, adenylate cyclase activity was globally depressed, p<0.01, whether stimulated by ISO (56%), fluoride (70%), or forskolin (57%) as compared to saline pump controls. There were also fewer agonist high affinity binding sites in animals with ISO pumps (6±6%) as compared to animals with saline pumps (48±13%). However, ß-adrenergic receptor density was not different from values observed in dogs with saline pumps (63±8 vs. 59±8 fmol/mg). Thus, chronically elevated ISO levels induce marked physiological desensitization, with a mechanism distal to the ß-adrenergic receptor.

92.1

DIETARY GAMMA-LINOLENIC ACID (GLA) REDUCES BLOOD PRESSURE AND AORTIC REACTIVITY. Mary B. Engler and Marguerite M. Engler. UCSF, San Francisco, CA 94143

The hypothesis that dietary GLA alters blood pressure and functional properties of aortic smooth muscle was tested in the rat. Male Sprague-Dawley rats were fed a purified diet containing either 11% (wt/wt) sesame oil (SES) rich in oleic acid or borage oil (BOR) rich in GLA for 7 weeks. Blood pressure by tail cuff technique and weight were measured weekly. Aortic rings were isolated and mounted in a smooth muscle bath. The rings were immersed and equilibrated for 60-90 mins. in Krebs-Ringer bicarbonate buffer solution (pH 7.4) and gassed continuously with 95% O_2 and 5% CO_2 at 37±0.5°C. Isometric force was measured. Blood pressure was significantly decreased ($p < 0.05$) in the BOR group as compared to the SES group. Weight gain was similar in both dietary groups. Aortic vascular responses to angiotensin II ($5x10^{-7}$M) and norepinephrine ($1x10^{-9}$M -$5x10^{-7}$M) were significantly decreased ($p < 0.05$) in the BOR group when compared to the SES group. KCl and serotonin contractile responses were similar in both groups. These findings suggest that dietary enrichment with GLA reduces blood pressure and attenuates the vasoconstrictor influences of exogenous angiotensin II and norepinephrine. These results are consistent with the hypothesis that dietary GLA favorably alters vascular smooth muscle tone. The alterations in vascular reactivity may be responsible for the beneficial effects of GLA on blood pressure.

92.2

PARATHYROID HORMONE: STRUCTURE-ACTIVITY RELATIONSHIPS. K.W. Chiu and P.K.T. Pang. Chinese University of Hong Kong and Univ. of Alberta, Canada.

Bovine parathyroid hormone-(1-34) [bPTH-(1-34)] has been reported to possess two distinct biological activities, viz. hypercalcaemic and hypotensive. These activities appear to locate at different sites of the molecule. Structure-activity studies of bPTH, rPTH and hPTH have recently been reviewed. In this study, porcine PTH-(1-34) was tested for its vasorelaxant effect on rat tail artery strips, and this effect was compared with those of bPTH-(1-34), Ala^1-pPTH and Nle^8-pPTH-(1-34). pPTH-(1-34) relaxed AVP- and NE-preconstricted strips in a dose dependent manner (30, 100, 300, 1000 ng/ml) but not in KCl-preconstricted ones. In AVP-preconstricted strips, Ala^1-pPTH-(1-34) and Nle^8-pPTH-(1-34) were also effective in promoting dose dependent relaxation. The sensitivity of these AVP-preconstricted strips to these PTHs to relax is in the following order: bPTH-(1-34), Ala^1-pPTH-(1-34), pPTH-(1-34), Nle^8-pPTH-(1-34). Data indicate therefore the importance of the N-terminal amino acids Ala and Met of the PTH molecule in regulating vascular smooth muscle activity. (Support from the Alberta Heritage Foundation for Medical Research)

92.3

EFFECT OF ANGIOTENSIN CONVERTING ENZYME INHIBITION ON THE SINU-ATRIAL NODE. **Paresh K. Patel*, David A. Mary* and Stephen G. Ball*. (SPON: Ian F. Hampton). Leeds University, Leeds LS2 9JT, U.K.**

Studies were undertaken to determine the effect of ramiprilat, a non-sulphydryl ACE inhibitor, on the sinu-atrial node in situ. Chloralose anaesthetised dogs, with their carotid sinuses vascularly isolated and perfused at constant flow, were artificially ventilated and acid-base balance and temperature maintained. Atropine (0.5 mg kg^{-1}), propranolol (0.5 mg kg^{-1}) and bretylium tosylate (10 mg kg^{-1}) were given. These doses completely blocked changes in heart rate in response to supramaximal stimulation of efferent cardiac vagal and sympathetic nerves and to reflex changes due to activation of the atrial receptors and carotid sinus baroreceptors. In 20 dogs, the baseline heart rate was 168 beats min^{-1} (mean; range 116-237), and aortic blood pressure was 20.4 kPa (10.8-28.2). After autonomic blockade they were 126 beats min^{-1} (101-177) and 13.3 kPa (6.3-21.1) respectively. With the prevention of any significant change in aortic blood pressure, intravenous ramiprilat (0.25 mg/kg) significantly decreased (paired *t*-test; $p<0.0001$) the heart rate to 121 beats min^{-1} (85-172). Our findings in anesthetised dogs with vagal and sympathetic blockade indicate that ramiprilat has a direct effect on the sinu-atrial node and reduces its rhythmicity.

92.4

REFLEXES FROM VENTRICULAR RECEPTORS AND THE CORONARY CIRCULATION. M.J. Drinkhill* J.K.A. Al-Timman*, and R. Hainsworth* (SPON: I. Hampton). Department of Cardiovascular Studies, University of Leeds, Leeds LS2 9JT, England.

Previously we have shown that simultaneous increases in aortic root and left ventricular systolic pressures result in reflex vasodilatation. In this study we examined the responses to independent changes in either aortic root or ventricular systolic pressure. Dogs were anesthetized with chloralose (100 mg/kg i.v.), artificially ventilated and the chest opened. A cannula, inserted into the ascending aorta and connected to a pressurized reservoir, allowed control of aortic root pressure. Left ventricular systolic pressure was controlled by transferring blood in either direction between the left ventricle, via a cannula inserted through its apex, and the aortic reservoir. Left atrial pressure was also controlled. The aortic and carotid baroreceptors were perfused at constant pressure while the lower part of the animal was perfused at constant flow through the descending aorta. Simultaneous increases in venticular systolic pressure and aortic root pressure, in six dogs, resulted in a decrease in arterial perfusion pressure of 37% (range 18-59). An increase only in aortic root pressure in the absence of a change in ventricular pressure decreased perfusion pressure by 27% (range 15-47). An increase in ventricular systolic pressure, in the absence of a change in aortic pressure only decreased arterial perfusion pressure by 13% (range 5-22). These results indicate that the major part of the reflex vasodilation arises from receptors stimulated by changes in aortic root pressure. The likely site of these receptors is in the coronary circulation.

92.5

HEMOGLOBIN SATURATION AND VENTILATION DURNG PRESYNCOPAL LOWER BODY NEGATIVE PRESSURE. J. Timothy Lightfoot*, J. Weir*, H. Klein*, M. Whitehurst*, M. Lyons* (SPON: S. M. Fortney). Florida Atlantic Univ., Boca Raton, FL 33431

Previous work has shown that lung diffusing capacity decreases during lower body negative pressure (LBNP; Dowell, et al. J. Appl. Physiol. 26:352, 1969). Therefore, the purpose of this study was to determine if the alteration in diffusion capacity caused a change in hemoglobin oxygen saturation (SaO_2) before the onset of presyncope. Fifteen subjects (27.1±1.2 yrs, 171.5±1.3 cm, 65.1±2.9 kg; mean±SE), underwent an LBNP test terminated at presyncope. SaO_2 was monitored using pulse oximeters (Nellcor) at the left index finger and at the bridge of the nose. At presyncope, expected decreases in heart rate (HR), blood pressure (MAP), and forearm vascular resistance (FVR) occurred. The following values (mean±SE) reflect observations at rest, one min before presyncope (PS-2), 30 sec before presyncope (PS-1), and at the onset of presyncope (PS) (*significantly different from Rest, $p<0.05$):

Variable	Rest	PS-2	PS-1	PS
FBF (ml/100 ml/min)	5.7±1.0	2.5±0.5*	2.5±0.8*	3.4±1.4*
SaO_2 nose (%)	96.0±0.6	94.3±1.3	94.1±1.6	93.9±1.1
SaO_2 finger (%)	98.7±0.4	98.5±0.5	98.0±0.7	97.5±0.7*
Ve (l/min)	8.0±0.4	10.0±0.7*	10.2±0.8*	10.6±0.7*
VO_2 (ml/min)	208±19	224±26	214±21	238±27

Because FVR increases during LBNP, finger SaO_2 might be expected to decrease. However, with an altered diffusing capacity during LBNP, the trend ($p=0.07$) toward a decreased nose SaO_2 might represent a mechanism influencing ventilation and cardiovascular homeostasis immediately before presyncope. It appears that these alterations maintain VO_2 at baseline levels.

