

The American Physiological Society was founded in 1887 for the purpose of promoting the increase of physiological knowledge and its utilization. The APS Constitution and Bylaws appears in the FASEB Membership Directory. Officers: *President*, Howard E. Morgan, Pennsylvania State University, Hershey, PA; *Past President*, John B. West, University of California, La Jolla, CA; *President-Elect*, Franklyn G. Knox, Mayo Medical School, Rochester, MN; *Council*, Shu Chien, Harvey V. Sparks, Jr., Norman C. Staub, Aubrey E. Taylor; *Executive Secretary-Treasurer*, Martin Frank, 9650 Rockville Pike, Bethesda, MD 20814.

A Publication of the American Physiological Society, Martin Frank, Editor	Volume 28, Number 6	December 1985
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The Physiologist (ISSN 0031-9376) is published bimonthly by the American Physiological Society, 9650 Rockville Pike, Bethesda, MD 20814. Subscriptions: Distributed with the Physiology Teacher to members as part of their membership; nonmembers and institutions, \$60.00 per year in the United States; elsewhere \$75.00. Single copies and back issues, including Fall Abstracts issue, when available \$12.00 each. The American Physiological Society assumes no responsibility for the statements and opinions advanced by contributors to *The Physiologist*.

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Editorial A Century of Progress

As we approach our Centennial Celebration, it is time for us to look to the future of physiology and the potential for new and exciting discoveries. However, it is also time to look back at a century of progress in physiology and consider the vision of our founders. Did Mitchell, Bowditch, Martin, Chittenden, and Curtis have the vision to contemplate the degree to which we currently understand the internal workings of the living organisms? I sense that their vision, like that of many of us, might have been more shortsighted. However, these five men did have the vision to hold the first meeting of APS on December 30, 1887, and thereby provide physiologists with a means to facilitate the exchange of their research findings. As a result, APS has provided a forum for thousands of investigators to share new levels of physiological understanding.

Our founders' vision of a society of physiologists has contributed to the great discoveries made over the last century: from cardiac physiology to cardiac transplantation; from nerve conduction to neural circuitry; from DNA to gene therapy. One hopes that these men might have envisioned some of these discoveries and the role APS would play in them. For our founders, physiological research was performed in research laboratories on terra firma. One wonders whether they would have anticipated the potential for research performed by John West at the heights of Mt. Everest. Or could they envision physiological research being performed 100 miles above earth by APS member, Robert Phillips, on the NASA Space Shuttle Life Sciences Laboratory. While the potential for research at that altitude is phenomenal, the scheduled February 1987 launch will be a fitting tribute to "A Century of Progress in Physiology."

During 1986, the APS staff will strive to prepare the Society for its Centennial Celebration in 1987. FASEB '86, the IUPS Congress, and the Fall APS Meeting will all provide focus to the birthday celebration. In addition, the Centennial Committee is preparing a gala celebration for FASEB '87 (see page 467), a celebration

Proposed Amendment to the Bylaws for Society Sections and Affiliations

The following amendment to the Bylaws approved by Council will be offered for vote at the Society Business Meeting, Wednesday, April 16, 1986.

ARTICLE X. Society Sections and Affiliations Current Bylaw

SECTION 2. Society Affiliations. The Society shall maintain membership in such organizations as determined by Council.

Proposed Bylaws

SECTION 2. Society Affiliations. The Society shall maintain membership in such organizations as determined by Council. The Council shall authorize affiliation of societies having mutual interests to the Society upon approval of the membership.

that, hopefully, the entire APS membership will be able to attend.

Looking toward the future, in 1986 the Society will embark on a joint venture with the IUPS in the publication of *News in Physiological Sciences* (NIPS). Distinguished scientists will contribute timely reviews of trends in physiology that will have an impact on the profession by providing a forward and dynamic vision of our science. This new international journal will include an update on developments in physiology worldwide and will be mailed to APS members with *The Physiologist*.

Beginning in 1986, *The Physiologist* will undergo a change to become a 16-page newletter catering to the needs of the membership and serving as the organ for communcation of APS news and information. While some of the current features will be lost or moved to other APS journals, a number of new features will be added. In fact, some of the new features have been included in the current issue. *The Physiologist* will continue to be distributed to all APS members.

Mark you calendar for March 29, 1987. The Centennial Celebration starts today but culminates in Washington, DC, on that date. Remember, for the founders of APS, the future is now!

Martin Frank Executive Secretary-Treasurer

Affiliate APS Societies

During the past several years, the APS Council has been in the process of negotiating possible affiliations with a number of societies in the field of physiology sciences which possess mutual interests and goals of the Society. It should also provide a mechanism to stimulate new growth and interest in APS. As a result of these discussions the Council is pleased to announce the pending affiliation of the Microcirculatory Society with APS.

The concept of affiliation has arisen because both "APS and the Microcirculatory Society have a mutual interest in certain areas of scientific investigation and reporting," and "... the two societies draw some of their membership from the same segment of the scientific community." The affiliation of The Microcirculatory Society, or for that matter any society, with the APS should enable both societies "... to accomplish their purposes in an efficient basis and to improve communication between the two societies and among the members of the two societies and with the public at large."

As part of the Compact for Affiliation, the APS will provide the Microcirculatory Society with a number of services for which APS will be reimbursed. In addition, members of the Affiliate Society will have access to a number of APS privileges as described in the compact. The total text of the compact will be published in the February issue of *The Physiologist*.

To facilitate the affiliation of the Microcirculatory Society, as well as other societies, with the APS, it is necessary to amend our Bylaws. At the Fall Meeting in Niagara Falls, the APS Council recommended that the Bylaws be amended to require the membership to approve the affiliation of another society with APS. The proposed amendment to the Bylaws is shown in the adjacent shaded box and will be voted on at the Spring APS Business Meeting.

"From Russia With Love"

Part I

At the end of June, I spent two weeks visiting laboratories in the Soviet Union at the invitation of the USSR Academy of Sciences. The actual invitation came from Academician Oleg Gazenko, Chief of the Institute for Biomedical Problems in Moscow and President of the Physiological Society of the USSR. This institute is responsible for much of the space physiology in the Soviet Union and also has a strong interest in highaltitude physiology, so my original understanding was that I was invited because of my interests in these areas. However, when my wife and I arrived, it became clear that one reason for the invitation was that I was President of the American Physiological Society, and my hosts wanted to improve links between the Physiological Society of the USSR and our own. Dr. Orr Reynolds and his wife were also invited but had to postpone their trip. Several of the institutes that I visited were chosen because the directors were Vice Presidents of the Physiological Society of the USSR. I therefore thought that a short account would be of interest to readers of The Physiologist.

I hope it is not necessary to emphasize that visiting the Soviet Union is not to condone its political system. However, it was an extraordinarily interesting two weeks, one of the most interesting visits to a foreign country that I have ever made.

We visited Moscow, Leningrad, Tbilisi (capital city of Georgia), and a small village in the Caucasus at the foot of Mount Elbrus (highest mountain in Europe). I saw about ten research institutes which I will not enumerate here, but I have full notes if anyone is interested. I saw enough neurophysiology to last me for a very long time; there is a big emphasis on what is called "higher nervous function," which stems from the work of Pavlov for whom there is clearly considerable veneration. I also visited laboratories of space, cardiovascular, renal, and respiratory physiology, although the last does not have a high priority in the USSR.



Oleg Gazenko, President, All Union Physiological Society named after I. P. Pavlov.

It is interesting that the Soviets draw a very sharp line between research and the teaching of medical students. Most of the institutes had only tenuous links with universities. The only exception of my visit was the Institute of Normal Physiology in Moscow, which is within the medical school of Moscow University. Even here, different faculty are used for research and teaching, and the teaching faculty were on vacation because it was summer and the students were away. I was told that the people who teach physiology to medical students have an enormous load of lectures and do not have time for research. My impression was that working in one of the research institutes was far more prestigious.

Everybody was extremely friendly, and the hospitality was outstanding. However, the attitude to visitors to the laboratory was somewhat different from our own. For example, we generally sit a visitor down with a graduate student, postdoctoral fellow, or faculty member, go over data, and discuss what it might mean. We are always very interested in any new ideas that the visitor may have. By contrast, I was generally presented with an interpretation of a study, and there seemed to be little interest in other ways of looking at the data. As a matter of fact, I saw very few primary data.

Many of the laboratories had surprisingly few foreign visitors. On two or three occasions, I complimented my host on his command of English only to be told that I was the first English-speaking visitor for many months. It is important to appreciate how difficult it is for many Soviet scientists to maintain contact with the West. Of course some attend international meetings, and Western journals are available in the large libraries, but there is not the tradition of international visitors that we enjoy.

I met a number of senior people associated with the Physiological Society of the USSR or All-Union Physiological Society. Reference has already been made to Academician Oleg Gazenko, who is currently President. As chief of the huge Institute for Biomedical Problems in Moscow, his main interest is environmental physiology including space, high-altitude, and underwater physiology. There are three Vice Presidents of the Society: Professor Pavel Simonov, Director of the Institute of Higher Nervous Activity and Neurophysiology in Moscow, and a corresponding member of the Academy of Sciences; Professor Nicolay Suvorov, Director of the Pavlov Institute of Physiology just outside Leningrad; and Professor O. S. Adrianov, Director of the Brain Research Institute in Moscow. I also met the Secretary of the Physiological Society (not a staff position). He is Professor Alexei Ivanitsky, Chief of the Electrophysiological Laboratory at the Serbsky Institute of General and Forensic Psychiatry in Moscow. All these people were extremely interested in the APS including its governance, types of membership, meetings, publications, etc. Our Society seems to be more coherent and active than theirs at the national level, although they have more regional meetings. I was repeatedly told that they are interested in forming stronger links between the two societies.

We were actually taken around by Dr. Eugene Gippenreiter, a physiologist at the Institute for Biomedical Problems, who works with the cosmonauts and who is



Left to right: Pavel Ilyin, O. E. Reynolds, and Eugene Gippenreiter.

also very interested in high-altitude physiology. He was on the physiological team that was responsible for the choice of the climbers for the very successful Soviet ascent of Mount Everest in 1982. One of the highlights of the trip was a completely unexpected walk up to an altitude of 4,200 m (13,800 ft) to Refuge 11 on Mount Elbrus (5,633 m. 18,481 ft). This was done in sneakers on hard packed snow with no hat and in brilliant sunshine, and I completely lost the skin off my face over the next five days.

Among the host of impressions that remain, the ones that stand out include the vastness of the country (three times the area of the continental USA), the many memorials to World War II (in which the Germans advanced to within a few kilometers of both Moscow and Leningrad and the Soviet Union lost twenty million people), the friendliness of individual Russians and their interest in the United States (when we came to a long line for an art gallery, Eugene Gippenreiter would announce "Americanski" and we would be invited to the head of the line), and the warm, generous, outgoing nature of individual Russians. The last will not surprise anyone who has read Russian literature. It was memorable to have supper with Eugene Gippenreiter and his wife in their modest apartment with their son, Boris, who at sixteen is the same age as our son Robert. Such an occasion gives a special poignancy to the present confrontation between the two superpowers.

Perhaps with the upcoming centennial celebrations of the APS, it will be possible to strengthen links between the two physiological societies. There are many obstacles to be overcome, not least the enormous difficulty that Soviet physiologists have in obtaining permission to attend international meetings. But improving relations must be in everybody's best interests.

John B. West

Part II

As mentioned in Dr. John West's article just preceding, Marjorie and I were invited to visit the USSR on the same schedule as the West's but had to postpone the trip. We therefore made our visit following the Joint Meeting of APS with the (British) Physiological Society during the last week of September. Our itinerary was somewhat shorter than the West's but followed a similar pattern and included several of the same institutes. Both of us had visited the USSR several times before, so we were continually encountering old friends and knew something of the pattern of such visits. We were also efficiently guided by Eugene Gippenreiter and met with the principals of the All-Union Physiological Society of the USSR, who were most gracious and universally expressed eagerness for more communication with American physiology.

Three aspects of my experience differed from that of Dr. West. First, by the time of my visit, the summit meeting between Ronald Reagan and Mikhail Gorbachev was definitely scheduled, and great hopes for a relaxation of tension, allowing for easier scientific communications, were expressed. I wholeheartedly concurred in these sentiments, feeling that the wider the band of communications, the less likely a tragic error in international affairs could occur.

Second, in contrast to Dr. West's experience, I was shown a great deal of experimental equipment in use, as well as data, and given full opportunity to discuss experimental findings with the bench workers. Perhaps the fact that I did not visit so many institutes made this more feasible, and my previous involvement in space experiments on animals may have been conducive to detailed discussion of methods and results.

Third, I was quite openly drawn into discussion of the "status of physiology" in the USA, the USSR, and internationally. Oleg Gazenko, President of the All-Union Physiological Society, and the Secretary General, Professor Ivanitski, were especially concerned about danger of loss of standing, or "prestige," of the field and proposed an international campaign to restore the "image" of physiology.

The roles of integrative physiology and the evolution of function were discussed as foci for such a reinvigoration of the field. Oleg Gazenko specifically cited the APS Centennial as the appropriate occasion for initiation of such a campaign.

Orr E. Reynolds

American Physiological Society Endowment Fund

The APS Endowment Fund was established in 1977 to support programs for the development of physiologists and physiology; to encourage communication with other disciplines of science and the public; and to foster scientific and cultural relations with other parts of the world.

The APS Endowment Fund was established to encourage tax deductible contributions or bequests to the Society at any time and in any amount, for specific or general purposes. Upon request, the Society will provide to a donor or institution contributing a memorial gift a replica of the plaque bearing the name of the individual living or deceased in whose honor the gift was made. The family of, or the individual being honored by a donation to the fund will be advised formally of the donor's name, unless the contributor specifically requests that the donation be anonymous.

Donations to the APS Endowment Fund or queries should be addressed to the fund at 9650 Rockville Pike, Bethesda, Maryland 20814.

134th APS Business Meeting

Time: Wednesday, October 16, 1985, 11:00 A.M. Place: Convention Center, Niagara Falls, NY

I. Call to Order

Calling the meeting to order, President Howard Morgan welcomed the membership to the 134th Business Meeting of the Society and announced the selection of Dr. John West as parlimentarian.

II. Report on Membership

President-Elect Franklyn Knox reported on the current status of membership and deaths since the Spring meeting.

A. Summary of Membership Status. The current membership has had a slight growth since the Spring meeting, reaching 6,248, with a distribution of 4,558 Regular, 14 Honorary, 134 Corresponding, 607 Emeritus, 763 Associate, and 172 Student members.

B. Deaths Reported Since the Last Meeting. The names of twenty-six deceased members were read by Dr. Knox. The membership observed a moment of silence in tribute to them (p. 475).

III. Election of Members

A. Appointment of Tellers. Tellers appointed by the President were Gabriel Navar, Clinton Webb, and George Hedge. The members were instructed to strike the name from the ballot if they did not wish to vote for a particular candidate, and the tellers were asked to collect the Ballots for Election of New Members.

B. Election of New Mémbers. Dr. Knox announced that all candidates on the ballot, who had been recommended by the Membership Committee and Council, were elected to membership (p. 472).

IV. State of the Society

Departing from the tradition of reporting actions of Council, Dr. Morgan said he wished to inform the group of current deliberations of Council on topics that have not had formal decisions. Input from the membership is desired to assist Council in making wise decisions. An opportunity was provided for discussion at the end of each topic. In addition, members were urged to send their recommendations directly to Council or through the Sections.

The first topic deals with governance and sectionalization of the Society. Sectionalization began about ten years ago, and in varying degrees, each section has a set of goals and procedures for electing officers and formalization of programs. In considering the Society governance, Council felt that formalization of section procedures was needed. As a result, the Long-Range Planning Committee has been charged "to evaluate the goals and procedures, particularly the election procedures, and to assist Council in defining minimal standards for sections of the American Physiological Society." The Long-Range Planning Committee, which met with the Section Advisory Committee, is in the process of formulating standards that will provide a mechanism for sections to participate in the governance of the Society. The first step is to ensure that sections are representative of a group and that section representatives are elected democratically so that one Society member would be represented by one vote through that person's section. For example, if one member belongs to multiple sections, it is likely that he/she would be required to indicate the section of primary interest. Following further meetings with representatives of the Section Advisory Committee, the Long-Range Planning Committee will submit recommendations to Council for consideration at the Spring meeting.

The process of sectionalization and governance relates to the Section Advisory Committee. The Committee, originally composed of current section chairpersons, has been in existence only two years. However, the need to establish a procedure for electing these representatives has become apparent to provide continuity. Therefore, it is proposed that committee members be elected for three-year terms. Accomplishing this, Council will be able to define the role of the Section Advisory Committee in the overall governance of the Society. It is believed that active participation of the Section Advisory Committee will provide broader representation of the membership in Society governance, and thereby make a stronger APS.

The membership was informed of Council's endorsement of the formation of an APS Teaching of Physiology Section petitioned by more than 100 members. In presenting a proposal to Council, Dr. Harold Modell stated that one of the main purposes of this section is to involve teachers of undergraduate physiology with ninemonth teaching positions and active research programs during the summer. This section could attract a new group of physiologists into the Society, who will strengthen the recruitment of graduate students and improve undergraduate teaching.

The Council entered into negotiations with the Microcirculatory Society to become an Affiliate Society of the American Physiological Society. The Microcirculatory Society usually holds its meeting two days preceding the APS Spring meeting, and many of its members are also members of the APS. However, some who are not, particularly those in the anatomical discipline, may not wish to become members. The Microcirculatory Society has made a proposal to become an Affiliate Society and that its members wishing to apply for APS membership would be assured of election as an Associate member. If Regular membership is desired, applications would be processed by the APS Membership Committee. Under the proposed agreement, the APS offices would conduct administrative functions of the Microcirculatory Society for which it will be reimbursed. A draft compact, which has been approved by Council, is being sent to the Microcirculatory Society members for approval. Admission of this Society as an Affiliate will require an amendment to the Bylaws published in The Physiologist (p. 462) and offered for vote by the membership at the Spring Business Meeting. Council looks at



APS Council (left to right): S. Chien, M. Frank, F. G. Knox, H. E. Morgan, J. B. West, A. E. Taylor, N. C. Staub, and H. E Sparks, Jr.

this as representing the first of a number of affiliations of societies sharing common interests with APS. Indirectly, this will strengthen physiology and has the prospect of increasing APS membership.

Last Spring, the Program Committee recommended a thematic approach to the APS Fall meeting, and Council approved its implementation at the 1986 Fall meeting in New Orleans (p. 467). However, free contributed papers, in either oral presentations or poster sessions, by all members on any topics will still be included. In addition to the broader base papers, there will be two themes. Seven sections will cosponsor the first theme, "Neurohumoral Regulation of Water and Electrolyte Balance," and the second, "Physiological Limitations to Performance: A Comparative Approach," will be sponsored by two sections. Two independent symposia, entitled "Endothelium-dependent Modulation of Vascular Reactivity" and "NMR Spectroscopy as an Investigative Technique in Physiology," are also scheduled under the sponsorship of the Society for Experimental Biology and Medicine and two APS sections. Overall, eleven to thirteen symposia, three tutorial sessions, and contributed papers will be programmed into a four-day meeting.

To support the activities of the Spring and Fall meetings, the Council, through the Liaison with Industry Committee, has appointed a group to represent the Society as a Program Endowment Fund Committee. The intention is to provide stability in the support of APS scientific programs. The goal of the Program Endowment Fund Committee, chaired by Theodore Cooper and three other members from the pharmaceutical industry, is to raise a \$250,000 endowment for APS program activities. Dr. Morgan believes this to be a fine beginning, although the Society actually needs an endowment of one million dollars to provide at least \$80,000 a year for symposia and other program activities. The endowment would avoid the repetitive approaches of members individually seeking funds for symposia. Dr. Cooper, who is enthusiastic about the prospect of raising \$250,000 over a two-year period, plans to have an organizing meeting in the near future. Dr. Morgan stated that program and publication activities are the cornerstone of the American Physiological Society, and Council is undertaking a series of steps to ensure stability in program as it has in the Society publications.

During the discussion of programming for the Fall 1986 meeting, George Hedge commented that concern was repeatedly expressed about having scheduled the Fall meeting within three months of the IUPS Congress. The major concerns are whether exciting symposia can be organized and whether the meeting will attract attendees. Has Council considered not having a Fall meeting or holding it in conjunction with the IUPS Congress whenever it is held on the North American continent? Dr. Morgan replied that concern has also been expressed in Council, but it is too late to cancel or change the meeting site at this time. The thematic meeting approach is an attempt to attract people who would not have been represented in Vancouver.

Another member from the audience expressed concern about the Fall meeting registration fee. When one is hit with a big registration fee at the FASEB meeting, it is obvious the Society has numerous obligations. However, this is not apparent at the Fall meeting. He aksed if there is some way to evaluate the Fall meeting registration fee policy. Dr. Morgan, who was not certain about the exact cost accounting for that meeting other than it does not always break even, said he will ask Council to review it in relation to the registration fee.

Two aspects of the publications program involve the appearance next year of the journal, News in Physiological Sciences (NIPS), edited by Knut Schmidt-Nielsen, and the new Physiologist, edited by Martin Frank. The combined publications will constitute what has appeared previously in the current Physiologist. In February 1986, The Physiologist will become a 16-page newsletter including such items as expanded material on public affairs, people and places, and available positions in physiology. NIPS will have 8-10 brief 3- to 4-page articles on important new findings. Dr. Schmidt-Nielsen has taken a great interest in NIPS and has rewritten some of the articles in terms understandable to people not in the field of the new discoveries. NIPS will offer a new approach of demonstrating that physiology is a vital, ongoing, and exciting science. The first combined issue of NIPS and The Physiologist will be mailed bimonthly to Society members.

Council was given an update on the plans for the Centennial (p. 467), with the major activities taking place at the 1987 Spring meeting in Washington, DC, March 29-April 3. Alfred Fishman is Chairman of the Centennial Committee with Orr Reynolds as Director of the Task Force. Current plans include an opening ceremony Sunday afternoon followed by a reception in the Washington Convention Center. A block of seats for two evenings at the Kennedy Center have been reserved for attendees. The meeting will conclude with a reception at the National Academy of Sciences for APS members to be hosted by the Academy. The general theme, "A Century of Progress in Physiology," organized by Michael Jackson, involves not only historical presentations but a look to the next century. Other FASEB societies will emphasize the role APS played in their genesis. The plans sound exciting, and we can look toward an important event of which its members can be proud.

Dr. Morgan took pleasure in announcing the most recent Soceity awards. For the first time this year, the Society was asked to administer the Procter and Gamble Fellowship and to present the award to a postdoctoral student. The selection was made by the Porter Development Committee, which supports minority students at the pre- and postdoctoral level. Darlene Racker was the recipient of the 1985-86 Procter and Gamble Fellowship in Physiology and received a cash award of \$9,500 to assist her in completing her PhD degree. Since the Spring meeting, two additional Perkins Fellowship Awards have been made to Dr. Jose M. Peinado from Granada, Spain, who will work with Dr. R. D. Myers at the University of North Carolina, and to Dr. Gouyling Bing of the People's Republic of China, who is to work with Dr. Paul D. Coleman at the University of Rochester.

Concluding his summary of the current deliberations of Council, Dr. Morgan expressed the desire to answer questions regarding Society activities. There being no questions and no new business, the meeting was declared adjourned at 11:45 A.M., October 16, 1985.

Franklyn G. Knox President-Elect

APS Sections Teaching of Physiology Section

Establishment of the Teaching of Physiology Section was approved by the APS Council at its Fall Meeting in Niagara Falls. In accordance with the Society Bylaws, a Statement of Organization and Procedures was adopted. The purpose of this organization is 1) to address issues relevant to physiology teaching and evaluation in undergraduate, graduate, and professional curricula, 2) to advise the American Physiological Society on matters of interest to physiologists engaged in teaching, and 3) to assist the Program Committee of the American Physiological Society in organizing and presenting open communication sessions, symposia, and other programs of interest to physiologists engaged in classroom teaching. APS members interested in becoming a member of the Teaching of Physiology Section are encouraged to contact the Membership Services at the Society headquarters.

MYOBIO Group Steering Committee Cell and General Physiology Section

Cardiac Muscle A. Fabiato Dept. of Physiol. Med. Coll. of Virginia Richmond, VA 23298

M. Lieberman Dept. of Physiol. Duke Univ. Med. Coll. Durham, NC 27710

Skeletal Muscle

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J. A. Rall Dept. of Physiol. Ohio State Univ. Columbus, OH 43210

M. J. Sicgman Dept. of Physiol. Jefferson Med. Coll. Philadelphia, PA 19107

Committee Reports

APS Centennial Celebration, 1887–1987

The Centennial of APS is fast approaching. Plans are moving ahead for the Centennail Celebration at the Federation Spring meeting in Washington, DC, March 29-April 3, 1987. The meeting will actually be a joint celebration, for at the same time that APS celebrates its 100th birthday, the Federation will be celebrating its 75th. The Federation was founded by APS and its two offshoot societies, the American Society of Biological Chemists and the American Society for Pharmacology and Experimental Therapeutics on December 31, 1912, during the 25th annual meeting of APS. By agreement with the Federation, the overall theme of the Federation meeting will be "A Century of Progress in Physiology." Michael Jackson, George Washington University, is chairing a Federation committee in charge of arranging a program that will develop the theme using symposia and plenary sessions in addition to contributed papers and posters. It is intended that the symposia, covering broad areas of physiological knowledge, will link present research, past heritage, and future directions in physiology and its daughter disciplines. In addition to the Federation symposia, APS will organize Society symposia. Twenty-five distinguished guests from abroad are expected to join us at the meeting and participate in the program.

Plans for the social as well as the scientific aspects are also well under way, taking full advantage of the unique opportunities for an international meeting afforded by Washington, DC. A grand opening ceremony and reception on Sunday, March 29th at the Convention Center for all Federation meeting attendees will launch the celebration. A more private reception for APS members and guests on the final evening of the meeting is being planned at the National Academy of Sciences. Seats will be reserved at the Kennedy Center so that visitors will have a chance to sample the performaing arts. Historical exhibits will be on display in the Convention Center and around town. Each member of the Society will receive the published Centennial history of APS now being edited by John Brobeck and Orr Reynolds. Medallions are being prepared as mementos of the occasion.

Suggestions about any part of this extraordinary event will be welcome.

Alfred P. Fishman Chairman, Centennial Celebration Committee Orr E. Reynolds Director, Centennial Task Force

Program Executive

The Program Executive Committee (PEC) met at 12:00 noon on Monday 14 October to review the theme and symposia proposals submitted to the Program Advisory Committee (PAC) at their meeting on 12 October. The PEC is delighted to report the successful implementation of the thematic approach to the Fall Meeting of the Society. The committee recommends the following themes for presentation at the 1986 Fall Meeting in New Orleans: 1) Neurohumoral Regulation of Water and Electrolyte Balance and 2) Physiological Limitations to Performance: A Comparative Approach. The first theme is cosponsored by seven sections including Neural Control, Endocrine and Metabolism, Nervous System, Comparative, Cardiovascular, Renal, and Water and Electrolyte. It will consist of four half-day symposia, three tutorial lectures, and volunteer papers. The second theme is cosponsored by the Comparative and Environmental, Thermal and Exercise Sections. It will consist of three to five half-day symposia and volunteer papers. In addition to these aspects of the themes, Dr. David Randall of the University of Kentucky has proposed that the APS institute a Workshop in Systems Physiology at future Fall meetings on the topic "Integrative Study in Physiology and Medicine." This concept was enthusiastically received by the PAC and PEC. The PEC therefore recommends that Dr. Randall be notified of the themes approved by Council and encouraged to develop workshops consistent with the theme topics.

In addition to the themes, the PEC also recommends the following independent symposia for presentation at the Fall Meeting: 1) Endothelium-dependent Modulation of Vascular Reactivity and 2)NMR Spectroscopy as an Investigative Technique in Physiology. The first is cosponsored by the Society for Experimental Biology and Medicine as well as the Muscle Group and Cardiovascular Section. It will consist of two half-day sessions. The second is cosponsored by the Comparative and ETE Sections and will also require two half-day sessions.

The committee also discussed elements of the 1986 FASEB meeting and recommends the addition of the following two symposia to those already approved last Spring: 1) Update in Cardiovascular Neurobiology and 2) Using a Computer and Video to Enhance Lectures/ Discussions. The first symposium is cosponsored by the Neural Control and Cardiovascular Sections and will be a sequel to the highly successful consortium of sessions that were presented during FASEB 1985. The second symposium would certainly be appropriate in light of Council approving the creation of a Teaching Section in the Society.

In addition to these issues, the committee also discussed a proposal by Dr. William Kachadorian from the National Institute on Aging to sponsor an annual symposium on the "Physiology of Aging" at the FASEB meeting. This concept was enthusiastically received by both the PAC and PEC. The recommendation of the PEC is to have this symposium organized in cooperation with one or more of the Sections and to have the proposal presented to the PAC by a Section.

C. V. Gisolfi, Chairman



APS Fall Meeting Poster Sessions. 468

36th Annual APS Fall Meeting 13-18 October 1985, Niagara Falls, NY

The 36th Annual Fall Meeting of the American Physiological Society has been much more of an international scientific forum than a meeting for physiologists only. Joining with the APS were the Canadian Physiological Society, the American Society of Zoologists Division of Comparative Physiology and Biochemistry (ASZ/DCPB), the Canadian Society of Zoology's Section on Comparative Physiology and Biochemistry (CSZ/DCPB), the IUPS Commission of Gravitational Physiology (IUPS/ CGP), and the American Society for Gravitational and Space Biology (ASGSB). In addition, among many non-North American scientists, six Soviet space physiologists/biologists were included as participants in the IUPS/GCP scientific sessions.

The most recent joint meeting of the American and Canadian Physiological Societies took place in 1980 in Toronto. Traditionally, since 1972, the Society has met every other year by the ASZ/DCPB. In 1979, in New Orleans, the IUPS/CGP joined with the APS for the Society's Fall Meeting and has continued that association in every third year of APS Fall Meetings. Founded in 1984, the ASGSB was invited by the APS to be a conjoining Society for this meeting in view of its common interest with part of the APS program and, especially, the objectives of the IUPS/CGP.

The scientific program for this 1985 Meeting consisted of the traditional refresher course, 3 workshops, 21 tutorial lectures, 18 symposium sessions, and 675 volunteered papers. Including the invited papers delivered in the refresher course (10), workshops (18), tutorial lectures (23), and symposium sessions (102) the number of presentations totaled more than 825 scientific reports.

The refresher course on "Exercise Physiology and its Clinical Applications" was organized by the local committee of the State University of New York at Buffalo (SUNY). The three workshops were IUPS/CGP-sponsored. Fourteen, six, and one of the tutorial lectures were sponsored, respectively, by the APS, CPS, and CSZ/ DCPB. The majority of the APS-sponsored tutorial lectures were from the group proposed by the APS Education Committee.

The following number of symposium sessions originated within the societies: APS, 7 sessions; SUNY, 5 sessions; CPS, 3 sessions; IUPS, 2 sessions; and APS/ IUPS, 1 session. One of the APS Symposium sessions, a bicentennial tribute to William Beaumont, was organized by the APS History of Physiology Section and related to "William Beaumont's World." Preceding the APS Meeting, SUNY offered a "Satellite Symposium on Environmental Physiology" dedicated to Hermann Rahn, APS Past-President, 1963.

In addition to its sponsorship of more than 50 volunteered papers, the ASGSB developed a special session of 10 reports devoted to the "Use of the Space Station for Biologic Research." A special APS/NASA/ASGSB session consisted of a poster discussion on 33 reports of the Spacelab 3 Bioscience Mission Results.

Dr. Martin C. Moore-Ede was the 1985 Bowditch Lecturer, speaking on "Physiology of the Circadian Timing System."

The sources of volunteered papers for the slide and poster sessions were as follows: from scientists in the United States, 551; Canada, 86; Mexico, 3; and non-



FIG.2. VOLUNTEERED PAPERS BY PHYSIOLOGIC CATEGORY APS FALL MEETINGS -- 1984 ¢ 1985

Catogory	Number of Papers	Percent of Total	Number of Papers	Percent of Total	CHANGES
Aging	4	0.85	3	0.44	•
Cell and General	0		5	0.74	A
Comparative	19	4.00	56	8.30	A
Endocrine and Reproductive	33	6.99	20	2.96	V
Environmental, Thermal	53	11.23	51	7.56	
Gravitational	2	0.46	133	19.70	
Gastrointestinal and Liver	10	2.12	21	3.11	A
Heart and Circulatory	97	20.55	100	14.81	
Membrane and Transport	7	1.48	10	148	
Epithelial Transport	5	1.06	12	1.78	A
Metabolic	11	2.33	10	1.48	
Muscle	30	6.36		6.07	A
Neurobiology and Neural Biophysics	16	3.39	35	5.19	A
Regulatory and Integrative	25	5.30	20	2.96	•
Renal and Electrolyte	23	4.87	18	2.67	۲
Respiratory	121	25.64	121	17.93	
Water and Electrolyte	11	2.33	15	2.22	•
Teaching	5	1.06	2	0.30	•
HISTORY	0		2	0.30	▲
Total	472	100.02	675	100.00	

North American countries, 35. The Society sponsorship of these short communications was as follows: APS, 548; CPS, 33; AXZ/DCPB, 25; IUPS/CGP, 21; and ASGSB, 35. The discrepancy between country of origin and Society sponsorship, e.g., Canada/CPS, is due to many Canadian sponsors indicating "APS" as their Society membership on the abstract form. Of the papers volunteered 138, or 20.44%, were "first-authored" by women in physiology.

Of the American-sponsored volunteered papers 164, or 26.97%, came from Physiology Departments; 45, or 7.40%, from Physiology/Biophysics; 70, or 11.51%, from Biologic Sciences; 37, or 6.09%, from Medicine; 23, or 3.78%, from Biochemistry; and 10, or 1.64%, from Pharmacology. The remainder (42.61%) originated in some 44 other types of academic departments and institutes, e.g., Nursing (3), Pediatrics (13), Veterinary (5), etc. Of the volunteered papers, 78 came from scientists in US Government laboratories, predominantly NASA Centers and the USVA. Only two papers were submitted by NIH personnel.

The Canadian volunteered papers came from scientists of 23 academic institutions; 25, or 29.07%, of the 86 Canadian papers originated in Physiology Departments. The three papers from Mexico were from the University of Mexico's Department of Biophysics and Biomathematics. Twenty of the 30 volunteered papers from non-North American contributors, representing 23 institutions in 16 countries, came from Departments of Physiology.

Programming of Volunteered Papers

Figure 1 shows the programming of volunteered papers into sessions representative of the APS sectional or specialty areas. One hundred eighty-one papers fell within the scope of the Section on Environmental, Thermal, and Exercise Physiology; 121 and 103 in Respiration and Cardiovascular Physiology Sections, respectively. These constitute 60% of the volunteered papers programmed. As can be seen, 426 papers or 62.96% were scheduled for presentation in POSTER sessions. Although not all were generated by a given APS section(s), symposia sessions and Tutorial Lectures are indicated as they relate to these specialties.

For comparison with the 1984 Fall Meeting, Figure 2 is indicative of a 1985 increase of 203, or 42.92%, more volunteered papers. Close inspection of Figure 2, and keeping in mind that five other Societies joined APS, shows large increases in gravitational physiology, i.e., 133 (1985) vs. 2 (1984). One could assume that without IUPS/CGP and ASGSB there might perhaps have been only a few such papers, decreasing the 1985 total by some 100 volunteered papers to 575. Papers in Comparative Physiology might not have increased so much in 1985 without the ASZ and CSZ contributions. Thus one could speculate that, on the whole, and with APS alone, there might have been much less than a 42.92% increase in volunteered papers in 1985 compared with 1984.