92.6

CARDIOVASCULAR ADAPTATIONS TO REPEATED FOOTSHOCK STRESS DIFFER BETWEEN TRAINED AND NONTRAINED FEMALE BORDERLINE HYPERTENSIVE RATS. JE Steele, DE McCoy, RH Cox*, RL Wiley*, AND GJ McGuire. Miami University, Departments of Zoology and Physical Education, Health, and Sports Studies. Oxford, OH 45056

The influence of exercise training on heart rate (HR) and blood pressure (BP) during novel and repeated footshock stress in the borderline hypertensive rat (BHR) was investigated. Forty-seven female BHRs were used in this study. Twenty-three BHRs were exercise trained (ET) by 2 hours of daily swimming for 8 weeks begining at 8 weeks of age. The remaining 24 BHRs served as nontrained (NT) age-matched controls. The novel groups (ET n=14, NT n=15) were exposed to one 15-minute session of footshock stress (1 s, 0.6 mA every 40 s). The experienced groups (ET n=9, NT n=9) were exposed to 10 sessions of footshock stress over 2 weeks prior to the recording session. Resting HR was lower in ET BHRs than NT BHRs in both groups, but it was unchanged in ET BHRs (347 vs 345 bpm) and was 22 bpm lower in NT BHRs (386 vs 364 bpm) after repeated exposure to the stress. ET BHRs of both groups maintained a lower HR than NT BHRs during footshock, but the differences between ET and NT BHRs diminished with repeated exposure. Resting BP was nearly identical in ET and NT BHRs exposed to novel or repeated footshock. However, BP was slightly lower (5 mmHg) in NT and ET BHRs after repeated exposure to footshock. BP in ET BHRs was higher than NT BHRs during novel exposure to footshock, but after repeated exposure ET BHRs had lower BP than NT BHRs during footshock. The BP response to footshock decreased in both groups after repeated exposure, but the decrease was greater in ET BHRs than in NT BHRs (30 mmHg vs 10 mmHg). These results suggest that cardiovascular adaptations to repeated footshock stress appear to differ between ET and NT BHRs, with HR changes more pronounced in NT BHRs and BP changes more pronounced in ET BHRs.

92.7

PARASYMPATHETIC TONE INCREASES IN TRAINED AND NONTRAINED FEMALE BORDERLINE HYPERTENSIVE RATS AFTER REPEATED EXPOSURE TO FOOTSHOCK STRESS. RH Cox*, JE Steele, DE McCoy, RL Wiley*, and GJ McGuire. Miami University, Departments of Zoology and Physical Education, Health, and Sports Science. Oxford, OH 45056

The influence of exercise training on the relative contributions of the sympathetic and parasympathetic nervous systems on heart rate (HR) and blood pressure (BP) during novel and repeated footshock stress in the borderline hypertensive rat (BHR) was investigated. Forty female BHRs were used in this study. Twenty-two BHRs were exercised trained (ET) by 2 hours of daily swimming for 8 weeks begining at 8 weeks of age. The remaining 18 BHRs served as nontrained (NT) age-matched controls. The novel groups (ET n=13, NT n=9) received either i.v. atropine sulfate (1.0 mg/kg) or propranolol (1.0 mg/kg) injection prior to 2, 15-minute footshock stress sessions (1 s, 0.6 mA every 40 s) over a 3 day period. The experienced groups (ET n=9, NT n=9) were exposed to 10 footshock stress sessions over 2 weeks and received either i.v. atropine methyl bromide (1.0 mg/kg) or atenolol (10 mg/kg) injection before each of 2 recording sessions. ET BHRs of both groups maintained lower HR than NT BHRs during footshock, but the differences between ET and NT BHRs were diminished following repeated footshock exposure. These HR differences remained following sympathetic blockade but were eliminated by parasympathetic blockade. BP in ET BHRs was higher than NT BHRs during novel footshock exposure but lower after chronic footshock exposure. BP responses to parasympathetic and sympathetic blockade were diminished following repeated exposure to footshock. These data suggest that ET BHRs maintain a higher degree of vagal tone than NT BHRs during footshock stress and that, with repeated exposure to stress, sympathetic influence is unchanged and vagal tone increases in both ET and NT BHRs.

NEUROENDOCRINE

93.1

PRENATAL ETHANOL EXPOSURE DOES NOT ALTER EARLY PATTERNS OF LH, FSH AND PROLACTIN IN FEMALE SPRAGUE-DAWLEY RAT OFFSPRING. R.T. Savoy-Moore, K.H. Swartz*, A. Cheng*, J. Gibson*, B. Williamson*, E.L. Abel*. Department of OB/GYN, Wayne State University, Detroit, MI, 48201.

We have previously reported (Soc Study Reprod Abs 321, 1989) that prenatal ethanol exposure advanced vaginal opening, the first sign of puberty, in Sprague-Dawley rats. In this study, we examined whether hormones known to be involved in the onset of puberty [LH, FSH and prolactin (PRL)] were altered during early development by prenatal ethanol exposure. Pregnant Sprague-Dawley rats were fed liquid diets containing 0%, 17.5%, or 35% ethanol-derived calories (EDC), or rat chow ad lib, from gestation day 8 to term. At birth, litters were culled to 10 with preference for females (up to 7), and weaned on day 21. Females ($n \geq 8$/group/time) were sacrificed on days 1, 5, 9, 13, 17, 21, and 25. Only 1 rat per litter was killed at any age, but serum was pooled for radioimmunoassay of LH, FSH and PRL. The anterior pituitary (AP) was removed and weighed. Age significantly affected AP weight (wt), AP wt adjusted for body wt, PRL and FSH (MANOVA, $p < .05$), but not LH. Prenatal ethanol exposure decreased AP wt, and AP wt adjusted for body wt ($p < .01$), but did not alter hormone values. We conclude that while prenatal ethanol reduced AP weight, it did not have a major impact on the reproductive hormone pattern during early development. Supported by NIAAA P50AA07606.

93.2

REDUCED TRANSCRIPTION OF PITUITARY GROWTH HORMONE IN NONINSULIN-DEPENDENT OBESE-DIABETIC MICE. Richard Fehn. Department of Biology, California State University, San Bernardino, CA 92407

C57 BL/KsJ db/db diabetic mice are obese, hyperglycemic and insulin-resistant and serve as a model for Type II diabetes mellitus. Western blot analysis of pituitary proteins revealed that young diabetic animals (4-5 wks) developing obesity had about 30% less Growth Hormone (GH) than lean littermates and this deficit persisted through the stable diabetes stage (2-18 mo.). Dot blot hybridization of total pituitary RNA using a rat GH gene probe showed a 30% reduction in GH-specific mRNA in stable diabetic animals. Transcriptional suppression of GH is suggested. Older diabetic animals exhibit relative increases in pituitary GH and GH mRNA. Pituitary GH content of end-stage diabetics, however, exceeds that of lean animals and coincides with a dramatic weight loss in diabetics. Diabetic animals present hyperthyroidism and hypercorticosteronemia that are known to reduce GH transcription, thus may contribute to reduced GH-induced lipolysis and its subsequent restoration during obesity onset and decline, respectively. Supported by American Society for Biochemistry & Molecular Biology.