The APS provided support for 8 of the 13 symposia sessions approved by the APS Program Executive Committee for presentation. Support of the Beaumont and SUNY Satellite Symposia was also provided by APS. The organizer, Dr. Charles Williams, of the APS-sponsored symposium (2 sessions) on "Malignant Hyperthermia," independently generated support from sources other than APS. Contributions for the "Malignant Hyperthermia" Symposium were obtained from the RGK Foundation, Marion Laboratories, Boehringer Ingelheim Animal Health, Norwich Eaton Pharmaceuticals, Astra Pharmaceutical Products, Burroughs Wellcome, and Vital Signs.

Joseph F. Saunders Membership Services

Ohio Physiological Society

Wright State University and its School of Medicine in Davton is a young place surrounded by a number of well-established sister schools within the State of Ohio. However, there is no physiological society in the state. As the new chairman of a new department, I invite everybody within the university system of Ohio (and of course from the outside) to join me to form the Ohio Physiological Society with its founding seat in Dayton, Ohio. A founders meeting is planned for 6-7 May 1986 on the campus of Wright State University and will be held in conjunction with the 1986 Biomedical Science Program Symposium, Properties and Regulation of Water and Salt Transport Systems in Health and Disease. Information about attending the founders meeting: Dr. P. K. Lauf, Department of Physiology and Biophysics, Wright State University School of Medicine, Dayton, OH 45401-0927. Phone: 513/873-3025.

Honors and Awards AAMC Award

Eric Kandel, a member of APS since 1964, was awarded the 1985 AAMC Award for Distinguished Research in the Biomedical Sciences. Dr. Kandel is a leading researcher on the cell and molecular mechanisms of behavior and learning. He has demonstrated that memory is associated with changes in the membrane properties of specific nerve cells and in the synaptic connections between cells. Dr. Kandel received his MD degree from New York University, interned at Montefiore Hospital, and was a research associate in the Laboratory of Neurophysiology at NIH. Since 1974. Dr. Kandel has been Professor of Physiology and Psychiatry and Director, Center for Neurobiology and Behavior, College of Physicians and Surgeons. Columbia University. Dr. Kandel is a fellow of the National Academy of Sciences and a Fellow of the American Association for the Advancement of Science.

APS Member Named to DRR Advisory Board

Dr. Stuart Bondurant, an APS member since 1960, has recently been appointed to the Division of Research Resources' (NIH) National Advisory Research Resources Council. The Council is responsible for the review of grant applications and to advise the Director, DRR, on the program-related matters. Dr. Bondurant, Professor of Medicine and Dean of the University of North Carolina School of Medicine, Chapel Hill, since 1979, is recognized for his clinical research on circulatory and respiratory dysfunctions. He has been honored with the Duke University Distinguished Alumnus Award (1975); as a Fellow, Royal College of Physicians (1981); and as a Fellow, AAAS (1982).

Carl A. Schlak Award

Dr. Ronald Dubner, APS members since 1968, is the 1985 recipient of the Carl A. Schlack Award. The award is presented annually by the Association of Military Surgeons of the United States to the dentist in one of the five Federal services who has made outstanding contributions in either dental research or education. Dr. Dubner is Chief of the NIDR Neurobiology and Anesthesiology Branch.

Symposium in Honor of Hermann Rahn

A Satellite Symposium on Environmental Physiology in Honor of Hermann Rahn was held in Niagara Falls, NY, on Friday and Saturday, October 11 and 12, just before the commencement of the APS Fall meeting. Organized by Leon Farhi and Charles Paganelli of the University of Buffalo, the symposium, attended by some 150 people, consisted of four half-day sessions, each devoted to an area of physiology in which Dr. Rahn has made significant contributions. Many of the speakers had worked with Dr. Rahn at the University of Buffalo or the University of Rochester. At the banquet on Friday evening, it was announced that the Laboratory of Environmental Physiology of the Department of Physiology at the University of Buffalo would be renamed the Hermann Rahn Laboratory of Environmental Physiology. Dr. Rahn was also presented the Meritorious Award of the US Air Force by Dr. Billy Welch, Chief Scientist, Aeorspace Medical Division, for thirty years of research in respiratory physiology and its practical applications. Dr. Rahn has been a member of APS since 1944 and served as President of APS in 1963-64. Associated with the Department of Physiology at the University of Buffalo since 1956, Dr. Rahn "officially" retired in August 1985, but his research is respiratory physiology continues. The symposium papers will be published by Springer-Verlag.

Honorary Members

Since the establishment of Honorary Membership in the American Physiological Society, the following distinguished scientists have been elected. The year of their election is indicated.

- E. D. Adrian[†], Cambridge, UK (1946)
- J. Barcroft[†], Cambridge, UK (1946)
- E. Braun-Menendez[†], Buenos Aires, Argentina (1959)
- F. Bremer[†], Brussels, Belgium (1950)
- A. Dastret, Paris, France (1904)
- P. Dejours, Strasbourg, France (1981)
- J. C. Eccles, Canberra, Australia (1952)
- T. W. Engelmann[†], Berlin, Germany (1904)
- D. P. Feng, Shanghai, People's Rep. of China (1983)
- B. Folkow, Goteborg, Sweden (1982)
- R. Granit, Stockholm, Sweden (1963)
- R. A. Gregory, Liverpool, UK (1981)
- E. Gutman[†], Prague, Czechoslovakia (1971)
- O. Hammarsten[†], Uppsala, Sweden (1907)
- W. R. Hess[†], Zurich, Switzerland (1950)
- A. V. Hill[†], London, UK (1946)
- A. L. Hodgkin, Cambridge, UK (1952)
- F. Hofmeister[†], Strassburg, Germany (1904)
- B. A. Houssay[†], Buenos Aires, Argentina (1941)
- A. Hurtado[†], Lima, Peru (1959)
- A. Huxley, London, UK (1981)
- H. E. Huxley, Cambridge, UK (1981)
- G. Kato[†], Tokyo, Japan (1965)
- B. Katz, London, UK (1985)
- A. Kroght, Copenhagen, Denmark (1946)
- Y. Kuno†, Yokyo, Japan (1959)
- J. N. Langley[†], Cambridge, UK (1904)
- L. Lapiquet, Paris, France (1946)
- G. Liljestrand†, Stockholm, Sweden (1950)
- C. Monget, Lima, Peru (1952)
- G. Morruzzi, Pisa, Italy (1959)
- L. A. Orbeli[†], Leningrad, USSR (1946)
- I. R. Pavlov[†], Russia (1904)
- E. Pflüger[†], Bonn, Germany (1907)
- W. T. Porter[†], Dover, MA (1948)
- F. J. W. Roughton[†], Cambridge, UK (1957)
- E. Sharpey-Schaefer[†], UK (1912)
- C. Sherrington[†], Oxford, UK (1904)
- E. T. A. Teorell, Uppsala, Sweden (1985)
- K. J. Ullrich, Frankfurt/Main, FRG (1985)
- H. H. Ussing, Copenhagen, Denmark (1950)
- K. von Frisch[†], Munich, Germany (1952)
- C. von Voit[†], Munich, Germany (1970) H. H. Weber[†], Heidelberg, Germany (1959)
- †Deceased

Bernard Katz

I became interested in the general field of neurophysiology as a preclinical medical student at Leipzig, Germany, during the early 1930's, and I did some experimental work which led to a MD thesis, in the Physiology



Department headed by Professor Martin Gildemeister (who himself was a pupil of Ludimar Hermann and so a "grandpupil" of Emil DuBois Reymond). But I received my real scientific education, and indeed much more than that, after I arrived in A. V. Hill's laboratory, at University College London, early in 1935. Being accepted by Hill as a physiological "apprentice" was the most important event in

my career and has had the greatest influence on all my subsequent activities. Since 1935, I have been working almost continuously on various problems of excitation in nerve and muscle and of the special processes occurring at the neuromuscular junction and at interneuronal synapses. Shortly before World War II, I received an invitation from Jack Eccles to join him in his laboratory in Sydney, Australia, which I accepted and which led incidentally to my friendship and collaboration with young Stephen Kuffler, whom I met on my arrival in Sydney in 1939. I became naturalized in Australia in 1941. Soon afterard I enlisted with the Royal Australian Air Force and spent the rest of the war as a Radar Officer in the South West Pacific Area. This was the only long-term intermission in my career as a neurophysiologist. At the end of the war, I married a young Australian lady, and when A. V. Hill asked me to return to University College London to help him rebuild his laboratory, we both followed his invitation. I have been working here in London ever since, first as Hill's assistant, then as head of a newly created Department of Biophysics, and since 1978 as an emeritus professor. I published my papers mostly in the Journal of Physiology and the Proceedings of the Royal Society; there are also general reviews, here and there, and three monographs: Electric Excitation of Nerve (1939, Oxford Univ. Press); Nerve, Muscle and Synapse (1966, McGraw-Hill); and The Release of Neural Transmitter Substances (1969, Liverpool Univ. Press).

Future N	Aeetings
1986	and the second state
FASEB Annual Meeting	April 13-18, St. Louis
APS Fall Meeting	October 5-10, New Orleans
1987	
*FASEB Annual Meeting	March 29-April 3, Washington, DC
APS Fall Meeting	October 11-16, San Diego
1988	
FASEB Annual Meeting	May 1-6, Las Vegas
Joint APS/ASPET Fall Meetin	ng October 9-14, Montreal
*APS Centennial Celebration	

To J. B. West:

I wish to thank you and your Council most heartily for your letter of June 10 and for the great honour of electing me to Honorary Membership of the American Physiological Society. I remember my great teacher A. V. Hill telling me of his election in 1946, and ... I am absolutely delighted to follow in A. V. Hill's footsteps by this election.

B. Katz University College London WC1E 6BT, United Kingdom

E. Torsten A. Teorell

Torsten Teorell was born in Stockholm on July 23, 1905. He was educated at the Karolinska Institute and graduated doctor of medicine. He held faculty positions there from 1926 to 1936 and then at Uppsala to the present. His research interests cover general physiology including permeability of the gastric mucosa and erythrocytes, membrane kinetics, and excitability. His name has been associated with major contributions to our understanding of bioelectric phenomena and correlated transmembrane ionic fluxes in a variety of tissues. He is a member of the Royal Swedish Academy of Sciences, the Royal Society of Sciences of Uppsala, and the American Academy of Arts and Scienses of Uppsala, and the American Academy of Arts and Sciences (Boston), and he has been decorated by Sweden and Brazil.

To J. B. West:

This is to acknowledge and thank you for my election to be an Honorary Member of the American Physiological Society. I am very proud of this distinction . . . and am very happy indeed of the honor you have bestowed upon me. I feel it is one of the greatest I have ever received.

E. T. A. Teorell University of Uppsala 75123 Uppsala, Sweden

Karl J. Ullrich

I was born in 1925 in Würzburg, a University town in Franconia, but grew up in a small village nearby where my father was a high school teacher. In 1935 my parents



sent me to the "Neues Gymnasium" in Würzburg. During the following years I learned Latin and Greek and acquired some knowledge of French. From 1943 to 1945 I served in the army but returned to civilian life three months before my 20th birthday. In 1945, I was a student of biology at the University of Erlangen. In 1946 I changed to medicine in Würzburg where my main interest was

in chemistry and biochemistry. After graduation in medicine 1951 I spent the internship in the Hospital for Internal Medicine in Würzburg. Very much influenced by Homer Smith's book *The Kidney in Health and*

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Disease (1951), I designed clearance experiments on human volunteers to study the orthostatic effects on renal blood flow and glomerular filtration.

In 1952 I joined the group of Prof. Kurt Kramer at the Physiological Institute in Marburg, where I first worked on heart function, and in January 1954 I started to study urine concentration mechanism in the countercurrent system of the renal medulla. In 1955 I followed Prof. Kurt Kramer to the University in Göttingen, where he became head of the Physiological Institute. In the following three decades my achievements in renal physiology were mainly influenced by establishing and applying new or improved methods.

In 1962 I was elected for the chair for physiology at the Free University of Berlin. In the following years I was mainly interested in solute reabsorption and secretion in the proximal and distal tubule. In 1967 I became the head of the Physiological section at the Max-Planck-Institut for Biophysics in Frankfurt. During the last 17 years my work has concentrated on the proximal renal tubule and collecting duct function. Since 1982 my investigations have concentrated on contraluminal transport step of the proximal tubule and transport of dicarboxylates, sulfate, hexoses, phosphate, and paraaminohippurate.

Max-Planck-Institut für Biophysik 6000 Frankfurt/Main 70, FRG

Membership Status

Regular	4,558
Emeritus	607
Honorary	14
Corresponding	134
Associate	763
Student	172
Total	6,248

NEWLY ELECTED MEMBERS

The following, nominated by Council, were elected to membership in the Society at the Spring Meeting, 1985.

Regular Members

ALBERS, H. ELLIOTT UNIV. OF MASSACHUSETTS

ANDERSEN, OLAF S. CORNELL UNIV. MED. COLLEGE

BAERTSCHI, ALEX J. UNIV. OF VIRGINIA

BEREITER, DAVID A. RHODE ISLAND HOSPITAL

BROWN, D. LESLIE UNIV. OF NORTH CAROLINA

BRUCKNER, GEZA G. UNIV. OF KENTUCKY

BULLOCK, JOHN UMDNJ-NJ MEDICAL SCHOOL

BURNETT JR, JOHN C. MAYO MEDICAL SCHOOL

BUSHINSKY, DAVID A. UNIV. OF CHICAGO

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CECH JR., JOSEPH J. UNIV. OF CALIFORNIA - DAVIS

CHUNG, JIN M. MARINE BIOMEDICAL INSTITUTE CLOUGH, DAVID L. UNIFORMED SERVICES UNIV.

CONSIGNY, P. MACKE

MEDICAL COLL. OF PENNSYLVANIA CORBET, ANTHONY J. BAYLOR COLLEGE OF MEDICINE

DANIEL, EDWIN E. MCMASTER UNIV.

DILLON, PATRICK F. MICHIGAN STATE UNIVERSITY

EVANS, JOHN N. UNIV. OF VERMONT COLL. OF MED.

FAHEY, PATRICK J. Loyola Univ. Medical center

FAIRMAN, RALPH P. MEDICAL COLLEGE OF VIRGINIA

FARKAS, GASPAR A. UVA MEDICAL CENTER

FAVUS, MURRAY J. UNIV. OF CHICAGO

FELDER, ROBERT B. UNIV. OF IOWA HOSPITALS GALLANT, ESTHER M. UNIV. OF MINNESOTA

GERRITY, TIMOTHY R. UNIV. OF ILLINOIS AT CHICAGO

GEWIRTZ, HENRY RHODE ISLAND HOSPITAL

GIDDA, JASWANT S. BRISTOL-MYERS CO.

GOTTFRIED, STEWART B. CASE WESTERN UNIVERSITY

GRIDER, JOHN R. MEDICAL COLLEGE OF VIRGINIA

HANRAHAN, JOHN W. YALE UNIV. SCHOOL OF MEDICINE

HARPER, SCOT L. UNIVERSITY OF SOUTH ALABAMA

HORTON, EDWARD S. UNIV. OF VERMONT COLL. OF MED.

IADECOLA, COSTANTINO CORNELL UNIV. MED. COLLEGE

INGRAM, F. DUANE BAYLOR COLLEGE OF MEDICINE

IWAMOTO, HARRIET S. UNIV. OF CALIFORNIA

JOHANSON, CONRAD E. UNIV. OF UTAH SCHOOL OF MED.

JOHNSON, DOUGLAS C. MASSACHUSETTS GENERAL HOSPITAL

JOHNSON, III, GERALD ORAL ROBERTS UNIV. MED. SCH.

KAJI, DEEPAK M. VA MEDICAL CENTER, BRONX, NY

KEEF, KATHLEEN D. UNIVERSITY OF ARIZONA

KESSEL, RICHARD G. UNIVERSITY OF IOWA

KLUG, GARY A. UNIV. OF COLORADO

KUTSKY, PHYLLIS B. TEXAS COL. OSTEOPATHIC MED.

LAU, YING-TUNG MICHIGAN CANCER FOUNDATION

LITTLE, WILLIAM C. UNIV. OF TEXAS HEALTH SCI. CTR

MCELLIGOTT, MARY ANN MERCK INST. THERAPEUTIC RES.

MORELAND, ROBERT S. BOSTON UNIVERSITY MEDICAL CTR.

MOREY-HOLTON, EMILY R. NASA-AMES RESEARCH CENTER

MORGANROTH, MELVIN L. UNIVERSITY OF MICHIGAN HOSP.

MYERS, ADAM K. GEORGETOWN UNIVERSITY

PANDOL, STEPHEN J. VA MEDICAL CENTER, SAN DIEGO

PAULSON, DENNIS J. CHICAGO COLL. OSTEOPATHIC MED.

PELLEG, AMIR LANKENAU MEDICAL RES. CENTER

PITTMAN, QUENTIN J. THE UNIVERSITY OF CALGARY

REZVANI, AMIR H. UNIV. OF NORTH CAROLINA

ROSENFELD, CHARLES R. UNIV. TEXAS HEALTH SCIENCE CTR

SAID, HAMID M. VANDERBILT UNIV. SCH. OF MED. SHELLOCK, FRANK G. CEDARS-SINAI MEDICAL CENTER

SIEGEL, NORMAN J. YALE UNIV. SCHOOL OF MEDICINE

SILBAUGH, STEVEN A. LILLY CORPORATE CENTER

SOLOMON, RICHARD J. ROGER WILLIAMS GENERAL HOSP.

SPECK, DEXTER F. UNIV. OF KENTUCKY MEDICAL CTR.

STEFFEN. JOSEPH M. UNIV. LOUISVILLE SCH. OF MED.

VINTEN-JOHANSEN, JAKOB BOWMAN GRAY SCHOOL OF MEDICINE

WALKER, W. ALLAN CHILDREN'S HOSPITAL, BOSTON

WATKINS, DON W. GEORGE WASHINGTON UNIV.

WELLS, MARION R. MIDDLE TENNESSEE STATE UNIV.

WEST, NIGEL H. UNIV. OF SASKATCHEWAN

WOLIN, MICHAEL S. NEW YORK MEDICAL COLLEGE

WU, JANG-YEN MILTON S. HERSHEY MEDICAL CTR.

Corresponding Members

ANTUNES-RODRIGUES, JOSE RIBEIRAO PRETO SCH. OF MED.

BAUER, CHRISTAN M. UNIVERSITAT ZURICH

BOUTELLIER, URS UNIV. OF ZURICH-IRCHEL

BREZIS, MAYER L. HADASSAH UNIVERSTY HOSPITAL

FERNANDEZ-MORAN, HUMBERTO V. UNIV. OF CHICAGO

ILIAS, WILFRIED K. UNIV. OF AUSTRIA

RODENSTEIN, DANIEL O. CLINIQUES ST. LUC, BRUSSELS

SEJERSTED, OLE M. INST. MUSCLE PHYSIOLOGY, OSLO

SHULKES, ARTHUR UNIVERSITY OF MELBOURNE

TIMO-IARIA, CESAR UNIV. OF SAO PAULO

Associate Members

ADAMSON, SUSAN LEE HOSP. FOR SICK CHILDREN, TORONTO

BAILE, ELISABETH M. ST. PAUL'S HOSP., VANCOUVER

BELL, DAVID R. UNIV. OF MICHIGAN

GWOSDOW, ANDREA R. JOHN B. PIERCE FOUNDATION LAB.

HUBBARD, JOHN W. UNIV. OF TEXAS HEALTH SCI. CTR

MCCULLY, KEVIN K. UNIV. OF PENNSYLVANIA

MOLONY, DONALD A. UNIV. OF TEXAS HSC-HOUSTON

PETZEL, DAVID H. Cornell University

PINSON, C. WRIGHT OREGON HEALTH SCIENCES UNIV. RAJ, J. USHA

HARBOR-UCLA MEDICAL CENTER

ROBY, FRED B. UNIV. OF ARIZONA

ROESS, DEBORAH A. COLORADO STATE UNIVERSITY

SEGAL, STEVEN S. UNIV. OF VIRGINIA SCH. OF MED.

STRIFFLER, JOHN S. WRIGHT STATE UNIV. SCH. OF MED

SUMPIO, BAUER E. YALE UNIV. SCHOOL OF MEDICINE

THOMPSON, LOREN P. UNIV. OF MICHIGAN

Student Members

ARABADJIS. PETER G. SUNY AT BUFFALO

BOSSUT, DANIEL F. B. Medical college of Virginia

BREDLE, DONALD L. INDIANA UNIVERSITY BRODOWICZ, GARY R. OHIO STATE UNIVERSITY

DONAHUE, HENRY J. UNIV. OF CALIFORNIA

DURKEE, TIMOTHY J. UNIV. OF ILLINOIS AT CHICAGO

KOWALCHUK, JOHN M. McMASTER UNIV. MEDICAL CENTER

LAW, WILLIAM R. UNIV. OF ILLINOIS AT CHICAGO

NADLE, THOMAS M. UNIV. OF CALIFORNIA

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Evelyn M. Anderson (1899-1985)

Evelyn M. Anderson was born in Willmar, Minnesota, on March 20, 1899, the daughter of Swedish immigrants. At Carleton College, in Northfield, Minnesota, she was encouraged in her desire to become a doctor by Dr.



Mary Lathrop Benton, Dean of Women, who helped her through the University of California School of Medicine. To meet the University of California's requirement of a year of intership or equivalent year of research in some scientific discipline, Anderson spent 1924-25 in the laboratory of Herbert M. Evans at Berkeley. As a result

of her work there, she presented at the annual meeting of the Anatomists two papers on vitamin A and on nutrition introduced by Evans. She received her MD in 1928, graduating at the head of her class. During her clinical training as an intern, assistant resident, and chief resident in medicine at the University of California Hospital in San Francisco, she co-authored three more papers with some of the outstanding clinicians of the Department of Medicine, H. Clare Shepardson, J. J. Sampson, and Hans Lisser.

With the support of Dr. W. J. Kerr, Chairman of Medicine, and others, Anderson obtained an NRC Fellowship to continue her scientific training at McGill University with J. B. Collip, who was then working on problems of hormone isolation from the pituitary gland. She remained in Collip's laboratory from 1931 to 1935, completing work for a PhD in Biochemistry in 1934 with a thesis on the anterior hypophysis and the thyroid. In that year she was elected a member of APS. Anderson's most memorable scientific achievement, and one of which she was especially proud, was the codiscovery of ACTH. In 1933, Collip, Anderson, and D. L. Thomsom published in Lancet (2: 347-348, 1933), research showing that an extract that they had obtained from the anterior pituitary contained an adrenotropic hormone. Also memorable was her discovery with Collip in 1934 of anti-TSH, a substance capable of counteracting pituitary thyroid-stimulating hormone (TSH) and for elucidating the principle of antihormones (Lancet 1: 76-78, 1934 and 1: 784-786, 1934).

In October 1935, Anderson returned to the University of California first as instructor and then as assistant professor of medicine (she was promoted to associate professor in 1946-47, while on leave). She also held a concurrent appointment as research associate at the Herbert M. Evan's Institute of Experimental Biology at Berkeley, where she undertook studies of thyroid function. As a clinician she became interested in the clinical phenomenon described by Harvey Cushing and known as Cushing's disease or syndrome. She published in 1937 with Webb Haymaker, whom she married in 1936, the first experimental evidence that Cushing's disease is due to hyperfunction of the adrenal cortex and not to the anterior hypophysis per se (Science 86: 545-546, 1937). After World War II, she worked with Joseph A. Long, then professor emeritus of zoology, in the Institute of Experimental Biology, on an apparatus to perfuse the isolated rat pancreas and on attempting by bioassay techniques to determine the ability of the preparation to secrete insulin (Endocrinology 40: 92-103, 1947). Many years later, the isolated pancreas technique was revived by others and the perfusion apparatus, in a modified form, was coupled with an immunochemical assay for insulin giving rise to a considerable body of literature.

Following a year sabbatical as a Guggenheim Fellow, working with Philip Bard in the Department of Physiology at Johns Hopkins in 1946, Anderson accepted the position as first chief of the Section on Endocrinology. National Institute of Arthritis and Metabolic Diseases (NIAMD) at NIH. Beginning in 1955, she also served as visiting professor of physiology at Howard University. Anderson's laboratory at NIH focused on the study of the hypothalamic regulation of metabolism. Anderson also continued at NIH efforts to assay blood insulin levels using bioassay techniques. One of her notable accomplishments in this period was bringing Nobel Prize winner Bernardo A. Houssay to NIH in 1949 when he was ousted from the University of Buenos Aires by the Peron regime. In 1962, Anderson and her husband returned to California, where she headed a research unit on neuroendocrinology at NASA's Ames Research Center until her retirement in 1969.

The author of over a hundred scientific papers, Anderson was the recipient of several awards, among them honorary doctorates from Carleton College in 1954 and from Woman's Medical College of Pennsylvania in 1961. She was one of six women to receive the 1964 Federal Woman's Award. She was a chairman of the Neuroendocrine Discussion Group, one of the informal special interest groups that met annually during Federation meetings, and also served a term (1951-52) as vice-president and program chairman of the Endocrine Society, the second woman (after Jane A. Russell) to attain this honor.

Her last years were almost entirely devoted to her family. Married at age 37, she promptly had three children and, by her retirement years, had eight grandchildren, whom she liked to encourage to enter science or medicine. She died in Baton Rouge, Louisiana, on June 8, 1985, after a lengthy illness. Her husband of 48 years, Webb E. Haymaker, a noted neurologist, neuropathologist, and historian of neurology, had died in 1984.

This notice was written from material contributed by Leslie L. Bennet, Evelyn Haymaker Dolven, and Robert O. Scow.

James Daniel Hardy (1904-1985)

Professor Hardy is best remembered by his fellow physiologists and scientific friends worldwide for his emphasis of physical principles in understanding thermal physiology.

His distinguished career extended over a half a century. After his undergraduate and masters training at the



University of Mississippi in mathematics and physics (1925), he received his physics PhD at Johns Hopkins University (1930) in visual and infrared optics. He was a NRC Fellow in Infrared Astrophysics at U. Michigan (1930-32). The Great Depression of the 1930's redirected his career into physiology with Professor Eugene F. DuBois and the Russel Sage

Human Calorimeter at Cornell Medical University, New York (1932). His pioneering development of radiometric procedures for measuring skin temperature and his research on the thermal and physical properties of the skin laid the sound physical basis that was necessary for future studies of the skin in thermoregulatory and sensory processes. He early recognized that a radiant heat source could serve as a prime stimulus of warmth and pain without the complicating sense of touch and was able for the first time to correlate these two sensations with accurately measured thermal stimuli.

Following five years of active duty during World War II (1941-46) as a line officer and physicist in the US Navy, Hardy resumed his research at Cornell Medical School as associate professor of physiology (1946); in 1953 he became Research Director, US Navy Aviation Medical Acceleration Lab at Johnsville and held a joint appointment as professor of physiology, University of Pennsylvania. In 1961 he became Director, John B. Pierce Foundation Laboratory and professor of physiology, Yale University Medical School, where he continued after retirement in 1974 in emeritus status as a consultant to the Director, A. B. DuBois.

Professor Hardy's primary scientific objective during the postwar years was the understanding of the "Physiology of Temperature Regulation." His concepts and scholarship in this area are clearly set out in a monograph with this title in Physiol. Rev. 41: 521-606, 1961. He used simple physical control theory to relate physiological responses to cold and heat and thermal sensors within the central nervous system's structure. In 1960, with H. T. Hammel, Hardy developed an ingenious method for cooling or warming the hypothalamus in conscious dogs. With T. Nakayama (1961) and R. F. Hellon (1963), he was one of the first to discover heatand cold-sensitive neurons in the anterior hypothalamus and preoptic area of the brain. Hardy was early in the literature to devise an electrical analogue of man's thermoregulatory system (1961). With J. A. J. Stolwijk (1966) and other associates at the Pierce Laboratory he developed a series of dynamic digital models which have proved remarkably useful and accurate in predicting the thermoregulatory processes of man.

Professor Hardy served physiology in many capacities: member, Executive Council of APS (1956-64); member for physiology, National Board of Medical Examiners (1959-65); section editor (Environmental Physiology), APS Journal (1966-72); the first chairman of the IUPS Commission for Thermal Physiology (1970-72), whose sponsorship resulted in publication of the first comprehensive "Glossary of terms for thermal physiology," edited by John Bligh and K. G. Johnson and published in J. Appl. Physiol. 35: 941-961, 1973; editorial board, Journal of Applied Physiology (1976-78). He served on many working committees of the National Research Council and National Institutes of Health throughout his career.

Professor Hardy was elected a member of the National Academy of Sciences (1975). He was the third recipient of our Ray Daggs Award (1976). He received honorary degrees from universities here and abroad and many awards from medical and engineering societies allied to physiology.

For his wartime service in the US Navy, Professor Hardy was awarded the Purple Heart and Legion of Merit. In 1946, he joined the Naval Reserve as Commander and continued to serve in varying positions of policy and increasing responsibility until he retired in 1964 as Rear Admiral.

Professor Hardy and his wife Augusta, who passed away three weeks before him, are both buried in Arlington National Cemetery.

A. Pharo Gagge

Deaths Reported Since the 1985 Spring Meeting

Channing, C. P., Baltimore, MD (4/8/85) Evarts, E. V., Bethesda, MD (7/2/85) Fox, E. L., Columbus, OH (4/83) Gemmill, C. L., Charlottesville, VA (6/7/83) Glickman, N., Miami Beach, FL (9/27/84) Gordon, R. S., Jr., Kensington, MD (8/2/85) Greeley, P. O., Canyon Country, CA (9/19/85) Guthrie, M. M., Madison, WI (3/24/85) Guttman, R., Brooklyn, NY (10/12/83) Hardy, J., New Haven, CT (9/6/85) Haymaker, E. A., Baton Rouge, LA (6/8/85) Hilliard, J., Santa Ana, CA (3/6/85) Hoff, E. C., Richmond, VA (2/17/85) Hoffert, J. R., East Lansing, MI (11/21/84) Keyl, M. J., Oklahoma City, OK (7/2/85) Lacy, W. W., Nashville, TN (9/2/85) Nasset, E. S., Berkeley, CA (3/16/85) Rabin, D., Nashville, TN (10/26/84) Salzano, J. V., Durham, NC (3/23/85) Spehlmann, R., Chicago, IL (10/15/84) Spiegel, E., Philadelphia, PA (1/26/85) Thompson, A. M., Kansas City, KS (3/7/85) Wieth, J. O., Copenhagen, Denmark (5/30/85) Wearn, J. T., Awendaw, SC (9/26/84) Webster, M. E., Winter Park, FL (7/6/85) Whitehead, R. W., Denver, CO (11/3/84) Wolf, G., New York, NY (9/19/85)



Letter to Arthur Otis:

Edward Adolph writes: "My colleagues of the Department of Physiology, University of Rochester, recognized my 90th birthday by hosting a symposium. Former graduate students and other associates gathered here and described some of their professional experiences. Of those who came, Bruce Dill (94 years old) traveled from his home in Nevada. That was the site of our desert expedition together with others in 1937.

"A unique feature of my lifetime in Rochester is that I have occupied the same room and desk for 60 years. During that period, colleagues have come and gone. What a grand succession of fellow workers!

"'Old' is variously defined in the history of mankind. The essayist Charles Lamb (1775-1834) was retired as being 'superannuated' at age 50 years. He had worked as a clerk in the East India Company for 10 years beyond the average age (40 years) of men's survival in his time and place.

"When I was born the expected survival was 47 years; today it is 74 years. Those added years can be not only a privilege but also a responsibility. Formal education occupies two to three times as long now as in Lamb's day. Our prolonged education may fit us to work profitably in the added years now available.

"In recent times Sir Charles Sherrington (1857-1952) added enormously to scholarship in the years from 75 to 93 of his remarkable life. True, the old projects that anyone has stored for later action may lose their glamor. But novel projects may replace them. Health permitting, good hunting may reward the superannuated scientist."

Thomas K. Cureton, Jr., at the age of 84, is still a world-class athlete ... "still training very hard, and winning. ... My swimming is my 'means of staying fit.' I competed in Japan in January 1985 and set a new National Japanese record in the 100-meter Individual Medley, of 2:12 in my age class. I was No. 1 in this age class for the USA in 1982 and 1983 and have just won that rating again in the 1985 long and short course Championship Meets."

Harold M. Kaplan writes that he retired from the Southern Illinois University School of Medicine in 1977 but continues to serve there as visiting professor. He is coauthor of a *Handbook of Endocrinology* and coeditor of a work on *Creative Discovery*. Teaching in a human physiology course and consulting for an R and D laboratory also occupy his time. His advice to younger colleagues: "... stay healthy and continue to contribute, although I have no formula for this advice."

Edward H. Lambert writes: I retired from the Mayo Clinic in Rochester, Minnesota at the end of August 1985, after a career of 42 years. My research laboratory already has been moved en toto to the Department of 476 Neurology, University of Minnesota, 80 miles to the north, where retirement at 70 is not mandatory. I am continuing my research on diseases of neuromuscular transmission with NIH support, which fortunately also has no age limitation. My wife, Vanda Lennon, is remaining in Rochester where she has a very active neuroimmunology laboratory. We expect to spend alternate weekends in Minneapolis or Rochester and we look at this lifestyle as having some interesting aspects, an opportunity for uninterrupted work during the week and a more complete break from work on weekends together than we have had before."

J. Henry Wills writes that he is still a visiting professor in the Department of Pharmacology at the Uniformed Services University of the Health Sciences, Bethesda, MD. He gives a course for graduate students, participates in the medical course of Pharmacology, and has carried on some research. Currently he is in the preliminary stages of writing two books.

Letter to Edward F. Adolph:

Ruth E. Conklin writes from Poughkeepsie, New York, to thank the Committee on Senior Physiologists for greetings on her 90th birthday. Since retirement her time has been occupied a great deal by family cares, such as taking care of her older brother.

Letters to E. B. Brown:

Theodor H. Benzinger sends his thanks for his 80th birthday greeting from the Committee on Senior Physiologists.

Walter Ehrlich writes that "I am still working in the Division of Physiology of the Department of Environmental Health Sciences in the Johns Hopkins School of Hygiene. My long-standing endeavor to understand the mechanisms which adapt the cardiac output of mammals to the metabolic needs of the organism has been successful. We have established that the essential regulating mechanism, which triggers, enhances, or limits the functions of all the other mechanisms, is the intrinsic adaptation of the arterioles to the metabolic demands of the various organs. Now we are working in the field of nervous effect on circulation and respiration of awake, intact mammals."

Letters to Roy Greep:

Lawrence Bennet in response to greetings on his 80th birthday that despite "spare-parts" surgery he has been enjoying golf and shop work, summers in Colorado, and winters in Arizona." He and his wife "are active volunteers in programs of a very wonderful church in the summer and a new hospital in the winter."

Donald S. Farmer writes that

I respond to your good letter of 29 April. "With the generous approval of my chairman, I was able to use the last quarter before retirement for research at the Max-Planck-Institut für Verhaltensphysiologie in Andechs. Thereafter came a lecture at a CNRS Symposium in western France, a research conference in Copenhagen, a symposium at Copper Mountain in Colorado, followed by the dismantlement of my laboratory, and the transfer of the contents of my office to a much smaller room. ... With coeditors James R. King and Kenneth C. Parkes, I am now working on volume IX of *Avian Biology*. I also continue as a coeditor of *Cell and Tissue Research* and coordinating editor of *Zoophysiology*."

Congress Establishes Broader National Policy For Lab Animal Welfare

After six years and the consideration of more than three dozen bills and resolutions, the Congress has enacted one legislative proposal and is about to approve a second action concerning the care and treatment of laboratory animals.

Enacted in October was the bill (HR 2409) renewing the authorities of the National Institutes of Health. Included as an amendment to the renewal authorization was a bill proposed by Rep. Doug Walgren (D-PA), which gives the Public Health Service policy and procedures a statutory foundation and mandate.