93.3

HIGH DOSAGES OF GONADOTROPINS DECREASE BOTH QUANTITY AND VIABILITY OF EMBRYOS OBTAINED FROM TREATED MICE. Barbara A. Shirley and Hassan Serry*. Univ. of Tulsa, Tulsa, OK 74104

Pregnant mares' serum gonadotropin (PMSG) and human chorionic gonadotropin (hCG), hormones that are used to stimulate ovarian follicle development and ovulation, were given to mice in twelve dosage combinations (PMSG: 5, 10, 20, or 40 IU; hCG: 0.5X, 1X, or 2X the PMSG dosage) to test the relationship of gonadotropin dosages to yield and viability of embryos. Mice were mated and embryos at the two-cell stage of development were taken from them, counted, and cultured. The lowest dosages of PMSG and hCG (5 IU and 2.5 IU respectively) resulted in an embryo yield of 39.4 $\pm$ 6.6 embryos per mouse and 92.4% of the embryos developed to blastocysts in 72 hrs of culture whereas the highest dosages of PMSG and hCG (40 IU and 80 IU) resulted in an embryo yield of 2.2 $\pm$ 2.1 embryos per mouse and none of the embryos developed to blastocysts. When the dosage of either PMSG or hCG was held constant and the dosage of the other gonadotropin increased, a decrease in embryo yield and inhibition of embryo development occurred within some part of the dosage range tested. Effects of a 20 IU dosage of either PMSG or hCG were so pronounced that dosages greater than 20 IU were in most cases without further effect. Results indicate that increases in dosages of either PMSG or hCG ultimately cause both embryo quantity and viability to decrease. (Supported by the Egyptian Cultural and Educational Bureau and by Hillcrest Infertility Center, Tulsa.)

93.4

ULTRASTRUCTURAL MORPHOMETRY OF TORPID PEROMYSCUS PINEALOCYTES CULTURED WITH NOREPINEPHRINE. William H. Yenke* and Edward B. Pivorun. Clemson Univ., Clemson SC, 29631.

Mammalian pineal gland involvement in torpor via norepinephrine/melatonin effects has been demonstrated in various species. In deermouse pineals, unique membrane-bound portions of cytoplasm apposed by mitochondria were present, dense-core vesicles (DCV) and synaptic ribbons were few, and light/dark pinealocyte morphometry revealed planimetric differences. Cell organelle and structural composition was different in all light, dark, torpid and euthermic cell combinations. Light cells contained numerous protein synthetic, storage and secretory organelles (which were more pronounced in euthermic animals). The dark/light cell ratio was 3.5:1; dark cells had fewer organelles characteristic of light cells and contained numerous mitochondria. Small clear vesicles (20-30nm) filled many dark cell end-bulbs. Flocculent-filled vesicles (FFV) were numerous in euthermic cells but few in torpid cells. Pineal organ culture changed pinealocyte substructure; this culturing effect was incorporated into the morphometry. Norepinephrine increased organelles related to protein synthesis in euthermic cells including DCV and depleted FFV in all cultured cells. Light/dark/torpid/euthermic cell organellar changes suggested a single transforming pinealocyte population with functional stages staining differentially as light and dark cells.

93.5

HOT FLUSHES RELATED TO OTHER SYMPTOMS AND SIGNS IN THE CLIMACTERIC?

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Health surveys of normal populations can yield important pre-clinical and clinical leads. Questionnaires were sent to 10598 women aged 39 to 60; 7256 complete replies were searched for the relation between climacteric status and frequency/severity of 25 common complaints. Pill users, women with a hysterectomy and/or ovariectomy were excluded from analysis; 5213 replies were used. Only hot flushes and their consequence: sweating, were found typical for the climacteric; confirming all previous studies. However, in early perimenopausal women an increased incidence of "fatigue" complaints was found, while only in peri- and postmenopausal women with hot flushes there is a second peak incidence of both "stress" (palpitations and tenseness) and "fatigue" complaints. These two consecutive peaks (with respect to time) suggest different mechanisms. Moreover the frequency of hot flushes matches in time the temporarily increased bone resorption in the late peri- and early postmenopause as found by Elders et al: [Bone & Mineral 1988; 5:11-19]. These temporal relations suggest new leads for neuroendocrine studies into flushes and other symptoms and signs in the climacteric. [This study was supported by the International Health Foundation, Brussels, Belgium and the Dutch Ministry of Health.]

93.6

CHANGES IN PLASMA BETA-ENDORPHIN CONCENTRATIONS DURING PICHINDE VIRAL INFECTION IN STRAIN 13 GUINEA PIGS. Z.M. Guo*, C.T. Liu, and C.J. Peters*. U.S. Army Med. Res. Inst. of Infect. Dis., Ft. Detrick, MD 21701-5011

Naloxone, an opiate antagonist, has been found to prolong the survival of strain 13 guinea pigs (S13-GP) infected with Pichinde virus (Fed. Proc. 44:1836, 1985). This finding suggests that endogenous opiates secreted by the pituitary and hypothalamus may be involved in the pathogenesis of Pichinde virus-induced disease. The present study was undertaken to determine whether plasma beta-endorphin concentrations were modified after Pichinde viral infection. Twenty-three S13-GP were allocated into control (N=9), infected I (N=6), and infected II (N=8) groups. Infected animals were inoculated with 10^4 plaque-forming units of Pichinde virus. Experiments were performed on post-inoculation day (PID) 7 for infected group I, and on PID 12 for infected group II. Blood samples of all S13-GP were collected from the common carotid artery under pentobarbital anesthesia. Plasma immunoreactive beta-endorphin was measured with a radioimmunoassay kit, and results (pg/ml) were 84.2 ± 13.1 (control), 202.1 ± 17.9* (infected I), and 154.2 ± 21.4* (infected II), (*$p<0.01$). Both Pichinde viral infection (Curr. Top. Microbiol. Immunol. 134:6, 1987) and intravenous administration of beta-endorphin (Proc. Natl. Acad. Sci. 75:6240, 1978) significantly depress cardiac functions. Our data suggest that an increase in plasma beta-endorphin may be partially responsible for the pathogenesis of Pichinde virus-induced disease.

93.7

EFFECTS OF AFTERNOON INJECTIONS OF MELATONIN ON WATER METABOLISM OF MALE SYRIAN HAMSTERS. Bruce A. Richardson, Colleen M. Kennedy* and Eugene H. Studier*. Univ. of Michigan-Flint, Flint, MI 48502

Melatonin (mel), a pineal indoleamine, when properly administered mimics the effects of the pineal gland on mammalian physiology. The present study was designed to determine: 1) what effects afternoon injections of mel would have on water metabolism of adult male hamsters and 2) the temperal relationship between mel treatment and these metabolic effects. Male hamsters maintained singly in metabolic cages on a 14L:10D (lights on 0600h) were injected daily with either vehicle or 25 µg of mel at 1600h for 86 consecutive days. Daily measurements of water consumption and urine production were made for each animal. Osmotic pressure, calcium, sodium and potassium concentrations were determined in urine samples collected at weekly intervals. After 10 days, mel injections resulted in significant increases in water consumption and urine production. Concomitantly, mel induced significant decreases in osmotic pressure as well as in urine concentrations of calcium, sodium and potassium. These findings indicate that exogenous mel affect renal function in the hamster. Supported by a Faculty Development Grant (UM-F) to B.A.R.

93.8

DOES CHRONIC EXPOSURE TO ADRENALINE AFFECT POST-TREATMENT CLEARANCE RATES IN RAINBOW TROUT?: APPLICATION OF A NEW METHOD FOR VENTRAL CANNULATION.
A. Kurt Gamperl and R.G. Boutilier. Dept. of Biology, Dalhousie University, Halifax, N.S. CANADA. B3H 4J1.

In the past, ventral aorta cannulations in fishes have been plagued by low success and short-term patency. However, a new method for ventral aorta cannulation enables pre-branchial blood sampling and pressure measurements to be obtained for a period in excess of a week. Other advantages of this technique are: 1) a double cannulation can be performed in 5-7 minutes; and 2) no leakage from the ventral aorta occurs because the cartilaginous tissue surrounding the aorta closes in tightly around the cannula. The ventral cannulation technique is being used to investigate the effect of chronic administration of adrenaline (epinephrine) on clearance rates in rainbow trout (Oncorhynchus mykiss). Fish were injected with adrenaline (Sigma Chemical Co.; 7.0 mg/kg; approx. blood conc. 250 nmol) or saline six times daily for one week. On the eighth day, fish are injected via the ventral aorta with [^{3}H]-adrenaline and [^{14}C]-sucrose (both from New England Nuclear) and blood samples were collected via the dorsal aorta at 0, 1, 2, 4, 8, 20, 40 and 60 minutes post-injection. Plasma radioactivity was measured without further processing to determine the rate of adrenaline extraction from the blood. Radiolabeled sucrose was used as an inert volume marker.