Expected to receive Congressional approval by December is the 1985 farm bill, which includes as an amendment a bill (S1233) by Sen. Robert Dole (R-KS) that would expand some provisions of the Animal Welfare Act. The Senate in October added the Dole bill as an amendment to its version of the farm bill.

The passage of the two legislative measures would, in effect, broaden the national policy for the care and treatment of laboratory animals by giving statutory authority to both the Department of Agriculture and the Department of Health and Human Services. Since 1966 the only statutory authority concerned with animal welfare was in the Department of Agriculture.

To ensure that the two agencies do not conflict in carrying out their policies and procedures for research institutions, the Congress is requiring the following specific actions by the departments:

• The Secretaries of the Departments of Agriculture and Health and Human Services will consult with each other before promulgating conforming regulations.

• No regulations shall be construed to prescribe methods of research.

• Research facilities' privileged information or confidential trade secrets, commercial and financial information will be protected by law with penalties for violations.

• The role of the research facilities' attending veterinarians will include the determining of the choice and use of anesthetics, analgesics, and tranquilizing drugs and the overseeing of exercise of the research animals. The Dole proposal requires as a new standard of care the exercising of both dogs and nonhuman primates but grants the veterinarian the authority to implement this provision on a case-by-case basis.

• Assurance that the composition and operation of the Institutional Animal Care Committees established by

the two authorities is consistent so that duplication of effort is avoided.

A language change in the description of the Institutional Animal Care Committee's role was made by the Senate to reflect broader responsibilities for the care and treatment of the animal models by all committee members. In earlier versions of both the House and Senate proposals the concern for the animal subjects was limited to only the nonaffiliated member of the committee—thus a tacit implication that neither the researchers nor veterinarian members of the committee have such concerns for the animals.

The Senate's description of the committee now states: "(All committee) members shall possess sufficient abilities to assess animal care, treatment, and practices in experimental research as determined by the needs of the research facility and shall represent society's concerns regarding the welfare of the animal subjects used at such facility."

In describing the role of the nonaffiliated member of the committee, the Senate version states that individual is "intended to provided representation for general community interests in the proper care and treatment of (all) animals."

The Senate version also adds to provision that requires federal research facilities to establish Institutional Animal Care Committees with the same responsibilities as the committees in nonfederal institutions.

The Senate's approval of the Dole amendments to the Animal Welfare Act climaxes a three-year effort by the American Physiological Society. The APS Council in early 1983 adopted a strategy that amending the Animal Welfare Act was preferable to any of the legislative reforms being proposed and provided the concept to Dole at that time.

Plan to Balance Budget Could Hurt NIH Funding

The enactment of the Gramm-Rudman-Hollings bill to reduce the federal deficit by \$36 billion dollars a year and provide for a balanced budget by 1991 could have major implications for the programs of the National Institutes of Health.

The bill, sponsored by Sens. Phil Gramm (R-TX), Warren Rudman (R-NH), and Ernest Hollings (D-SC), proposes to eliminate \$36 billion dollars each year from 1987 through 1990 by reducing spending in federal programs with Social Security, entitlements, and some defense programs being exempted. The brunt of the effort to seek a balanced budget will come from nondefense discretionary programs that now represent only 16% of the federal budget.

Should the Gramm-Rudman-Hollings bill become law, it has been estimated that the NIH budget would be reduced by as much as \$400 million annually in Fiscal Years 1987 and 1988 and by \$700 million annually in Fiscal Years 1989 and 1990.

William M. Samuels, CAE

ACDP Survey on Use of Animals in Teaching Physiology

GILBERT S. GREENWALD Department of Physiology University of Kansas Medical Center Kansas City, Kansas 66103

At the behest of the Office of Technology Assessment (OTA), George A. Hedge, President of the Association of Chairmen of Departments of Physiology (ACDP), was asked to gather information on the use of animals in laboratory teaching for a forthcoming publication prepared for Congress of "Alternatives to Animal Use in Research, Testing and Education." The report issued in the fall of 1985 will serve as the benchmark for all future surveys on animal usage. The ACDP survey was completed in six weeks and a return of 65% on such short notice indicates how seriously this issue is viewed by physiologists.

The OTA has adopted the definition of "alternatives" to include any method "that replaces the use of laboratory animals altogether, reduces the number of animals required, or *refines* existing procedures or techniques so as to minimize the level of stress endured by the animals." If we consider the three R's in terms of teaching physiology, the ACDP survey shows that they are already being practiced. Over the past decade, 6 schools have dropped labs completely and 52 report a 63% reduction in the number of animals used (question 25). The reasons for the drop are multiple (see questions 26 and 27) and obviously have nothing to do with pressure by the animal welfare community. Another factor, not listed, is the ultimate obsolescence of polygraphs, transducers, etc., with equipment in most schools 10 or more years old and with little likelihood that administrators will view this as a top priority for replacement.

For various reasons, in some schools laboratories are no longer in vogue, but 84% of respondents still have them and of these 89% have laboratories using animals and 59/74 have dog laboratories. It is noteworthy that for 18 schools the number of dogs used in teaching physiology amounted to <% of the number disposed of by local pounds (question 19). Space does not permit printing of the anecdotal comments, but they range from a minority view that animal laboratories are unnecessary and can be replaced by computer models to a majority emphasizing that they are irreplaceable for the student's learning experience. There are unfortunately no objective criteria available to validate either viewpoint.

I thank Darlene Limback for carrying out the computer analysis of the data.

- 1. Number of copies of survey mailed to ACDP members: 135
- 2. Number returned: 88 (65%)

Breakdown of primary affiliation:	
U.S. Medical Schools	76
U.S. Osteopathic Medical Schools	2
U.S. Veterinary Schools	3
U.S. Dental Schools	2
U.S. Other (Univ.)	4
Foreign Medical Schools	4
Canadian - 3	
Other - 1	

- 3. Number of full time faculty in responding departments: MEAN 12.6 RANGE 3-28
- 4. How many students are taught in the following disciplines each year by your department:

	Number of Departments	Mean Number of Students	Range
Graduate	81	22.4	1-200
Medical	79	131.1	24-300
Veterinary	6	72.5	4-120
Osteopathic	4	118.3	58-215
Dental	23	88.3	25-150
Pharmacy	13	78.4	2-125
Allied Health	36	79.2	9-285
Nursing	34	100.6	2-282
Undergraduate	22	181.2	2-800
Other	14	44.7	7-120

- 5. How many schools have organized laboratorics: 74/88 (84%)
- 6. How many schools have required laboratories: 61/74 What percentage of students participate: 96.4 = ±.85*
 * = SEM throughout
- 7. How many school shave optional laboratories: 17/74What percentage of students participate: 73.3 ± 7.2
- 8. What percentage of the student's final grade is based on laboratory performance: (66 replies) RANGE 0-22%
- 9. What percentage of the student's laboratory grade is based on the following:

	Range	Number of Schools
Practical examinations; laboratory performance	22-100%	7
Oral examinations: laboratory performance	10-100%	4
Written examinations	5-100%	31
Written reports	10-100%	13
Oral reports	10-45%	3
Other	10-100%	5

- 10. How many schools have labs using animals: 66/74 (89%)
- 11. How many departments have dog labs: 59/74 (80%)
- 12. How many student laboratory sessions involve the following experimental subjects:

	Number of	Sessions Per School			
	Schools	Median	Average	Range	
Students	59	3	$3.9 \pm .3$	1-13	
Frogs	37	1	$2.1 \pm .4$	1-14	
Turtles	14	1	$1.4 \pm .2$	1-3	
Dogs	57	2	$3.1 \pm .5$	1-18	
Cats	6	1	2.3 ± 1.3	1-9	
Rabbits	12	1	$1.8 \pm .7$	1-10	
Rats	25	1	$2.0 \pm .5$	1-10	
Other mammals	5	1	$1.2 \pm .2$	1-2	
Invertebrates	5	1	1.0	1	
In vitro	10	1	$1.9 \pm .5$	1-6	

13. Which subspecialty areas have dog laboratories:

	Number of Schools
General Physiology	1
Electrophysiology	1
Neurophysiology	2
Cardiovascular Physiology	48
Respiratory Physiology	16
Renal Physiology	16
Gastro-intestinal Physiology	2
Endocrinology	1

14. How many departments have cat laboratories: 6

15. Is it feasible to replace dogs or cats used in labs with another species:

	Number of Schools
Yes	8
No	50

16. Chart animal usage in your school:

Demonstrations

		Numbers of Animals			
Species	U	Used		Euthanized	
	Total	Range	Total	Range	of Schools
Dogs	153	1-30	136	0-20	30
Cats	3	1-2	3	1-2	2
Rabbits	14	1-6	14	1-6	4
Rats	300	2-270	30	0-12	5
Other	39	1-10	39	1-10	6

Laboratories:					
	U	sed	Euth	anized	Number
Species	Total	Range	Total	Range	of Schools
Dogs	2917	5-240	2917	5-240	54
Cats	83	6-45	75	0-45	4
Rabbits	189	1-60	189	1-60	14
Rats	2002	8-400	1811	0-400	24
Mice	305	25-250	275	0-250	3
Guinea Pig	8	2-6	8	2-6	2
Hamsters	30	30	30	30	1
Other	3198	4-675	2695	4-675	30
10	.1. 6 .	1	1	. `	

(Species: turtle, frog, toad, fish, cow, goat)

17. For schools with dog laboratories, what is the source of animals: Source Number of Schools

Pound	14
Licensed Dealers	38
Pound and Licensed Dealers	7

18. How many dogs are used by your department per year: Number of Dogs Used Number of Schools

Number of Dogs Used	Number of Schools
0	28
1-10	8
11-20	10
21-30	9
31-40	8
41-50	5
51-60	4
61-70	4
71-100	3
101-200	6
> 200	2
Average Number Dogs Used Per	Year: 52.9 ± 6.4 Range: 2-256

19. If figures are available, how many dogs were euthanized last year by local pound (18 respondents):

	Total Dogs Used By School	Dogs Disposed of By Pound
MEAN RANGE	61.8 ± 14.6 2-256	$\frac{11,139 \pm 2,625}{200-35,000}$
	Dogs Used in Laboratories Compared To Dogs Disposed of by Pounds	= 0.55%

20. How many departments reuse animals in more than one lab: 6

Species	Number of Schools
Rat	4
Rabbit	6
Cat	2
Dog	3

21. What method of euthanasia is used at the end of lab: (60 Replies)

	Number of Schools
Anesthetic overdose	45
Potassium chloride injection	21
Pneumothorax	5
Fibrillation by electrical shock	3
Magnesium sulfate injection	1
Decapitation (small rodents)	3
Pithing (frogs, toads, turtles)	5

22. In laboratory exercises using animals, how many students work in a group:

Number of Students Per Group	Number of Schools
3	3
3-4	2
4	25
4-5	12
5	8
6	7
6-7	1
8	2
10	1
16	1
Average Number of Stude	nts Per Groups: 4.95

- Range: 3-16 23. Which alternatives to live animals models are being used in your
- school: Number of Schools

Replacements	
Computer simulation	28
In vitro techniques	10
Mannequins	5
Physical/chemical models	8
Videotapes and audio/visual aids	56
Invertebrate species	6
Greater reliance on students as subjects	32
Reductions	
Demonstrations	34
Larger groups of students sharing	16
Using single animals for multiple	
procedures	10
Greater reliance on students as subjects	23
Refinements	
Noninvasive methods (Imaging, e.g.)	2
Alter protocols to reduce pain	4
Substitute lower species	5
Other	2

24. What other basic science departments in your school have student animal laboratories:

	Number of Schools
None	33
Pharmacology	35
Psychology	2
Biological Science	1
Veterinary Anatomy	1
Microbiology	2
Physiological Chemistry	1
Surgery	2
Toxicology	1
Pathological Science	1
Anatomy	1

25. Has the number of animals used in lab increased or decreased significantly (percentagewise) over the last 10 years: (76 replies)

	Number of Schools	Average Percent Change	Range	N
No Change	19			
Increased	4	38.3 ± 6.0	30-50	3
Decreased	52	62.9 ± 4.8	10-100	42
Dropped labs	6			
entirely	(7.0%)			

26.	If your	animal	usage	has	decreased,	what	is	(are)	the	reason((s)	1:
-----	---------	--------	-------	-----	------------	------	----	-------	-----	---------	-----	----

	Number of Schools
Development of valid alternatives	23
Cost factors	43
Student pressure	16

Opinions

Statement for Panel Discussion American Physiological Society, 24 April 1985

My name is Thomas Jukes, and I have been a member of the American Society of Biological Chemists since 1935. I believe we should view the animal rights question as extending far beyond the humane care of animals, a subject on which scientists are in agreement. We should not delude ourselves that guidelines for the welfare of laboratory animals will appease animal rights activists.

The animal rights alliance has a program that includes acts of revolutionary terrorism, such as fire-bombing the house of Nobel laureate Sir John Vane, in London, January 1985. The book *Love and Anger* by Richard Morgan (5) is an organizing handbook for activists in the struggle for animal rights. Morgan says "the designation of and agitation for animal rights is part of a revolutionary process aimed at restructuring the major institutions of our society. Indeed, in struggling to change the way humans treat animals... we work toward nothing less than the transformation of the world."

Morgan warns against democratic procedures and says that decisions should be taken by core-group members rather than being made in meetings. The inorganic chemist and vegetarian Alex Hershaft has stated (2):

The fresh idealism and excitement of animal rights advocates provided a fitting complement to the experience, resources, and credibility of ethical vegetarians. Clearly, the time had come for the two movements to merge and to make a major impact on the social and economic fabric of American society.

	Number of Schools
Public pressure	4
Faculty attitudes	24
Other	20

27. What advantages do you see in using alternatives to live animals in medical education:

		Number of Schools
	Savings in costs	50
	Savings in time	35
	Reduction in number of animals	31
	Ability to isolate mechanisms/events	10
	Reduction in pain for the animals	10
	Greater control over variables	23
	Other	7
28.	 What disadvantages do you see in using alternatives to animals in medical education: 	
		Number of Schools
	Further distancing the teaching from	
	the ultimate subject (man)	63
	Artificial nature of the system	55
	Inability to study interactions in the	53
	complex system	53
	inability to study species-specific	12
	Loss of student experience of working	12
	with live subjects	73
	Loss of student exposure to practicality	15
	and complications of gathering valid	
	data	60
	Other	15

It was precisely with this goal in mind that, in the summer of 1980, we formed Action for Life-a framework for arranging conferences and seminars to train and mobilize animal rights and vegetarian advocates.

The newspapers have just described the lawlessness and destruction practiced in the raid on the University of California, Riverside, April 20, 1985.

Speaking as a biochemist, I am impressed with the interrelationship of living organisms. This is shown by many biochemical facts, such as similarity of genes for homologous proteins. Cytochromes c, as shown in Figure 1, show evolutionary descent from a common ancestor. No matter whether we decide to be omnivores, carnivores, or vegetarians, we shall kill and eat our relatives. The difference between them and us rests in nucleotide sequences in DNA molecules. Some vertebrates are carnivores that eat other vertebrates, other





Evolutionary similarities to and differences from humans as measured by cytochrome c amino acid sequences.

vertebrates devour insects or plants. There are also plants that eat insects.

The use of laboratory animals is a main target of animal rights activists because of the ease with which emotions are aroused in the public, especially about domestic pets or "companion animals." Probably some opponents of laboratory use of animals are or will be diabetics who depend on insulin, which was discovered by use of dogs that had their pancreases removed in laboratory experiments at the University of Toronto in 1922. The dogs recovered and were kept in good health by injections of the new substance. I am sure that many of you have seen the famous picture of Banting and Best with the thriving depancreatized dog on the roof of the Medical Building at Toronto. Let us remind ourselves of the use of the newly discovered insulin in 1922 as shown in Figures 2 and 3, and that people, too, have rights. Following its therapeutic triumphs, insulin was used by Frederick Sanger to found the modern science of molecular biology.

The agricultural wing of animal rights wants to stop animals from being raised for meat. For example, Hershaft said on January 24, 1985 (3): "a traditional wholesome humane family farm of yesteryear has been displaced by a giant, mechanized, medicated, impersonal factory farm."



Figure 2

Response to treatment with insulin. Diabetic girl before (*left*) and after (*right*) start of insulin injections. [Cases of the late Dr. Gayelin, published in the Journal of Metabolic Research, 1922. In: The Story of Insulin, edited by G. A. Wrenshall, G. Hetenyi, Jr., and W. R. Feasby. Toronto: Max Reinhardt (Canada), 1962, p. 80.]



Figure 3

Mother with her child, almost in the terminal stage of diabetes (*lefi*), and the same child shoveling snow 32 days after insulin treatment had been started (*right*). [In: *The Story of Insulin*, edited by G. A. Wrenshall, G. Hetenyi, Jr., and W. R. Feasby. Toronto: Max Reinhardt (Canada), 1962, p. 81.]

Drug abuse, once confined to large urban ghettos, he said, was alive and well on factory farms, where the feed of farm animals was "laced with subtherapeutic doses of antibiotics to keep them alive and growing in the face of deadly stress.... Chickens that once roamed a barnyard, scratching in the dirt, are now crowded, four and five in painful wire cages the size of a folded newspaper, stacked on top of one another in endless batteries."

In contrast, the Swann Committee report said (6): "Disease is one of the principal causes of suffering in animals, and in all types of animals the use of antibiotics to control infection reduces the suffering and makes an important contribution to animal welfare." By opposing this use, the American Humane Society and other proanimal groups show that they do not care about suffering by animals. They merely want to obstruct production of meat.

Many animal lovers are presumably sincere people who evidently make the mistake of thinking that farm livestock have the same feelings as people about their surroundings—that they don't like to be crowded and that they become claustrophobic and unhappy in confinement. Of course, this isn't even true for people, who happily jam themselves into cocktail parties and football stadiums. Farmers have a different perception, because they know that if animals are uncomfortable, they grow more slowly; cows give less milk and hens lay fewer eggs. Therefore farmers plan the care of animals to produce maximum yields. Overcrowding and discomfort defeat this purpose.

Many experiments on biological effects require the use of intact animals and cannot be replaced by tissue cultures or computer simulations.

As Jacques Monod has noted, the majority of the public has no understanding or appreciation of science. He said (4): "Modern societies . . . have scarcely even heard . . . the demand for a total break with the old animist tradition. Armed with all the powers, enjoying all the riches they owe to science, our societies are still trying to live by and to teach systems of values already blasted at the root by science itself."

The media eagerly give free publicity to animal rights activists, who have learned that the more bizarre the act of terrorism, the greater the coverage. In contrast, the journal *Nature* in editorials has been very helpful to science in this matter (1). The fight against the animal rights movement is not an argument about the size of cages but, rather, is part of a struggle by scientists to maintain the existence of science.

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The University of Kentucky was founded as a result of The Morrill Act of 1862 by which either land or scrip (money) was given to states to form agricultural and mechanical colleges. To take advantage of this offer, the Agricultural and Mechanical College was established in Lexington in 1865 by the state legislature as one of the colleges of a denominational school already in existence called Kentucky University. In 1878 the Agricultural and Mechanical College was separated by an act of the state legislature to become the State College of Kentucky. The latter, in the course of time, became the present University of Kentucky. The act of separation specifically stated that "the said Agricultural and Mechanical College shall forever remain a State Institution, free from all ecclesiastical entanglements or control" (1). The difficulty of forming a viable state institution in Kentucky may be attributed to constant interference from various religious denominations to obtain control of the several previous schools however impecuniously and sporadically supported by the state. The Morrill Act was the belated opportunity to separate school from church.

James Patterson, the first president of the State College, had a good eye for scientific talent. In 1890, he



persuaded Joseph William Pryor to take the chair of Anatomy and Physiology. Pryor, born in Missouri in 1856, had come to Lexington in 1882 to practice medicine. He had obtained an M.D. from the University of Missouri and practiced in that state for a short time. For a period, he was Medical Examiner of the State College so that he gave the entering

students physicals as well as lectures on sex education. He was personal physician to Patterson as well. Pryor expressed some anxiety about his appointment. "I was afraid I would not measure up to the views of what was then considered orthodox. I was a believer in a certain kind of evolution, I did not believe in a fiat creation, I was not a prohibitionist, and I often went to the races." (2)

Pryor was deeply interested in the preparation of undergraduates for medical school. Shortly after his appointment, he visited the Universities of Illinois. Chicago, and Wisconsin and learned that human physiology was not taught at any of the Arts Colleges at these institutions. Only Ohio State was doing so. He also took a summer course in Human Physiology in the Medical School at the University of Chicago. He began to teach premedical courses in 1894. At this time there were few, if any, requirements for entrance to the various medical schools. Many required only a high school diploma. Believing that a physician should be an educated person. Pryor first introduced a four-year curriculum, then, following pressure from state physicians, a two-year curriculum. Ultimately, the department offered a threeyear curriculum with the bachelor's degree granted after completion. All of this occurred before the famous Flexner Report of 1910 turned medical education in the direction toward which Pryor had been steering all along.

Pryor's scientific interest was in osteology, in particular the early development of bone in humans and the differences between the male and female skeleton. Within months of the announcement of the discovery of Xrays by Roentgen early in 1896, these rays were produced by Professor Andersen of the Mechanical Engineering Department of the State College. Pryor asked Andersen to make a roentgenogram of a patient's hand with amputated fingers. Pryor saw the opportunity for research on the time of ossification. Together with Professor Pence of the Physics Department who had purchased equipment to produce the high voltages required for X-ray production, Pryor took about 50 roentgenograms of children from the public schools. These exposures of children were obtained through the cooperation of the Superintendent of Schools. He was also able to take pictures of 100 newborns! The chief finding of this work was that ossification took place earlier than had been suspected previously.

Other early investigators using X-rays, like Cannon at Harvard, suffered from radiation damage. This did not happen to Pryor whose apparatus was also unshielded. He continued publishing through his 90th year and died shortly before his 100th birthday.

Pryor retired from the chair in 1931. He was succeeded as chairman of the Department of Anatomy and Physiology by Richard S. Allen. Allen had arived at the University of Kentucky in 1927 as an assistant professor. His fundamental training had been with the discoverer of glucagon, John R. Murlin at the University of Rochester. Allen rose through the ranks during the Depression. These were very difficult times, when the staff at the University went unpaid for many months. There was little incentive for research and little was done. The situation improved with the United States entered World War II in 1940, and many soldiers were trained at various universities including the University of Kentucky. The general prosperity that ensued following the termination of the war led to the hiring of more researchoriented staff such as James W. Archdeacon (gastrointestinal physiology), now Professor Emeritus, and Louis L. Boyarsky (neurophysiology).

During the 1950's there was intense pressure to increase the number of physicians in the United States. Although a medical school already existed at the University of Louisville, some felt that the needs of the state, particularly of the indigent and of the eastern part of Kentucky, would be improved by the addition of a medical school at Lexington. Under the aegis of the then Governor of the Commonwealth, Albert B. "Happy" Chandler, a medical school at the University of Kentucky was authorized in 1956 by the Board of Trustees. William Willard, a progressive educator, was chosen vice-president for the Medical Center. He attracted a number of highly competent individuals to chair the new departments. Among these were William H. Knisely (Anatomy), George W. Schwert (Biochemistry), Kurt Deutschle (Community Medicine), Edmond Pellegrino (Medicine), and Loren D. Carlson (Physiology and **Biophysics**).



Loren Carlson, born in Davenport, Iowa, in 1915, was educated entirely in that state. He obtained the Ph.D. in zoology at the University of Iowa in 1941 under the direction of the well-known insect physiologist J. D. Bodine. The nation being at war, Carlson entered the Air Corps as Captain at Wright Field. A. Pharo Gaage says that "Loren for most of the

time he was at Wright Field was Chief of the Oxygen Branch, which at that time was responsible for the development of all oxygen equipment for the Air Corps. And as head of the Branch, he was frequently involved in high-altitude flights to 40,000 feet both in airplanes and simulated in the altitude chamber. He tested his own equipment and was also responsible for its development and production. . . As a result of his help, we have oxygen equipment that was fully developed and was ready to be put in all the jet planes that come in the 1950's." (3)

At the end of the war, Carlson became an assistant professor of physiology in the University of Washington Medical School, rising to professor in 1960. During his time at Washington, Carlson turned to the study of temperature regulation in humans and rats. His work in this area led to the discovery (with W. H. Cottle) of nonshivering thermogenesis in 1956 and to a series of papers on the control of this phenomenon by the endocrine system.

At the time of Carlson's arrival at the University of Kentucky in 1960, the old Department of Anatomy and Physiology in the College of Arts and Sciences was abolished and a new Department of Physiology and Biophysics was formed in the Medical School. R. S. Allen, J. W. Archdeacon, and L. L. Boyarsky of the old department were absorbed into the new one. Over the next few years, Carlson hired a number of scientists of either physiological or biophysical background. These included Joseph Engelberg (cell biology and biophysics), Henry Hirsch (neurophysiology), David Magirian (neurophysiology), Ernest McCutcheon (cardiovascular), Robert Smith (neurophysiology), David Wekstein (thermal regulation), Michael Wilson (circulation), Fred Zechman (respiration), and James Zolman (physiological psychology). Judith Pratt joined the department to coordinate the undergraduate teaching of physiology.

This was a time of material plenty. The department had much money from several governmental sources, including a training grant for predoctoral students. The department supported a strong graduate program toward the Ph.D. The master's degree was not ordinarily conferred. The training of graduate students was based on relatively few didactic courses with an emphasis on research and publication. To this end, only two courses were absolutely required of all entering graduate students: medical physiology and cellular physiology. The qualifying examination at this time consisted of three unsolved problems for which the student was expected to devise the appropriate experimental solutions after a literature search. In keeping with the spirit of the time, advanced graduate courses in systems analysis and biophysics for the graduate student of mathematical character were introduced.

Despite the diverse fields represented in the department, a unifying conceptual thread tied them together - the control of physiological systems. Most members of the department could be considered to be working on some aspect of control in their areas. Carlson continued to work on thermal regulation and attracted a considerable number of Japanese postdoctoral fellows. In this young department, there was a great deal of intellectual interaction culminating in either experimental or theoretical work. At the molecular level, Joseph Engelberg, who was a master of information theory, worked on cell replication in the laboratory. He and Henry Hirsch published several seminal papers on the theory of cell replication. David Wekstein and James Zolman studied thermal regulation in the chick.

In 1966, Carlson left to become chief of Sciences Basic to Medicine at the new medical school at Davis, California. Such departures were commonplace among the chairmen, some of whom, like Carlson himself and Ed Pellegrino, later become national figures. Carlson served as president of the American Physiological Society in 1969. L. L. Boyarsky was acting chairman for the two years following Carlson's departure. The next chairman, Fred Zechman, was a long-standing member of the department. He had received his PhD in physiology from Duke University in 1956. Born in 1928 in Youngstown, Ohio, he attended Otterbein College (BS) and the University of Maryland (MS). At Duke, he trained under Frank G. Hall and Weyland Hull in the field of respiratory control and ventilatory mechanics. After a short period at Miami University in Ohio, he came to the University of Kentucky as an assistant professor in 1961. In 1968 he became professor and chairman of the Department of Physiology and Biophysics. Zechman had started his studies of respiratory control using added resistive and elastic loads as system perturbations, but he became interested in the mechanisms subserving detection and scaling of these loads which he has continued to investigate in normal and paraplegic subjects.

During his tenure of 12 years as chairman, the department grew considerably in staff and space. The individuals and their areas of specialization added during this period were Donald Frazier (neurophysiology), Lu-Yuan Lee (respiration), Sandra Legan (endocrinology), Cobern Ott (renal physiology), Bert Peretz (neurophysiology), David C. Randall (circulation), and Dan Richardson (circulation). The addition of these young faculty members kept the department intellectually alive.

Collaboration with other departments accelerated during Zechman's chairmanship. This was especially true in clinical areas closely related to physiology such as respiration, circulation, and kidney. In the late seventies a National Institutes of Health Program Project (the first awarded at the University of Kentucky) in which Zechman was principal investigator, included not only neurophysiologists (Frazier and Boyarsky) but also clinical faculty from the Department of Medicine. David Randall and Dan Richardson have collaborated with the Wenner-Gren laboratory, an independently funded group under the direction of the Department of Mechanical Engineering. Cobern Ott continued to be coinvestigator on a project with the Department of Medicine. Collaborative efforts in the teaching of medical students involved professors in the various clinical departments. The education of the graduate students also continued as before, although the lack of a training grant meant that investigator's research grants, the Medical School, and the Graduate School had to supply the stipends.

Over the years a number of eminent physiologists have stayed in the department during their sabbatical leaves. These included Otto Gauer, John Krog, and Arnold Hsiah.

In 1980, Fred Zechman resigned his position as chairman and subsequently moved to become Associate Dean for Research and Graduate Studies for the Medical Center. The chairmanship was assumed by Donald Frazier in 1980.

Donald T. Frazier was born in Martin, Kentucky, in 1935, and attended the University of Kentucky, where he received his PhD in 1964. His dissertation work under L. L. Boyarsky involved cholinergic pathways in a primary afferent pathway.

During this period he also worked with Guiseppe Sant'Ambrogio, who was a postdoctoral fellow in Boyarsky's laboratory. After obtaining the PhD, he went to the new medical school at the University of New Mexico as assistant professor of physiology. During this period, he was a Grass Fellow and had begun a collaborative effort with T. Narahashi which continued at Wood's Hole, Massachusetts, on the effect of various local anesthetics on the giant axon of the squid. In 1969, he returned to the University of Kentucky, where he resumed his interest in the neural basis of respiratory control.

Three faculty members were added to the department in the last 6 years, Brian Jackson (renal physiology), Dexter Speck (neurophysiology), and John Diana (microcirculation). The latter heads a laboratory in the Tobacco and Health Institute.

In the 22 years of its existence the department has produced 57 graduate students: 40 have obtained the PhD and 17 the MS. Twenty-five postdoctoral fellows have worked in all the areas of physiology represented in the department. Most of the graduates and fellows have gone on to teach and do research in a department of physiology of a medical school. The best celebrated of the graduates is Story Musgrave, presently an astronaut who has been on two missions in the shuttle program. The greatest part of the original staff from Carlson's time remain. Their research interests have changed as the Medical Center itself has enlarged and altered its original aims. The formation of a Center on Aging drew Wekstein and Richardson: Wekstein, who is not its associate director, as the major architect in its formation, and Richardson to work on the microcirculation of the aging human. Hirsch, who began as a biophysicist, also works on aging but on a theoretical level. Among the more innovative changes is the Program for Integrative Studies directed by Joseph Engelberg. This program is an attempt to initiate and coordinate special seminars and colloquia that are truly interdisciplinary, drawing on people from the humanities, the engineering sciences, and the Medical Center.

Such innovations have become the exception rather than the rule. The Medical Center and the department have become more conservative. For example, the graduate qualifying examination is now largely of the classical comprehensive kind. The research that members of the department do is more applied in nature. Almost all are working on problems with an obvious clinical connection. No doubt this is a result of national forces that direct the funding toward centers with an applied bent and transcend the departmental level of organization.

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In the Beginning

The State of Oklahoma was constituted in 1907 from lands formerly comprising the Oklahoma and Indian Territories. Physiology was taught in that region long before statehood was attained. In the proclamation by the President of the United States opening these lands to settlement, a certain portion of land was reserved from settlement for university, normal school, and agricultural college purposes. The lands so reserved were then appropriated for this purpose by an Act of Congress and leased for the benefit of the proposed institutions.

The first legislative assembly of the Indian Territory in 1890 established the University of Oklahoma which, with David Ross Boyd, MA, as its first President and Professor of Mental and Moral Sciences, admitted the first students at Norman in 1892. An early bulletin of the University of Oklahoma states that "Norman, the seat of the University, . . . is a growing town of 3,500 inhabitants, situated eighteen miles south of Oklahoma City on the Atchison, Topeka and Santa Fe Railroad. It stands on high ground sloping to the Canadian River and is preeminently healthful. The winters are mild and the atmosphere dry and bracing."

Physiology, as a biological subspecialty, was definitely taught at the University of Oklahoma starting in 1898. In that year Albert H. Van Fleet came to the faculty of the College of Arts as professor of a new Department of Biology and as ex-officio territorial geologist. Van Fleet had earned the PhD degree at the University of Leipzig and, along with Edwin De Barr who taught chemistry and pharmacy, was one of the only two members of the faculty who held an earned doctor's degree. Biology Course 3, entitled Human Physiology, carried five credit hours and was given in the first semester. The course consisted of lectures and recitations. Martin's *Human Body* was the required textbook.

The biological laboratories consisted of six rooms at the east end of the science building. One of these, a large room on the first floor, was reserved for work in botany, physiology, and general biology. This room was fitted with tables for the accommodation of 40 students. It contained the herbarium and could be darkened to use the lantern. A set of anatomical models for illustrating the work in physiology and anatomy was also stored in this room.

Although several medical colleges existed in the territories at that time, these were essentially academies providing instruction in certain of the simpler practical procedures. By 1900 increasing demands had arisen for the establishment of professional departments in the University, where students might prepare themselves for professional work after completion of the four-year course leading to the BS degree. Accordingly, a premedical course sequence was set up that amounted to the establishment of a two-year medical school. The aim of this program was to prepare the students for advanced standing in accredited medical schools, where the last two years of work leading to the MD degree could be completed. Physiology, as a discipline, was taught in this curriculum from the beginning.

Teaching Pioneers

The responsibility for overseeing this professional training program was given to Lawrence Northcote Upjohn, MD, who might properly be regarded as the first dean of the University of Oklahoma Medical School. The 1902 catalog lists him also as instructor of anatomy and physiology. He later resigned and went into business with other members of his family who had established the pharmaceutical firm in Detroit.

Roy Philson Stoops, MD, joined the faculty of the University of Oklahoma in 1903 as instructor of physiology. He became the director of the Medical School in 1904 and might be regarded as the second dean. He continued to teach physiology and anatomy until 1906, when a separate Department of Physiology was organized in the School of Medicine. It was difficulty to attract a top-notch medical scientist to head this newly formed department. Fortunately Mr. Edward Marsh Williams, instructor in pathology and histology, was willing to double as teacher of physiology for the next two years until the first head of the Department of Physiology was recruited. John Dice Maclaren, MD, a graduate of Columbia University's College of Physicians and Surgeons, arrived in 1908. For two years he served as professor of physiology and therapeutics. In 1911 he ventured even further west and accepted the call of the University of Oregon in Portland as professor of medicine.



Left: Lawrence N. Upjohn (1901-1903); right: Roy Philson Stoops (1903-1906).

Two years were to elapse again before a permanent successor to Dr. Maclaren was named. In the interim two local physicians were able to serve the school as teachers of physiology. Dr. Albert Clifford Hirshfield had been a practicing physician in Norman since 1909 and donated his services as professor of physiology at the University of Oklahoma for the year 1911-12. It is interesting to note that he returned to the faculty of the School of Medicine in 1916 as instructor in gynecology. Dr. Richard Leland Foster, another practicing physician, served as acting professor of physiology for the academic year 1912-13.

The Formation of a School of Medicine

The University of Oklahoma School of Medicine began with what would today be regarded as a premedical course in 1900; it was not until 1910 that it became a full-fledged four year school of medicine. The need for offering a basic course in physiology was recognized from the beginning, and the administration was usually able to secure one of the well-trained physicians on the staff to help teach this discipline. In 1907, the year Oklahoma attained statehood, a building to house the College of Medicine was purchased in Oklahoma City. The courses for the first two years, however, continued to be given in Norman until 1928. In June 1911 the first degree of doctor of medicine was conferred by the University of Oklahoma.

Leonard Blaine Nice joined the faculty of the School of Medicine in Norman in 1913 as chairman of the Department of Physiology. He had earned the PhD degree from Clark University the same year. In 1920 the departmental staff doubled when Alma Jessie Neill, PhD, was added to the faculty. During the late 1920's Arthur Brown Chase, MD, and Harry Coulter Todd, MD, served as part-time teachers in the Department of Physiology. Both Drs. Nice and Neill remained with the department until 1928 when a new School of Medicine building, modeled after the Medical School building of Washington University in St. Louis, was completed opposite University Hospital in Oklahoma City. In that year the basic science departments were transferred from Norman to Oklahoma City, and for the first time all four years of medical school were offered in one location.