AGING

94.1

A RAPID AGING MODEL IN RATS

R. F. Tislow, Harvard Univ. Med. School, Boston, MA 02115 and Marriott Lifecare Community, Haverford, PA 19041-1095.

A rapid aging within 2-3 days was observed by the author (also independently by R.O. Greep) in hypophysectemized 26-29 day old Sprague-Dawley rats with hypothalamic lesions (FASEB.J.2(6) ABSTR.8342(1988). An animal model should facilitate research on premature aging in rats, and provide clues for premature aging in man. It would require to ascertain whether hypophysectomy is essential preceeding a hypothalamic lesion (HL). The location of the HL and its molecular biology should give some clues about the aging mechanism, and result in an animal model for the study of its treatment.

94.2

PULMONARY PENTANE EXCRETION INCREASES WITH AGE IN HEALTHY SUBJECTS. Edwin J. Zarling, Sohrab Mobarhan, Phyllis Bowen, Savitri Kamath; Loyola Univ., Dept of Med, Maywood IL and Univ. of IL, Dept of Nutr, Chicago IL

Lipid peroxidation occurs to excess in the presence of inflammation or in the absence of adequate circulating antioxidants. However, even in health low levels of lipid peroxidation can be detected by measuring the pulmonary excretion of pentane. In order to test whether this pentane excretion is related to age, we measured fasting breath pentane in 47 healthy subjects (ages 21 to 79). We also measured the antioxidants vitamin E, retinol, beta carotene, lycopene and zinc. These parameters were then compared by linear regression.

	regr coeff ± SEM	p value
age vs pentane	0.028 ± 0.012	<0.05
pentane vs vita E	1.36 ± 1.18	ns
pentane vs retinol	0.019 ± 0.023	ns
pentane vs beta car	0.011 ± 0.015	ns
pentane vs lycopene	-0.030 ± 0.026	ns
pentane vs zinc	-1.46 ± 1.54	ns

CONCLUSIONS: In healthy subjects, 1) pentane excretion increases with age, and 2) this increase is independant of antioxidants levels.

95.1

SUBSTANCE P : A POSSIBLE INDEX OF PAIN IN PATIENTS WITH SPINAL ARACHNOIDITIS. Enzo Molina, Antonio Signorelli*, Lucio Gualandris*, Enrico Petroboni*, Rossella Merli* and Valentino Cassinari*. Inst. of Pharmacol. and Pharmacogn., University of Parma, Div. of Neurosurgery, OO.RR. Bergamo (Italy)

In 18 patients suffering from chronic low back pain caused by spinal arachnoiditis, and have been implanted with multipolar spinal cord stimulation (S.C.S.) system, we measured Substance P, Beta-endorphins, ACTH and Cortisol blood levels. A basal blood sample (B) was taken in the morning of the day before implantation, a further blood sample (I) was taken 5 days after, and another (II) after 10 days. The results are reported in the following table:

	B	I	II
Substance P			
pg/ml	129.1 ± 47 (*)	50.6 ± 21	40.5 ± 7
Beta-Endorphins			
pg/ml	44.5 ± 2	45.4 ± 2	47.9 ± 3
ACTH			
pg/ml	18.8 ± 5	19.6 ± 5	23.7 ± 6
Cortisol			
ng/ml	15.1 ± 1	19.6 ± 2	18.5 ± 2

(*) $p<.05$ Wilcoxon test. The basal values (B) of Substance P were particularly elevated even if compared to healthy subjects (2.3 ± 3). All our patients undergo a follow-up program involving blood samples withdrawal after six and twelve months. **Conclusion:** a good correlation between the positive analgesic effect of the S.C.S. system, clinically proved, and the variation of the Substance P blood levels was observed.

95.2

EVALUATION OF AN IN VIVO MODEL DESIGNED TO STUDY PROTRACTED EFFECTS OF LOCAL ANESTHETICS. N.A. Pahno*, V.E. Paris*, D.D. Rigamonti*, V.R. Jimmerson* and G.F. Seng* (SPON: H.S. Lowensohn). USAIDR, WRAMC, Washington, D.C. 20307-5300.

Lidocaine is used routinely in neurophysiological experiments to study typical responses to local anesthetics. However, the reported experimental and recommended clinical doses are apparently in great excess of that needed to produce conduction block in all fibers of a mixed nerve. The present study used a unique in vivo rodent model developed by Paris et. al. (Soc. Neurosci. Abstr., Vol 16., 1990) to evaluate anesthetic effects of lidocaine HCl (2%). Minute injections (<5 umoles) were made within the perineurium of the surgically exposed sciatic nerve using a glass micropipette (tip OD<30u). The average diffusion distance was 9mm (range 6-14 mm). Core temperature was maintained at 37.5 ± 0.3° C. Individual nerve fiber fractions were identified by their onset conduction velocities ($A\alpha$=64.6 ± 9.2; $A\delta$=3.3 ± 0.5; C=1.5 ± 0.1, m/sec), and conduction block and return of nerve function were studied for up to 10 hr. Both onset of block and recovery times were dose-dependent, and recovery varied among the fiber fractions. These results are consistent with recent in vitro, as well as in vivo clinical studies, but suggest that lidocaine is effective at minute experimental doses when administered intraneurally. Furthermore, these results demonstrate that the present model may be useful for evaluating the protracted effects of other local anesthetics.

95.3

CEREBROSPINAL FLUID (CSF) SAMPLING AND INTRACEREBROVENTRICULAR (ICV) INFUSION IN ANESTHETIZED STRAIN 13 GUINEA PIGS. C.T. Liu and Z.M. Guo*. U.S. Army Med. Res. Inst. of Infect. Dis., Ft. Detrick, MD 21701-5011

The strain 13 guinea pig (S13-GP) serves as a model for studying arenaviral hemorrhagic fevers in man. To study the possible brain-chemistry changes during arenaviral infection, techniques for repeated sampling of CSF and constant ICV infusion were developed by using anesthetized S13-GP (~700g). 1. CSF sampling: The head of the animal was placed in a stereotaxic device with anterioventral tilt at 30°. Cisternal punctures were made with an L-shaped, 23-gauge needle through the shaved skin. Clear CSF (~0.2 ml) was collected in 5-10 min at 2-hr intervals for 8-10 hr after IV saline infusion (10 ml/hr.kg^{-1}). 2. ICV infusion: Bilateral cerebroventricles were catheterized stereotaxically with two 20-gauge needles into the skull (5-6 mm depth). The location was 1 mm behind the anterior fontanelle and 1.5 mm to the left or right of the sagittal suture. Baseline values of left cerebroventricular pressure (CVP) were 0-4 cm H_2O. Although CVP reached 10-16 cm H_2O after artificial CSF was infused into the right ventricle at 0.5 ml/hr, cardiopulmonary functions remained unchanged. However, after an infusion at 5 ml/hr, minute volume and blood pressure increased initially and decreased thereafter, leading to shock. We found that about 1 ml of CSF can be obtained for biochemical analyses; an ICV infusion of <0.5 ml/hr in S13-GP was safe for delivery of certain drugs and substances into the brain.

95.4

THE EFFECT OF TEMPERATURE ON FLIGHT MOTOR PATTERNS IN LOCUSTA MIGRATORIA. J.A. Foster* and R.M. Robertson. Department of Biology, Queen's University, Kingston, Ontario, K7L 3N6, Canada.

In flying locusts the temperature of the thoracic nervous system can vary between 26°C and 40°C. Temperature influences neuronal properties and interactions but it is unknown how the operation of the flight circuitry in the thoracic ganglia is affected. Flight motor patterns were recorded from dissected, deafferented preparations perfused with saline at different temperatures and from intact locusts tethered in a wind tunnel at different ambient temperatures. Increasing the temperature of the nervous system by 10°C led to an average 2.7 Hz increase in the frequency of rhythmic motor output of the deafferented preparation. The same relationship was observed for the intact locusts. We conclude that the effect of temperature on wing beat frequency in the intact animal can be accounted for by changes in the operation of the central circuitry. We are investigating the changes in neuronal physiology that may account for these effects. Preliminary observations show a decrease in the latency of synaptic interactions with increases in temperature and a decrease in the amplitude of inhibitory synaptic potentials. This work was supported by the Natural Sciences and Engineering Research Council of Canada.