Medical Center Campus

Upon the establishment of the School of Medicine in Oklahoma City, Edward Charles Mason was appointed professor and chairman of the Department of Physiology. Dr. Mason had earned the MD degree at the University of Chicago and the PhD degree at Cincinnati. After some training at Henry Ford Hospital in Detroit, he became a fellow at the Mayo Clinic. He was in private medical practice in Springfield, Missouri, when he was tapped for the position at Oklahoma. Dr. Mason served as chairman of the department from 1928 to 1946 and continued to serve as a professor of physiology until his death in 1957, giving a total of 29 years of service to the university.

Dr. Mason was a member of the American Physiological Society and a Fellow of the American College of Physicians. He maintained a lively personal interest in research, working on such diverse problems as shock, water balance, burns, oxygen utilization, carbon dioxide production, and acid-base balance. He authored several papers on these and other topics and was probably the first physiologist from Oklahoma to present a paper abroad at an international meeting. This occurred in 1946 when the International Physiological Congress met in London, England.

Dr. Mason saw the need to expand the department both in terms of service to the Medical Center and of training personnel, who in turn could serve the Medical Center and train others. He added to the department several talented teaching assistants, who while pursuing their career in Medical School contributed to the teaching efforts of the department. He also recruited additional faculty members devoted to teaching and research, some of whom had already established a reputation before coming to Oklahoma. Mention must be made of one of these. Dr. Allan J. Stanley received the PhD degree at the State University of Iowa, where he trained in physiology of reproduction with Emil Witschi and in genetics with W. R. B. Robertson. In his more than two and a half decades of service to the department, he taught at least 2,000 medical students and was a productive investigator throughout his career. He has also served as president of the Oklahoma State Board of Examiners in Basic Sciences.

During the years of Dr. Mason's leadership the tendencies toward more faculty research activity, and offering advanced degrees in science became established. Twelve master's theses were written by students studying physiology in the School of Medicine.

In 1946 Arthur Alfred Hellbaum from the Department of Pharmacology chaired the Physiology Department while a permanent chairman was being sought. During that year Ardell Nichols Taylor, PhD, came to the Department and was appointed acting chairman in September 1947. Oklahoma-born and Texas-trained, Dr. Taylor returned to his native state from a position in the Physiology Department at the Medical Branch of the



Left to right: John Dice Maclaren (1908-1911); Leonard B. Nice (1913-1927); Edward C. Mason (1928-1946); Ardell N. Taylor (1947-1960).

University of Texas at Galveston. He showed an early interest in medical education and was appointed chairman of the Physiology Department in 1949 and associate dean in charge of Student Affairs in 1952. He continued in both capacities until 1960. During his association with the department a number of additional faculty were recruited. These included Drs. Joseph H. Perlmutt, James W. H. Smith, Paul P. Webb, Robert C. Troop, M. Jack Keyl, Michael T. Lategola, Joe M. Dabney, Robert M. Bird, and C. G. Gunn.

Dr. Bird also served as dean of the School of Medicine from 1970 to 1974. Dr. M. Jack Keyl served for some years as vice-chairman of the Department of Physiology and Biophysics and later as acting chairman. He had received the PhD degree at the University of Cincinnati under Victor Whittaker and spent his postdoctoral research experience with William Lotspeich in renal physiology.

Expanding Its Mission

Perhaps the most significant event taking place during Dr. Taylor's chairmanship was the decision of the Graduate Council of the University of Oklahoma in 1951 to grant the request of the medical faculty that it be permitted to offer work leading to the PhD degree in medical sciences. One of the events preceding this was Dr. Charles D. Kochakian's move from the Department of Physiology and Vital Economics of the University of Rochester to the newly established Oklahoma Medical Research Foundation as head of the Biochemistry Section. He was accompanied by two graduate students, who, only after arriving here and helping with the setting up of a laboratory, learned that there was no graduate work leading to the PhD degree offered at the Medical Center. The students returned to Rochester, but this incident served as impetus to establish a PhD program in Oklahoma City that was designed to prepare graduate students for a teaching and research career in the basic science departments of medical schools. In 1955 Paul B. McCay was the first student of physiology to be awarded the PhD degree. Kenneth K. Faulkner was the second. The purpose of creating this program was obviously achieved. Both Drs. Faulkner and McCay today hold important positions in other departments at the Health Sciences Center. Other early recipients of the PhD degree include Lou Ann Pilkington, who served for a number of years at Cornell University Medical College; Joe Dabney, who continued on the faculty of this department for a while and later taught at Michigan State University and the Uniformed Services University of the Health Sciences; and Abbas E. Kitabchi, who joined the University of Tennessee Medical Units faculty at Memphis. Over the years enrollment in the Graduate Division of the School of Medicine increased at a progressively rapid rate until today when there are nearly as many graduate students as there are medical students in the Health Sciences Center. Dr. James W. H. Smith, a member of the faculty in the Department of Physiology. served as associate dean of the Graduate School on the Medical Center Campus from 1953 to 1956.

The 10-year period from 1950 to 1960 was one of great expansion for the Medical Center as a whole. The hospital facilities were greatly enlarged, not only by additions to University Hospital but also by the erection of the Veterans Administration Hospital within the geographical region of the Medical Center campus. The Oklahoma Medical Research Foundation had come into being and was housed in a new building directly adjacent to the Medical School. These and other expansions brought to Oklahoma City many new individuals with excellent training and dedication, as well as a zeal for accomplishment in teaching and research.

In 1959 the Department of Physiology received a unique five-year training grant. For one month each summer the department offered a concentrated course in cardiophysiology, limited to 20 college professors. A portion of the grant provided for the acquisition of the traveling demonstration laboratory that could be brought to various colleges in the state during the regular school term. Through this program an upgrading of the teaching of physiology in the state was achieved. The grant also assisted in recruiting outstanding graduates, as well as medical students, for the degree programs.

Dr. Taylor took a leave of absence from the Medical Center to serve as associate secretary of the Council for Medical Education and Hospitals of the American Medical Association. He resigned from the University of Oklahoma in 1961 to continue his work with the Council and also to direct the American Medical Association's program for Allied Medical Professions and Services. In 1967 he became affiliated with the Chicago Medical School, first as dean, then as president and chancellor.

The Early 1960's

During the academic year 1960-61 Dr. M. Jack Keyl served as acting chairman of the department. In 1961 the department recruited as the new chairman Francis J. Haddy, who had earned both the MD and PhD degrees at the University of Minnesota. He had spent two years at the Mayo Foundation as a Fellow in Medicine, followed by service in the US Army. His assignments included a tour of duty as investigator at the US Army Medical Research Laboratories at Fort Knox. He came to Oklahoma after further training at the Veterans Administration Hospital in Chicago and teaching in the Department of Physiology of Northwestern University. Dr. Haddy's special field of interest was the peripheral circulation. He was known internationally for his many contributions in this area, writing numerous papers, giving special lectures, and participating in symposia. The department in Oklahoma City became a place where many outstanding scientists would visit to discuss matters of mutual interest with Dr. Haddy and to observe the techniques and experiments in his research laboratories. In 1966 Dr. Haddy was singularly honored when he became the first recipient of the Carl J. Wiggers Award and delivered the first annual Wiggers Lecture before the American Physiological Society.

In 1960 the Federal Aviation Agency established the Civil Aeromedical Research Institute in Oklahoma. This institute was located at first in temporary quarters in Norman and three years later moved into spacious new quarters in Oklahoma City. Many members of the highly trained professional staff who were attracted to this institute became part-time faculty members in several departments in the Medical Center. The Department of Physiology was among those profiting from this influx of new talent and gained 10 new faculty members: Drs. Robert T. Clark, Jess N. McKenzie, George T. Hauty, Larry O'Brien, Pei Chin Tang, Carlton E. Melton, P. F. Iampietro, Lerner B. Hinshaw, Bruno Balke, and Thomas Adams. They contributed to the department by lecturing to medical and graduate students in their special field of competency, by arranging and supervising teaching laboratories and demonstrations, and by presenting their research. Dr. Lerner B. Hinshaw subsequently moved to the Veterans Administration Hospital, where he has continued a particularly close association in both teaching and research as a geographically full-time member of the Department of Physiology.

When Oklahoma City University launched a program of upgrading its science curriculum in 1961, Dr. A. Kurt Weiss joined its faculty and also became a part-time faculty member of the Department of Physiology. Dr. Weiss received the PhD degree at the University of Rochester, where he trained with E. F. Adolph. He then became affiliated with the University of Miami Medical School and also served as an investigator with the Howard Hughes Medical Institute. In 1964 Dr. Weiss received a Research Career Development Award from the National Institutes of Health and became a full-time member of the department. Drs. Nicholas Werthessen, Jerry B. Scott, Robert Daugherty, Henry Overbeck, and Robert Edelberg also joined the department on a full- or parttime basis during Dr. Haddy's tenure as Chairman. Drs. Scott and Daugherty later joined the Department of Physiology at Michigan State University. Dr. Daugherty moved on to become dean of the Medical School of the University of Wyoming and then of the University of Nevada.

During the 1960's the department was very active in research and many staff physicians showed an interest in doing graduate work in physiology. The department then began offering the PhD degree in the area of physiology in addition to the PhD in medical science, which had already been in existence for some years, and many students were attracted to the department for graduate training.

The departure of Dr. Haddy and eight full- or parttime members of the faculty to Michigan State University in the summer of 1966 left the Department somewhat depleted and in need of reconstruction. During the period of Dr. Haddy's chairmanship, the department had established itself as a prolific research unit. Thus, in the period October 1964 to October 1965, over 60 separate publications listed at least one member of the department as author. A large number of graduate students were recruited and educated. In 1965 three PhD degrees and six master of science degrees were awarded in physiology. The Department of Physiology had gained a national reputation, especially for investigative work in peripheral vascular physiology.

The Late 1960's

The new chairman, Eugene D. Jacobson, came to Oklahoma from UCLA in the fall of 1966. He had received the MD degree from the University of Vermont and had been trained in internal medicine and in physiology at the State University of New York in Syracuse. He was a veteran of eight years in the US Army, mostly in a research capacity. Dr. Jacobson had been associated in research training with both cardiovascular and gastrointestinal physiologists (Drs. Gordon Moe, Donald Gregg, and Morton I. Grossman), and his own research activities had been in the field of the physiology of the splanchnic circulation.

The initial problems confronting the department in 1966 included the recruiting of additional full- and parttime faculty members and developing resources (funds



Left: Francis J. Haddy (1961-1966); right: Eugene D. Jacobson (1966-1971).

as well as space) to permit expansion of the department in educational and research activities. The strenuous efforts to recruit additional faculty yielded superb results. After Dr. Gerhard A. Brecher left Emory University, where he had been chairman of the Physiology Department for a number of years, he joined the Physiology Department of the University of Oklahoma as distinguished professor late in 1966. The author of numerous papers and several well-known books, Dr. Brecher had an international reputation in cardiovascular physiology based on significant contributions on the filling of the heart, venous return, and heart-lung machines. The holder of the PhD degree from the University of Hamburg and the MD degree from the University of Kiel, Dr. Brecher had been associated in research training with Gustav Schubert in Prague and with Carl J. Wiggers in Cleveland. Dr. Brecher was also an authority on the physiology of optics and the author of a textbook on this topic.

Roger Thies came to the department the following year as associate professor. A graduate of Harvard (MA) and Rockefeller Universities (PhD), he received further training in neurophysiology at University College, London, where he was associated with Bernard Katz. Dr. Thies' research centered on membrane functions at the myoneural junction. He had formerly also taught at Washington University in St. Louis and Makerere Medical College, Uganda.

Tushar Chowdhury arrived in Oklahoma in 1969 as associate professor of physiology and biophysics and director of the biophysics program. He had earned the PhD degree in biphysics at the State University of New York in Buffalo, where he worked with Fred Snell, and had also taught at George Washington University before coming to Oklahoma. His research interests included the electrophysiology of nerve, muscle, and cancer cells.

Leonard R. Johnson joined the department in 1969. He received the PhD degree from the University of Michigan, where he had studied with Horace Davenport and spent his postdoctoral research period with Morton I. Grossman. His research interests were primarily in the area of gastrointestinal hormones and, combined with those of Dr. Jacobson, made this department a strong center of research in gastrointestinal physiology.

Numerous individuals received part-time or joint faculty appointments in the department during Dr. Jacobson's leadership: from the Department of Medicine – Drs. T. E. Bynum, Edward D. Frohlich, Clarence A. Guenter, Robert Lindeman, John Naughton, Jack Tompkins, Stewart Wolf, and Andy Aniece Yunice; from the Department of Anesthesiology – Walter Massion; from the Department of Psychiatry and Behavioral Sciences – Arthur A. Zeiner; from the Department of Gynecology and Obstetrics – Darren Nelson and O. Ray Kling; and from the Civil Aeromedical Institute – E. Arnold Higgins and George Clark.

James W. Woods came to Oklahoma from Johns Hopkins University to become the first director of the new Basic Sciences Teaching Facility. He held joint appointments in the Departments of Pharmacology and Physiology. Richard Bell and Linda Shanbour, who at one time were students in the department, became faculty members also.

As a result of the influx of highly trained specialists in various areas of physiology, the department naturally underwent many changes and experienced a reorientation in its educational thrust without losing impetus in research. One of these changes was a pronounced shift into the areas of biophysics and neurophysiology; this also resulted in 1969 in a change of the official name to Department of Physiology and Biophysics.

The awarding of a National Institutes of Health Training Grant in 1968 to support graduate students and postdoctoral fellows in physiology and biophysics capped extensive efforts to acquire added funds for training. Institutional funds were generated to renovate unused space and create five new laboratory-office suites. Simultaneously, several new research grants from NIH, and contracts from the Department of Defense, the US Army, and the Department of Transportation infused needed funding into investigative programs conducted by the staff. Total funding of research in the department more than tripled in the period 1967-70. The following year, defying the national trend, research funding of the department increased by 25%. During the period October 1966 to October 1967, nearly 90 publications were prepared by members of the department; during the period October 1967 to October 1969, the number exceeded 100 each year. During the period October 1969 to October 1970, members of the department contributed 168 publications.

The Early 1970's

Dr. Jacobson resigned in 1971 to become the first director of the physiology program at the new University of Texas Medical School, then being assembled in Houston. He subsequently served as vice-dean for Academic Affairs at the University of Cincinnati School of Medicine. In 1985 he became dean of the University of Kansas School of Medicine.

Dr. M. Jack Keyl was named acting chairman and continued in this capacity for $6\frac{1}{2}$ years. Most members of the gastrointestinal research group followed Dr. Jacobson to Houston. With Dr. Allan J. Stanley's retirement in 1970, the full-time faculty size was further shrunk and with the expansion of the former Medical School campus to a Health Sciences Center, new teaching demands kept the faculty very busy. Dr. Robert J. Person, a graduate of the biological psychology program at this institution, joined this department in 1971 as assistant professor. With the anticipated opening of a Collge of Dentistry, funds were secured in 1971 to enlarge the faculty by bringing in Dr. Rex D. Stith, an endocrinologist. A native Oklahoman, he had been a graduate of Oklahoma State University and subsequently had earned the PhD degree at Purdue University, where he worked with Gerald D. Bottoms. At the same time the new chief of the Pulmonary Disease Section of the Department of Medicine, Robert M. Rogers, MD, and the new director of the Pulmonary Function Laboratories, Bernard E. Pennock, PhD, received adjunct appointments in the department and for the next few years provided most of the instruction for the department in the area of respiratory physiology.

The department entered a new era in 1976 when the Biomedical Sciences building was opened. In addition to the adminstrative offices for the dean of the College of Medicine, this building houses the Basic Science Departments. The Physiology Department occupies the entire sixth floor, and there is a separate central facility on the first floor for housing laboratory animals. Each faculty member has a small office and a larger laboratory. A bridge was built to connect this building with the Basic Sciences Education building.

The Late 1970's

In October 1977, Dr. H. Lowell Stone was appointed head of the Department of Physiology and Biophysics, and with his arrival another era of high achievements was instigated. Dr. Stone received the BS degree from Rice University and the PhD degree from the University of Illinois. After a postdoctoral stint in the laboratory of Arthur Guyton in Jackson, Mississippi, he joined the **Biodynamics Branch of the USAF School of Aerospace** Medicine at Brooks AFB in Texas. He then moved to Galveston, Texas, where he became director of Cardiovascular Physiology at the Marine Biomedical Research Institute and a professor in the Physiology Department of the University of Texas Medical Branch. His chief research interest was the neural control of the coronary circulation, especially in relation to changes during exercise.

Dr. Stone brought with him three of his faculty colleagues from Texas. Russell T. Dowell was an exercise physiologist who had earned the PhD degree by studying with Charles Tipton at Iowa. Robert D. Foreman graduated from Loyola University School of Medicine in Chicago with the PhD degree, having studied with Robert Wurster. During his postdoctoral training with William Willis in Galveston he learned techniques to investigate the ascending pathways for cardiac and other visceral pain. Kenneth J. Dormer, PhD, a graduate of UCLA, is experienced in three areas, neurocardiology, marine physiology, and cochlear physiology.