95.5

THERMOENCEPHALOSCOPY - NOVEL TECHNOLOGY FOR RESEARCH ACTIVATION OF CORTEX. A.M. Gorbach* and E.N. Tsicalov* (SPON: M. Frank). Inst. Higher Nerv. Activity, Butlerova St. 5a, Moscow, USSR, 117342

The new method of neuroimaging, Thermoencephaloscopy (TES), has been developed based upon the dynamic recording of the infrared radiation related to the brain cortex activity (the local metabolism of units, the local cerebral blood flow, the activity of cortical neurons and glial cells) from an unopened skull by a thermo and image processing technique. Parameters of the method are: thermosensitivity of up to 0.002°C, spatial resolution of up to 70 μm/pixel and temporal resolution of up to 40 msec. Thermomap consists of 16384 pixels; each reflects the temperature of a small region of the brain cortex. Infrared brain scans of rats, rabbits, cats and monkeys recorded during stimulation of different types and parameters (photic, acoustic, and electrodermal stimulation, conditioning, direct electrical cortical stimulation and cortical motor testing) demonstrated the existence of local dynamic effects in the primary and secondary projection fields of the cortex. Wave processes were found spreading over the cortex with a slow (1-10 mm/min. in the case of Leao's spreading depression) or a fast (1-33 mm/sec.) speed. Temperature dynamics and right side asymmetry on the dorsal surface of the brain were found during sleep cycles of a unconstrained rat. Thus our experiments with TES help to define the position, size and sequence of operation of activated (heated) and deactivated (cooled) cortical zones during different types of function.

95.6

PURINE AND AMINO ACID RELEASE FROM THE ISCHEMIC RAT CEREBRAL CORTEX. John W. Phillis, Richard E. Simpson and Gary A. Walter. Department of Physiology, Wayne State University, Detroit, MI 48201.

Estimates of the extracellular levels of adenosine and its metabolites and of the amino acids glutamate, aspartate, γ-amino-butyric acid (GABA) and glycine were obtained by measuring their concentrations in rat cerebral cortical cup superfusates. Artificial CSF samples were taken at 10 min intervals. Two sets of control superfusates preceeded 20 min of brain ischemia by bilateral carotid artery occlusion. HPLC measured levels of purines and amino acids were followed prior to, during and for 3 hrs 40 min of recirculation. Purines and the excitatory and inhibitory amino acids increased in the cortical superfusates during and immediately following ischemia. Purine levels in pre-ischemic cortical superfusates in nmole/litre were: adenosine 68.9±12.9; inosine 215.5±85.6; hypoxanthine 554.3±289.4; xanthine 537.0±165.2; and uric acid 722.5±159.4. With the exception of uric acid levels, these increased during the second ischemic collection to: adenosine 1082.2±196.3; inosine 1281.7±137.7; hypoxanthine 3421.5±287.1 and xanthine 947.4±155.2. Uric acid levels declined during the ischemic challenge to 496.3±144.9, but rose during subsequent collections to a peak level of 2004.4±446.3 nmole/litre at 40 min post-ischemia. Adenosine and inosine levels normalized rapidly upon reperfusion, followed sequentially by hypoxanthine, xanthine and uric acid. Control pre-ischemic levels of the amino acids in nmole/litre were: glutamate 975.9±364.3; aspartate 312.4±67.2; glycine 7804.8±968.9; GABA 173.9±68.2 and these increased to: glutamate 7257.4±1869.6; aspartate 1753.6±521.3 and GABA 3319.0±709.6 during the second ischemic collection. Glycine levels increased slowly after the ischemia reaching a peak of 9536.0±1407.0 nmole/litre at 40 min. Amino acid levels returned to normal within 90 min of reflow. High extracellular levels of the excitotoxic amino acids, glutamate and aspartate, may be involved in ischemia-induced neuronal loss.

95.7

ROLE OF NEUROTRANSMITTERS IN THE ANOXIC SURVIVAL OF TURTLE BRAIN. Peter L. Lutz and Göran Nilsson*, Marine Biology and Fisheries, RSMAS, University of Miami, Miami, Florida 3314 9

The turtle brain survives anoxia by depressing its metabolic rate to match a severely reduced energy supply, while maintaining its energy and ionic status. The mechanisms by which this is achieved are unknown but our results indicate that neurotransmitters are key players. Subjecting the turtle brain to anoxia produces a substantial rise in the tissue levels of the inhibitory neurotransmitter GABA and a decrease in the excitatory transmitter glutamate. There is an increase in alanine sufficient to inhibit pyrurate kinase activity and thus depress glycolysis. Surprisingly, the oxygen dependent monoamines serotonin, norepinephrine and epinephrine do not decline and may be stockpiled, being found in much higher concentrations in the turtle than in mammalian brain. Monitoring the release of the neurotransmitters during anoxia by microdialysis showed an initial transient release of adenosine followed by a massive and sustained release of GABA, taurine and glycine. However, extracellular glutamate levels do not change thus avoiding the uncontrolled release of glutamate thought to be a major cause of exitotoxic death in the mammalian brain.

95.8

MEMBRANE DEPOLARIZATION INHIBITS ASCORBATE UPTAKE IN ASTROCYTES. John X. Wilson and S. Jeffrey Dixon*. Univ. of Western Ontario, London, Ontario, N6A 5C1, Canada.

Astrocytes take up ascorbate through a concentrative and Na^+-dependent transport system located in the plasma membrane (J. Neurochem. 53:1064-1071, 1989; Neurochem. Res. 14:1169-1175, 1989). The purpose of the present experiments was to determine if astroglial ascorbate transport is electrogenic and therefore subject to modulation by agents which alter membrane potential. We observed in primary cultures of rat cerebral astrocytes that raising external K^+ concentration, so as to depolarize the plasma membrane, immediately decreased the initial rate of ascorbate uptake. The depolarizing ionophores gramicidin and nystatin also slowed ascorbate uptake, whereas the nondepolarizing ionophore valinomycin did not. Gamma-aminobutyric acid (GABA), a neurotransmitter which is known to depolarize the astroglial plasma membrane, rapidly (<1 min) inhibited cellular accumulation of the vitamin. Valinomycin prevented the inhibitory effect of GABA. Astroglial ascorbate uptake also was diminished by lowering external Ca^{2+} concentration. Qualitatively similar results were obtained whether or not astrocytes were pretreated with dibutyryl cyclic AMP for $\geq$1 week to accelerate their maturation. These data indicate an electrogenic Na^+-ascorbate cotransport system through which the rate of ascorbate uptake is modulated by agents, such as GABA, that alter glial membrane potential.

95.9

PLASMA LEVELS OF CATECHOLAMINES AND METABOLITES DURING ACUTE AND REPEATED IMMOBILIZATION STRESS. R. Kvetnansky*, D.S. Goldstein*, K. Szemeredi*, V.K. Weise*, C. Holmes*, G. Bagdy*, and I.J. Kopin* (SPON: M.S. Kafka). Clinical Neuroscience Branch, NINDS and Hypertension-Endocrine Branch, NHLBI, NIH, Bethesda, MD 20892.

During repeated immobilization stress (IMO), tissue rates of synthesis of catecholamines (CA), tissue contents of CA-synthesizing enzymes, and responses of plasma CA levels are increased. This study examined CA metabolism during IMO by measuring simultaneously plasma levels of norepinephrine (NE), epinephrine (EPI), dopamine (DA), and the deaminated metabolites dihydroxyphenylglycol (DHPG), dihydroxyphenylacetic acid (DOPAC), methoxyhydroxyphenylglycol (MHPG), and homovanillic acid (HVA) in conscious rats during acute and after repeated 2 hr intervals of IMO. Concentrations of these substances in 300 µl aliquots of plasma sampled at 5, 20, 60, and 120 minutes of IMO were measured using liquid chromatographic-electrochemical methods. Levels of all the substances significantly increased during acute and repeated IMO. After 7 daily 2 hr intervals of IMO, baseline levels were unchanged; responses of NE and DA were accentuated and of DHPG, DOPAC, and HVA attenuated; and responses of EPI and MHPG were unchanged. The results indicate that repeated IMO is associated with augmented release of NE and DA from sympathetic nerve endings without augmented adrenomedullary responsiveness. The lack of change in MHPG levels can be explained by the fact that MHPG is a metabolite of both NE and EPI. The metabolic data are consistent with inhibition of monoamine oxidase as a result of repeated stress.

95.10

POTENTIATING EFFECT OF PN200-110 (ISRADIPINE) ON ANTI CONVULSANT ACTIVITY OF 2-METHYL-3(3-METHYL-2-PYRIDYL)-4-QUINAZOLONE (MMPQ). Pushpa Bhargava*, Hans C. Kusters*, and Surendra S. Parmar, UND Sch of Medicine, Grand Forks, ND 58202 and Gary W. Omodt* and Chandradhar Dwivedi*, SDSU College of Pharmacy, Brookings, SD 57007

Anticonvulsant activity of MMPQ was reflected by its ability to provide protection against pentylenetetrazol (90 mg/kg, sc)-induced convulsions in mice. Dose dependent protection of 20%, 80% and 90% was observed with 40, 60 and 80 mg/kg, ip, respectively, of MMPQ. Decrease in anticonvulsant activity of MMPQ (100 mg/kg, ip) from 80% to 60% during 1 and 2 hr pretreatment, respectively, has provided evidence that biotransformation of MMPQ possibly decreases its effectiveness as an anticonvulsant. Pretreatment with PN 200-100 (20 mg/kg, ip) potentiated anticonvulsant activity and degree of protection observed with 40, 60 and 80 mg/kg, ip, of MMPQ was 70, 100 and 100%, respectively. Similar potentiation in anticonvulsant activity of diazepam (1 mg/kg, ip), flurazepam (1 mg/kg, ip) and chlordiazepoxide (3 mg/kg, ip) was observed by pretreatment with PN 200-110 (20 mg/kg, ip) and percent increase was 30, 50 and 50, respectively. These studies have provided evidence toward similar mechanism of action between MMPQ and benzodiazepines and that consequently specific neurotransmitter like serotonin, as evidenced by earlier investigations, could presumably be involved in the physiological functions of both these groups of anticonvulsant drugs.
(Supported in part by Max Baer and Hoffmann-La Roche Gts.)

95.11

Effects of chronic administration of imipramine on CNS alpha-2 receptors. C.A. Jiménez-Rivera[1], G. Santacana[1], G. Silva[2], D.D. Savage[3] and G. Weiss[4]. Departments of Physiology[1] and Pharmacology[2], Universidad Central del Caribe, School of Medicine, Cayey, P.R. and Dept. of Pharmacology[3] and Physiology[4], University of New Mexico, Medical School, NM.

Imipramine (IMI) is an effective antidepressant which blocks the reuptake of norepinephrine. In order to understand some of its basic mechanisms of action we investigated the effects of chronic imipramine administration (10 mg/kg, i.p., 21 days) on the population of alpha-2 receptors of several brain sites. In vitro autoradiography was employed using ^{3}H-Idazoxan to estimate the density of alpha-2 receptors. After the administration period animals were sacrified by decapitation, brains quickly removed and kept frozen (-70°C) until analysis. The densitometric analysis revealed a decreased number of receptors in the A2 region (25%) and LC (19%). No changes were observed in the amygdala, pyriform cortex, and bed nucleus stria terminalis. These results suggest that chronic IMI treatment selectively modulates the alpha-2 receptor population localized in the brain stem NE-rich nuclei and not the population present in limbic structures innervated by NE-terminal projections.

95.12

Inhibition of Nicotinic Action of (+)-Anatoxin-a on Guinea Pig Ileum by Thymopentin. Peter K. Chiang*, D. L. Butler,* S. T. Buckland*, Peter Kostka*, J. Katzhendler*, and N. D. Brown* (SPON: R. S. Fisher). Dept. of Applied Biochemistry, Walter Reed Army Institute of Research, Washington D. C. 20307-5100

Synthetic (+)-anatoxin-a was tested for its effect on guinea pig ileum contraction. It was found that anatoxin-a stimulated ileum contraction with a potency similar to acetylcholine (ACh). Even though the stimulation could be blocked by atropine, tubocurarine or hexamethonium, no specific inhibition of the binding of [^{3}H]N-methylscopolamine to ileum plasma membranes was observed in the presence of anatoxin-a. Preincubation of ileum with hemicholinium caused a 50% reduction in the ability of anatoxin-a to stimulate ileum contraction. Furthermore, the stimulation of ileum contraction by ACh itself was not blocked by hexamethonium or tubocurarine, thus indicating that the action of anatoxin-a might possibly be at the presynaptic nicotinic receptor sites. In addition, anatoxin-a failed to modulate the carbachol-stimulated secretion of alpha amylase from pancreatic acinar cells, a process that is controlled by muscarinic receptors. It was observed that thymopentin, a synthetic pentapeptide corresponding to positions 32-36 of thymopoietin, blocked the stimulation of ileum contraction by anatoxin-a. It may be inferred that anatoxin-a binds to presynaptic nicotinic receptors, thus releasing endogenous ACh, which in turn causes ileum contraction by interacting with the postsynaptic muscarinic receptors.

95.13

EFFECT OF ENDOTHELINS ON CYTOSOLIC FREE CALCIUM CONCENTRATION IN NEUROBLASTOMA NG108-15 AND NCB-20 CELLS. T.L. Yue*, M. Gleason, P.G. Lysko* and G. Feuerstein. SmithKline Beecham, King of Prussia, PA 19406-0939

The effects of endothelin (ET)-1, ET-2, ET-3 and Big ET on intracellular levels of Ca^{2+} ($[Ca^{2+}]_i$) were studied in neuroblastoma NG108-15 and NCB-20 cells. All ETs, except Big ET, induced an increase in $[Ca^{2+}]_i$ in NG108-15 cells in a dose-dependent manner, with EC_{50s}: 6.7, 11.2 and 71 nM, respectively. However, none of the ET increased $[Ca^{2+}]_i$ in NCB-20 cells. Calcium channel blockers diltiazem or nicardipine had no effect on ET-induced increase in $[Ca^{2+}]_i$, but extracellular Ca^{2+}-depletion significantly reduced the response of NG108-15 cells to ETs. NG108-15 cells exhibited a homologous desensitization to sequential addition of ETs, but no heterologous desensitization among ET, bradykinin and PAF was observed. These data suggest that ET-induced receptor activation results in increased intracellular Ca^{2+} via a non-voltage calcium channel mechanism and intracellular Ca^{2+} release.

95.14

DEPOLARIZATION OF SKELETAL MUSCLE BY CARIBBEAN PALYTOXIN IS INHIBITED BY CARDIAC GLYCOSIDES. G. Escalona de Motta, S. Ortiz*, M.B. Rodriguez de Salzberg* and H. Marrero*. Institute of Neurobiology and College of Natural Sciences, University of Puerto Rico, San Juan, PR 00901, USA.

Palytoxin (PTX), a potent marine toxin isolated from the zooanthids of various species of the genus Palythoa, including P. caribaeorum (Beress et al, Toxicon 21:285,1983), causes an irreversible, Na dependent depolarization of vertebrate nerve and muscle membrane. This action is proposed to be mediated by toxin binding to the membrane Na/K ATPase (Bottinger et al, Biochim. Biophys. Acta 861:165,1986). The depolarization caused by PTX (0.1 to 10 nM) on frog sartorius muscle membrane, recorded with intracellular microelectrodes, was inhibited in Na free solution and by cardiac glycosides, the monoglycosides being 2 to 3 times more potent than the triglycosides. The corresponding aglycones were also less antagonistic. Similar results were observed using the'loose'patch clamp technique. Current-voltage relations were obtained in the presence and the absence of 1 to 10 nM PTX. Lower threshold potentials were observed in toxin treated fibers, apparently due to an increased Na conductance. Thus, the action of PTX on intact muscle cells appears to be related to the ouabain-sensitive site of the Na/K ATPase. Structure-activity relationships observed for the toxin-inhibiting glycosides, suggest the mechanism involved does not require sodium pump inhibition.(Supported by NIH grants: RR08102 and NS07464)

NEURAL CONTROL OF BLOOD PRESSURE

96.1

EFFECTS OF SYMPATHETIC DENERVATION AND CONVERTING ENZYME INHIBITION ON TROUT PLASMA CATECHOLAMINES **D. Kullman, H. Xu, M. D. Kellogg and K. R. Olson. Dept. Biol. Sci., U. Notre Dame and Ind. U. Sch. Med., South Bend Ctr., U. Notre Dame, Notre Dame, IN 46556.**

The importance of circulating catecholamines in blood pressure regulation in fish is unclear. The present study examines the effects of sympathetic denervation (SDN) angiotensin converting enzyme (ACE) inhibition on plasma catecholamines in 250-550 g rainbow trout (*Salmo gairdneri*). SDN was produced by injection of 10, 15 and 60 mg.kg^{-1} 6OH-dopamine (6OH-DA) on days 1,2 and 6; blood was taken on day 7. The ACE inhibitor, lisinopril, was injected 45 min prior bleeding. 6OH-DA did not affect arterial pressure; lisinopril reduced pressure by ~30%. Plasma dopamine (DA), epinephrine (Epi) and norepinephrine (Ncpi) were measured in dorsal aortic plasma by radioenzymatic methods. 6OH-DA increased ($p<0.025$) Epi (1.8±0.1 to 6.9±0.7 nM.l^{-1}; mean±SE, n=10), increased Nepi in 8 of 10 fish (3.3±1.0 to 8.0±2.0; $p<0.05$, n=8) but did not affect DA. Lisinopril (n=7) increased plasma DA (0.9±0.3 to 3.8±0.8; $p<0.25$), Nepi (1.4±0.2 to 6.2±1.7; $p<0.5$). The Epi response (1.3±0.2 to 16.9±8.4; $0.5<p<0.1$) was quite variable. These results show that, in trout, plasma catecholamines increase in response to deficits in sympathetic neural tone and angiotensin activation and may thus sustain peripheral vascular resistance. **Supported by NSF Grant No. DCB 8616028.**

96.2

CARDIO-RESPIRATORY RESPONSES TO MICROINJECTIONS OF A GLUTAMATERGIC ANTAGONIST IN THE RAT CAUDAL DEPRESSOR AREA (CDA). R. Jung*, E.N. Bruce and P.G. Katona. Dept. of Biomedical Eng., Case Western Reserve University, Cleveland, OH 44106.

In urethane anesthetized (1.2 g/kg), spontaneously breathing rats tidal volume (Vt), respiratory rate (RR), MAP, and the baroreflex effects on pressure (BPR:elicited by left aortic depressor nerve stimulation) were measured. Ventral medullary surface (VMS) exposure was followed by microinjection of glutamatergic antagonist kynurenic acid (KYN) 1.7 mm lateral to the basilar artery, 0.9 mm under the VMS at the 2nd rootlet of the XIIth nerve in the CDA. Unilateral KYN injections (5 nmol, 50 nl; n=4) caused an immediate apnea for 7.8±3 (S.D) sec; Vt decreased, reaching ≤ 20% of control in 68±27 sec. Soon the animal had to be ventilated. RR increased from 127±49 to 356±172 breaths(b)/min. With a 1.58 nmol (31 nl) unilateral injection (n=4) the initial apnea was absent but Vt decreased to ≤ 20% in 143±85 sec and the animal had to be ventilated again. RR rose from 138±7 to 300±91 b/min. For both doses MAP increased. After bilateral injections MAP increased by 103±14 and 99±30 mmHg respectively, while the BPR response was -36±2 and -40±11 mmHg before KYN, and +5±3 and +3±12 mmHg after. Respiratory stimulation by ventilation with 5% CO_2 did not revive breathing (n=4). However, after 1-1.5 hrs, ventilation as well as BPR recovered. Injections of vehicle at the CDA site (n=6), or of 1.58 nmol KYN 2.5-3.2 mm rostral (n=7), or VMS application on the rootlets (0.025 umol, 0.5 ul; n=8) had no observable effect. The results suggest that 1) neural structures in the CDA are essential for sustained ventilation in this preparation; 2) the receptor sites for this are glutamatergic 3) these neural structures also affect tonic vasomotor tone and are essential for the baroreflex inhibition of arterial pressure.

96.3

NEUROPEPTIDE Y MODULATION OF CARDIAC VAGAL PREGANGLIONIC FUNCTION DIFFERS IN RATS AND GUINEA PIGS. B.J. Pardini, D.E. Puk, D.D. Lund, & P.G. Schmid. Veterans Affairs Medical Center and Cardiovascular Center, Dept. of Internal Medicine, University of Iowa, Iowa City, IA 52246.

Recent experiments from our laboratory indicate in an *in vivo* guinea pig model that infusion of neuropeptide Y (NPY), to simulate its release from cardiac sympathetic nerves where it is colocalized with norepinephrine, inhibits cardiac vagal preganglionic but not postganglionic function (FASEB J., 4(3):A832, 1990). The present experiments determined if NPY has similar effects in rats, a species that, unlike guinea pigs, demonstrates significant alpha adrenergic inhibition of cardiac vagal preganglionic function. Urethane-anesthetized rats were prepared with arterial and venous catheters, and ECG leads. The cervical vagi were sectioned and propranolol (1 mg/kg, iv) was administered to eliminate reflex changes in heart rate. To investigate parasympathetic preganglionic modulation by NPY, the right vagus nerve was electrically stimulated (0.5 mA, 0.5 msec, 1 to 10 Hz) before (CONTROL) and during NPY infusion at (1, 2, or 4 µg/kg/min). In the rat NPY did not inhibit vagal nerve stimulated bradycardia at the same dose that was effective in guinea pigs (1 µg/kg/min) or at twice the dose. However, when NPY was infused at 4 µg/kg/min, vagal nerve stimulated changes in heart rate (bpm; mean ± SEM; n=7; * = p ≤ .05 vs CONTROL) were:

STIM. FREQ.	1 Hz	3 HZ	5 Hz	10 Hz
CONTROL	30.9± 6.7	76.0± 7.6	95.9± 8.0	132.1± 7.2
NPY	*16.3± 2.7	*55.7± 6.7	*78.1± 6.9	128.1±10.8

These data indicate that NPY is a much less potent modulator of vagal effects in rats than in guinea pigs. We conclude that sympathetic inhibition of cardiac vagal nerve function occurs primarily through an NPY effect in the guinea pig and an alpha adrenergic effect of norepinephrine in the rat (Supp. by Dept. of Veteran Affairs, NIH HL38137, and AHA - Iowa Affiliate)

96.4

HORMONAL RESPONSE TO CAROTID SINUS PRESSURE ALTERATION IN THE CONSCIOUS DOG. Martha J. Brunner and Gary J. Gala. Department of Surgery, University of Maryland at Baltimore, Baltimore, Maryland 21201

The carotid baroreflex is known to contribute to the release of various stress hormones in anesthetized animals under different physiological conditions. We undertook a study in conscious dogs to determine the role of the carotid sinus in the release of these hormones. Male mongrel dogs were chronically instrumented to produce a carotid sinus isolation. On the day of experiment carotid sinus pressure was manipulated from 25 to 200 mm Hg. Each dog was studied in the intact and vagotomized condition. Blood samples were obtained at each carotid sinus pressure. Plasma was assayed for ACTH, cortisol, AVP, renin, AII and aldosterone by radioimmunoassay. Mean arterial pressure and heart rate demonstrated the classical hemodynamic response to change in carotid sinus pressure. Altering carotid sinus pressure resulted in changes in levels of cortisol, renin, angiotensin II and aldosterone. Renin, angiotensin II and aldosterone were characterized by increased levels at high carotid sinus pressure, and may be related to the concommitant fall in systemic arterial pressure. *Peripheral cortisol increased* at low carotid sinus pressure only in the vagotomized group. AVP levels were not altered by changes in carotid sinus pressure. We conclude that the carotid sinus baroreflex plays an important role in the cortisol response to hypotension. Supported by NTH Grant # HL-38316.

96.5

MODULATION OF ADRENERGIC AND CHOLINERGIC INOTROPY IN ISOLATED CANINE ATRIA BY SUBSTANCE P (SP). X. Cao, D.V. Priola and D.C. Smith. Univ. of NM, Albuquerque, NM 87131.

We have previously shown that SP inhibits both vagal and sympathetic inotropic effects in the isovolumic canine heart. We examined the effects of SP on nicotinic and muscarinic stimulation of isolated atria from both normal and denervated (DNV) hearts to better define this neuromodulation by SP. Atria from 10 control and 10 DNV dogs were placed in isometric muscle baths. Inotropic responses to nicotine (NIC), 0.5-1.0 X 10^{-6} and acetylcholine (ACh), 0.5-1.0 X 10^{-8} were measured alone and in the presence of 0.5-1.0 X 10^{-6} SP. NIC elicited a biphasic response in control atria. The initial negative effect averaged -52% and the secondary positive effect, 48%. ACh decreased contractility by 45-80%. SP alone caused no significant negative inotropy. However, SP given *with* NIC reduced the negative inotropy by about 50% without affecting the positive component. In contrast, SP did not modify the negative inotropic effect of ACh. Except for the absence of the positive component, DNV atria showed similar negative inotropic responses to NIC and ACh. Again, SP reduced the response to NIC but not to ACh. These data support the hypothesis that SP modifies the response to autonomic neurotransmitters at the cell body rather than the axon while not interfering with the effector cell's responsiveness to ACh. This hypothesis is also supported by the lack of a SP-modulating effect on the secondary positive response to NIC, one which involves catecholamine release from adrenergic nerve terminals. Physiologically, SP may be released from intramyocardial afferent nerve collaterals and directly modify the autonomic neural response in a classic negative feedback manner. (Supported by Grant #HL 18517 from the NHLBI.)

96.6

ROLE OF CARDIAC AND SINOAORTIC BARORECEPTORS IN RENIN RELEASE DURING HEMORRHAGE IN CONSCIOUS DOGS, Y-T. Shen*, S.F. Vatner, Dept of Medicine, Harvard Medical School, New England Regional Primate Research Center, Southborough MA 01772

The extent to which cardiac or sinoaortic baroreceptors control renin release during hemorrhage remains controversial. In part, the hypotension induced by hemorrhage, which is a potent stimulator of renin release, may confound the role of reflexes. To address this controversy, hemorrhage was performed in 4 groups of conscious, chronically instrumented, splenectomized dogs: 9 intact, 7 with chronic surgical or acute (intrapericardial lidocaine) cardiac denervation (CD), 6 with chronic sinoaortic denervation (SAD), and 8 with combined SAD and chronic or acute CD. To control for variable hypotension, the protocol was designed for hemorrhage to reduce mean arterial pressure by 20 mmHg over the same time period in all groups. Reductions in right atrial pressure induced by hemorrhage were similar in all groups. Hemorrhage increased plasma renin activity similarly in intact (from 0.9±0.3 to 4.5±1.2 ng AI/ml/h), CD (from 0.7±0.1 to 4.8±0.9 ng AI/ml/h), SAD (from 1.0±0.2 to 3.3±0.9 ng AI/ml/h) and SAD+CD (from 1.6±0.4 to 3.9±0.7 ng AI/ml/h) groups. Thus, neither cardiac nor sinoaortic baroreceptors play an important role in mediating renin release during controlled hypotensive hemorrhage in conscious dogs.

96.7

INHIBITION OF THE BARORECEPTOR REFLEX BY CONTRACTION OF HINDLIMB MUSCLES IN THE DECEREBRATE CAT. P.N. McWilliam* and T. Yang* (SPON: I. Hampton). Univ. of Leeds, United Kingdom.

There is evidence that the baroreceptor induced prolongation of R-R interval is reduced during exercise. This study tests the hypothesis that afferent impulses from receptors in contracting muscle are involved in this reduction of reflex bradycardia. Experiments were carried out on cats decerebrated under halothane anaesthesia. Carotid sinus baroreceptors were stimulated by injecting Ringer-Locke solution through the common carotid arteries and the changes in sinus pressure were measured via cannulae in the external carotid arteries. The reflex effect of baroreceptor stimulation on the heart was expressed as the maximum prolongation of R-R interval compared to the mean of ten R-R intervals immediately before pressure elevation. Muscle contraction was evoked by stimulation of L7 ventral roots. Under control conditions carotid baroreceptor stimulation prolonged R-R interval by 288±123 ms. However, a similar increase in carotid sinus pressure 1.2±0.4 s after the onset of hind limb contraction produced by ventral root stimulation at 50 Hz produced a smaller prolongation of pulse interval of only 172±65 ($P< 0.01$, paired t test). In some experiments inhibition of the cardiac component of the baroreceptor reflex has been observed after only 1 s of muscle contraction and with stimulation frequencies of only 10 Hz. It is concluded that afferent impulses from receptors in contracting muscle inhibit the cardiac vagal component of the baroreflex.

96.8

CUSHING RESPONSE DURING DEVELOPMENT IN SHEEP. R.C. Koehler, J.E. Backofen, A.P. Harris, M.D. Jones, Jr., and R.J. Traystman. The Johns Hopkins Medical Institutions, Baltimore, MD 21205

Mammalian fetuses can experience elevated intracranial pressure (ICP) when the compliant skull is compressed in the birth canal during labor. We contrasted the response to elevation of ICP at levels equivalent to normal baseline arterial pressure in near-term fetal (n=6), 1-week-old (n=8) and adult (n=8) sheep anesthetized with pentobarbital. With CSF infusion in 1-week-olds and adults, sustained increases in arterial pressure of 16 ± 1 and 22 ± 2 mm Hg, respectively, occurred over a 40 min period as a result of increased cardiac output. However, cerebral blood flow (radiolabeled microspheres) fell 66% and 57%, and cerebral O_2 uptake (sagittal sinus samples) fell 34% and 37%, respectively. In the fetus, arterial pressure increased by 11 ± 1 mmHg and cerebral blood fell 49% at 3 min of elevated ICP. However, by 15 min, arterial pressure increased further (+17 ± 2 mmHg) and cerebral blood flow was nearly restored. Fetal cerebral O_2 uptake remained unchanged throughout the 30 min period. The secondary increase in fetal arterial pressure was the result of profound vasoconstriction in intestines and skin. Placental blood flow and arterial blood gases were maintained. We conclude that the Cushing response is highly developed in near-term sheep and may play a critical role in preserving cerebral metabolism during parturition. (Supported by NIH HL 38285)

96.9

DAY-NIGHT VARIATION IN 24H-URINARY EXCRETION PATTERN AFTER OPENING OF "FEED-BACK LOOPS" INVOLVED IN Na-HOMEOSTASIS. H.W. Reinhardt, W. Boemke*, A. Jöckel*, Ü. Palm*, A. Hey*. Exptl. Anesthesia, UKRV, 1000 Berlin 19, FRG

Studies were performed in chronically instrumented female Beagle dogs, kept under standardized dietary and environmental conditions (14.5 mmol Na, 3.5 mmol K, 91 ml water /kgbw/24h). Data were collected via a computerized system (urine samples in 20 min periods over 24h, for details see AJP 258, R274-R280, 1990). "Feed back loops" were opened by long-term infusion of captopril 15 µg/min/kgbw (C), C combined with aldosterone iv. 10 µg/min/kgbw (C+A), and surgical interventions: adrenalectomy (AX), sino-aortic denervation (SAD), SAD+cardiac denervation (SAD+CD). To compare day-night-excretion rates (Ex) a ratio (R) was calculated (R = Ex 9:00 A.M. to 5:00 P.M. / Ex 5:01 P.M. to 8:59 A.M.). Paired Mann-Whitney test, * $P < 0.05$, mean ± SD

SODIUM	CONTROL	EXPERIMENTAL	H_2O	CONTROL	EXPERIMENTAL
C	3.0±0.9	1.85±0.4 *		1.58±0.6	1.10±0.3 *
C+A	3.0±0.9	2.01±0.7 *		1.58±0.6	0.97±0.3 *
AX	4.8±2.9	1.51±0.8 *		2.02±0.9	1.04±0.5 *
SAD	3.9±2.5	2.33±1.0 *		1.89±0.8	1.17±0.5 *
SAD+CD	4.9±2.7	2.70±1.3 *		2.36±1.0	1.43±0.6 *

Under all experimental conditions the daily excretion pattern for Na and H_2O was shifted to the night, regardless whether primarly a Na-retaining or Na-eliminating "feed back loop" was cut. CONCLUSION: Optimal function of the Na-balancing system can only be achieved if the investigated components are intact.