Wishing to build a department in which most areas of physiology were represented on the faculty by a specialist. Dr. Stone soon brought in additional faculty members: Jay P. Farber, Ph.D., who had studied with Leon Farhi at SUNY in Buffalo, as respiratory physiologist from the University of Iowa: Y. S. Reddy, PhD, University of Sri Venkateswara, India, with an interest in cardiac muscle biochemistry from the University of Texas Medical School, Houston; Bert A. Mobley, PhD, who had studied with Ernest Page at the University of Chicago, with an interest in muscle biophysics from Wayne State University; and Robert C. Beesley, PhD, who had studied with John Forte at Berkeley, as gastrointestinal physiologist, also from Wayne State. Close ties for research collaboration were established with the Departments of Pediatrics, Psychiatry, Neurosurgery, Medicine, and Pathology as well as with the Departments of Health, Physical Education, and Recreation on the University of Oklahoma Campus in Norman. Re-



Left: H. Lowell Stone (1977-1984); right: Robert D. Foreman (1984-).

newed efforts were made to recruit top-notch graduate students and postdoctoral fellows. In subsequent years additional faculty members were recruited: Robert W. Blair, PhD, Texas at San Antonio with Vernon Bishop, having spent his postdoctoral years in this department; George Billman, PhD, University of Kentucky; and W. Steve Ammons, PhD, Emory University. Dr. Stone was a prolific researcher, who, in addition to numerous NIH Grants, also held research contracts and collaborated in his research with the Air Force and with NASA. Dr. Peter J. Schwartz, professor of medicine, Cardiovascular Institute at the University of Milan, Italy, was appointed visiting professor and spends from one to three months each year in collaborative research at Oklahoma. Dr. Jean-Pierre Gagnol of Montpellier, France, where he heads the cardiovascular research of a large drug company, was appointed visiting associate professor and comes to Oklahoma frequently. Dr. Stone spent a considerable amount of time on collaborative work in other laboratories and was a frequent guest at the NASA-Ames Research Center, Moffett Field, California; in Milan, Italy; in Montpellier, France; and in Moscow, Russia, where he consulted on cardiac instrumentation of primates for space flights.

A number of faculty members served as peer reviewers for the National Institutes of Health, the National Science Foundation, and the American Heart Association. The department also entertained a steady stream of visitors who were interested in the experiments being conducted here on changes in neurocardiologic mechanisms during exercise, cardiac pain, the sudden death syndrome, weightlessness, initiation of respiratory control in the newborn, muscle physiology, adrenal receptor mechanisms, and other topics. The weekly seminar series gave these distinguished guests an opportunity to tell of their experiments. The department gave the impetus for establishing the Oklahoma Society of Physiologists, which holds an annual day-long scientific session, and the Red River Symposium Series. The latter is an annual weekend, usually held at Lake Texoma or Lake Murray, where investigators from this department get together with their scientific counterparts in other medical schools, primarily from Southwestern Medical College in Dallas, Texas Tech University in Lubbock, and the Health Sciences Center in San Antonio.

For many years Dr. A. Kurt Weiss served as course coordinator for all professional courses, taught for the Colleges of Medicine, Dentistry, and Pharmacy. In 1979 Dr. Weiss was appointed vice-head of the department, giving Dr. Stone more time for research.

In the years 1982-84 the Department of Physiology and Biophysics was awarded the largest amount of research funds among all departments at this Health Sciences Center, including the clinical departments. The total research support generated by the department from outside sources by far exceeded the total state budget allocation to the department.

At a time when the federal government curtailed its support of research and the standards for obtaining funded grants were elevated further, almost all members of the department had active grants and were heavily engaged in research. This activity was not without its rewards. Three faculty members (Drs. Farber, Foreman, and Reddy) were given Research Career Development Awards and Dr. Bert Mobley became an Established Investigator of the American Heart Association. In 1984 Dr. Robert Foreman was named the recipient of the Provost's Award for Excellence in Research and the Board of Regents of the University conferred upon Dr. Stone a George Lynn Cross Research Professorship. The undergraduate students elected Dr. Weiss to Honorary Membership in the Golden Key National Honor Society. In 1985 Dr. Lerner Hinshaw became another holder of the George Lynn Cross Research Professorship in the department.

There were some tragedies, too. On July 4, 1978, while visiting his brother in San Antonio, Dr. Tushar Chowdhury died suddenly of an aneurysm. On November 16, 1984, while on a combined business and hunting trip in Montana, Dr. Stone suffered a heart attack and died at the age of 48. Thus another era in the history of this department came to an end.

The Present

This is written a few months after Dr. Stone's death. Dr. Robert D. Foreman is serving as acting head of the department. A search committee for a new head has been activated. The department has shown cohesiveness and is carrying on. Two of Dr. Stone's graduate students were able to finish their dissertation research and have received PhD degrees. Already an NIH Program Project Grant in excess of three million dollars has been awarded for work on mechanisms and prevention of lethal arrhythmias, another large grant from a different source on the effects of carbon monoxide on lethal arrhythmias has also been received, and numerous smaller grants. The future for this department looks bright.

The advice and help in locating early source material given by the late Dr. Mark R. Everett, Regents' Professor of medical sciences and dean emeritus of the School of Medicine, and Dr. Allan J. Stanley, professor emeritus of physiology, is hereby gratefully acknowledged.

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History of Physiology at The Ohio State University

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The Beginnings

The laboratory of experimental physiology at The Ohio State University is one of the oldest in the United States. It was established by Dr. Albert M. Bleile in 1879. Dr. Bleile earned his MD degree at Starling Medical College in 1876 (a predecessor to The Ohio State College of Medicine) and then went to Europe, where he spent three years in postgraduate studies in Paris, Vienna, and Leipzig working under men such as Dubois Raymond and Helmholtz. Most important, however, was Carl Ludwig, the great teacher, who through his students had an extraordinary influence on the early history of American physiology.

Dr. Bleile spent a year in Carl Ludwig's laboratory. During this time, he carried out pioneer research on the control of blood sugar, a field in which the broad outlines had recently been delineated by Claude Bernard. In 1879, Dr. Bleile returned from Europe and accepted a position as Professor of Physiology at the Starling Medical College, where he set up a small but wellequipped experimental and teaching laboratory. This was only eight years after Henry Pickering Bowditch, also a student of Carl Ludwig, had established the first teaching laboratory of physiology in America at Harvard.

Dr. Bleile was one of Dr. Ludwig's favorite students, and the two men corresponded for a number of years after Dr. Bleile returned to the United States. A part of this correspondence is preserved in the Medical Section of the Ohio State Archeological and Historical Museum (Figure 1).

In 1914, when the combined Starling Medical College and Ohio Medical University were consolidated with The Ohio State University, Dr. Bleile's physiological laboratory became a part of the University. Dr. Bleile, himself, had been a professor of physiology at the University since 1891 and continued in this capacity until his death in 1933. When the University took over the Starling-Ohio Medical College, Dr. Clayton McPeek, with the rank of assistant professor, was chairman of the department (1914–16). Dr. McPeek continued as assistant professor of physiology until 1934, when he resigned his position at the University in order to devote full time to medical practice (3).

Departmental Growth

In 1916, Dr. Clyde Brooks was brought to Columbus from the University of Pittsburgh and was made chairman of the Department of Physiology. He continued in this position until 1920, when he resigned to accept a similar position at the University of Alabama. That same year, Dr. Roy G. Hoskins, who had been professor of physiology at the Starling-Ohio Medical College from 1910 to 1913, was brought back and made the departmental chairman. He continued in this position until 1928, when he resigned to organize and head the Memorial Foundation for Neuro-Endocrinology, which was housed in the laboratories of the Harvard Medical School in Boston. With the resignation of Dr. Hoskins, Dr. Raymond J. Seymour, who had been on the staff since 1917 and was noted as an outstanding teacher, was made chairman. He held the position until 1934, when he was succeeded by Dr. Frank A. Hartman, who came to Columbus from the University of Buffalo. Dr. Hartman was well and favorably known for his outstanding research on the functions of the adrenal gland. He was one of the first endocrinologists to prepare a physiologically active extract from the gland and received numerous honors in recognition of his work. Dr. Hartman resigned from the chairmanship in 1947 to become a

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Figure 1 Copy of letter from Carl Ludwig to Dr. Albert M. Bleile.

[†] Fred Hitchcock, who died in 1980, was an active member of the Department from 1923 to 1960 and wrote the history through 1958 (4). See "A Retrospective Look Through the Camera of Fred A. Hitchcock" [*Physiologist* 27(3): 128–130, 1984] for an interesting collection of his photographs.

research professor, and in 1954 he retired with the title of professor emeritus. During all these years, he continued his distinguished research in adrenal endocrinology and published numerous definitive studies of the adrenal gland (1).

When Dr. Hartman resigned from his administrative post, Dr. Fred A. Hitchcock, a member of the faculty since 1923, was asked to take over as acting chairman, until a suitable man could be found to head the Department. Charles A. Doan, dean of the College of Medicine, was desirous of having a physiology chairman with a clinical background who would be well qualified for a professorship in the Department of Medicine, as well as having outstanding qualifications as a physiologist. After a two-year search, Dr. Eric Ogden, who had worked with Ernest Henry Starling and was professor and chairman of the Department of Physiology at the University of Texas Medical Branch in Galveston, was appointed to the position. Dr. Ogden assumed his duties in the autumn of 1949 and continued to serve as chairman until he left to become chief of the Environmental Biology Division of Ames Research Center, Moffett Field, California, in 1962 after serving thirteen years as chairman.

As the College of Medicine expanded from 80 to 150 students, the department grew during the period 1949-1960 from 7 to 12 full-time staff, and there developed several well-rounded groups with varied interests in physiology. In the thirties and early forties, research interests were oriented toward endocrinology because both Dr. Hoskins and Dr. Hartman were distinguished as endocrinological researchers. Under Dr. Ogden, cardiovascular and respiratory physiology dominated the interests of the faculty. (See Table 1 for a complete list of departmental chairmen from 1897 through 1985.)

In the early twenties, the medical and dental schools were located on Park Avenue in Columbus, Ohio, adjacent to White Cross Hospital. This resulted in a sharp division between the instructors concerned with medical professional teaching and those on the campus who taught undergraduate scientific courses. At this time, the medical teaching was under the direction of Dr. Hoskins, with the assistance of Dr. McPeek and Dr. Paul H. Charlton, who gave up his connection with physiology in 1926 to become a member of the surgical staff, and two newly appointed instructors, Dr. Milton O.

Table 1 Chairmen of the Department of Physiology and Their Specialties Control of Blood 1879-1914 Albert M. Bleile, MD Sugar Clinical Physiology 1914-1916 Clayton McPeek, MD 1916-1920 Clyde Brooks, PhD Clinical Physiology 1920-1928 Roy G. Hoskins, PhD Neuro-endocrinology 1928-1934 Raymond J. Seymour, MD **Clinical Physiology** Adrenal Physiology 1934-1947 Frank A. Hartman, PhD 1947-1949 Fred A. Hitchcock, PhD Aviation Physiology (acting) 1949-1962 Eric Ogden, MD Cardiovascular Physiology 1962-1964 Robert C. Grubbs, MD Metabolism (acting) 1964-1973 Robert C. Little, MD Cardiovascular Physiology 1973-1985 Heinz P. Pieper, MD Cardiovascular Physiology



Figure 2

Dr. Seymour teaching a physiology class in Room 208 Hamilton Hall (ca. 1930's). Except for the smoked drums, this room is much the same today.

Lee and Dr. Hitchcock. Dr. Lee served until 1928 when he resigned to take a position in Boston with Dr. Hoskins. He later became the distinguished executive secretary of the American Physiological Society and of the Federation of American Societies for Experimental Biology, where he had far-reaching influence on biomedical research.

The teaching of physiology on The Ohio State University campus in the early years was carried on by Drs. Bleile and Seymour, with the assistance of Dr. E. P. Durrant, who was assistant professor from 1925 to 1930 and associate professor from 1930 to 1933. In 1933, Dr. Durrant retired as associate professor emeritus; he died on January 28, 1953. His son, Dr. Rollin R. Durant (who spells his name with one "r"), was an instructor in the department from 1925 to 1936 and assistant professor from 1936 to 1943, when he resigned to devote his entire time to the practice of medicine.

During Dr. Seymour's years as chairman, the department remained largely unchanged (Figure 2). Dr. Seymour, himself, was not research oriented, and to make up for this deficiency, he brought Dr. Leonard B. Nice, who at the time was professor of physiology at the University of Oklahoma, to the department. Dr. Nice was an endocrinologist particularly interested in reproductive endocrinology. He later served as professor and chairman of the Physiology Department at the Chicago Medical School.

Just before he resigned in 1923, Dr. Hoskins appointed Mr. Howard Hamlin to the departmental faculty. Mr. Hamlin had been on the staff at Simmons College and at the Sargent School of Physical Education. He was an instructor from 1927 to 1930 and assistant professor from 1930 to 1935, when he resigned to accept a position with the Ohio Department of Education.

Under Dr. Frank A. Hartman, the Department maintained its orientation toward endocrinology. In 1934, Katherine A. Brownell joined the Department as a research assistant in endocrinology and a candidate for the PhD degree. She worked many years with Dr. Hartman and received her PhD in 1940. In 1946, she was promoted to instructor and in 1953 to assistant professor, and in 1960 she was given the rank of associate professor. Drs. Hartman and Brownell wrote and published the first definitive text on the adrenal gland (1). After Dr. Hartman's retirement in 1947, the endocrinological activities of the Department were largely in the hands of Dr. Brownell. Dr. Robert C. Grubbs was appointed to the faculty as an assistant professor by Dr. Hartman in 1946. Previous to this, Dr. Grubbs, who obtained both his MD and MSc degrees at Ohio State, had been on the staff of the Physiology Department at the George Washington Medical School for nine years. In 1947, he was promoted to associate professor and, in 1956, Dr. Ogden appointed him vice-chairman of the department, followed by the rank of professor in 1957. Most of Dr. Grubb's time was occupied with his teaching and administrative duties.

In line with the general policy of The Ohio State University, the Physiology Department always had been a "service department." All physiology for students in various colleges was taught in this single department. In the twenties, under Dr. Hoskins, the dental students and the medical students were together in the same physiology course. This had the advantage of lessening the teaching load in the understaffed department. However, the arrangement was considered unsatisfactory by both the Department of Physiology and the College of Dentistry. It was the considered opinion of all concerned that a course in physiology for dental students should have a different orientation from a similar course for medical students. Therefore, a separate and distinct course was organized for dental students and taught by Dr. Rollin R. Durant. In compliance with a request by the College of Dentistry that the teaching and administration of the course in physiology for dental students be made the major assignment of a senior faculty member, Dr. Hartman asked Dr. Hitchcock to take the assignment. Dr. Hitchcock began teaching the dental class in the autumn quarter of 1936 and was in charge of the course for seventeen years. In the autumn of 1952, Dr. Milton A. Lessler, who had jointed the staff of the department in 1951, began assisting Dr. Hitchcock with the dental physiology class. Beginning with the 1953 class, Dr. Lessler was in charge of the course for 15 years. This arrangement made it possible for Dr. Hitchcock to devote his major efforts to aviation and space physiology research and to the direction of his many graduate students.

Teaching Philosophy

Throughout the history of the department, it has always been the responsibility of the chairman to take admininstrative charge of the physiology course for medical students and to play a major role in teaching. The lectures to medical students, however, were usually divided up among the various senior members of the faculty, each giving the lectures in his own field of specialty. This method is open to the criticism that lectures, given by a specialist on a specific physiological topic, are likely to be too technical and detailed for students with a limited background in the subject. The method may also lead to fragmentation and overspecialization in the staff. When the department was chaired by Dr. Hoskins, it was the rule that lecturers should speak on topics outside their field of specialization. Dr. Hoskins rotated these assignments from year to year so that each faculty member covered the entire field of physiology in the course of lecturing over a period of years. This kept each staff member up-to-date on subjects outside his specialty and served to lessen the tendency toward overspecialization.

Originally, physiology courses for the students in the College of Veterinary Medicine were taught by the Department of Physiology, and it was the policy of the Department to have on staff a man who, in addition to a graduate degree of physiology, also had a DVM degree. Such a man was Dr. Derwin W. Ashcraft, who for many years was in charge of teaching physiology to students in veterinary medicine. Dr. Ashcraft received his DVM degree in 1923, a MSc in physiology in 1928, and a PhD in 1932, all at The Ohio State University. Dr. Ashcraft was appointed an instructor in the Department of Physiology in 1928 and an assistant professor in 1932. He taught the courses for students in veterinary medicine with great success. As time went on, a certain amount of friction developed in regard to these courses, and the veterinary students complained that the courses were oriented toward human instead of animal physiology, while the medical students complained that they were taught nothing but frog and dog physiology. There was a feeling on the part of the faculty that a man whose major teaching duties and interests were in a college other than medicine may be passed over by his chairman and dean when it came to promotions and salary increases. These and other considerations led, in 1934, to the establishment by The Ohio State University of a Department of Veterinary Physiology and Pharmacology in the College of Veterinary Medicine. Dr. Ashcraft headed this department with the rank of associate professor until his death in 1944. Since 1934, the Department of Physiology has not been responsible for the teaching of students in the College of Veterinary Medicine.

The Hartman Years

There was considerable expansion of the department under the chairmanship of Dr. Hartman. He appointed Dr. Emil Bozler, who took his PhD in 1923 at the University of Munich, and Dr. Clifford A. Angerer, a PhD, from the University of Pennsylvania.

Dr. Bozler came to the United states as a Fellow of the Rockefeller Foundation and carried on research at the University of Rochester and at the Johnson Foundation for Medical Physics at the University of Pennsylvania. He joined the department at Ohio State in 1936 and held the rank of assistant professor until 1942, when he was made associate professor, and then advanced to the rank of professor of 1946. At The Ohio State University, Dr. Bozler (Figure 3) distinguished himself both as a teacher and as a leading research worker in the field of neuromuscular physiology. He retired in 1971 and was awarded



Figure 3 Emil Bozler in his laboratory (ca. 1980).

an honorary doctor of science degree by The Ohio State University in 1975, as well as many other honors by the international physiological community.

Dr. Clifford Angerer joined the department in 1939 as an instructor. He was advanced to assistant professor in 1943, to associate professor in 1947, and professor in 1954. His research was chiefly in the field of general physiology. In 1935, Dr. Hans O. Haterius, who had taken his PhD degree in physiology at the University of Iowa in 1928, was brought into the department with the rank of assistant professor. Dr. Haterius, an endocrinologist with a major interest in the field of reproduction. was brought to the University with the understanding that his research was to be in the field of reproduction and lactation of farm animals. These plans were never satisfactorily accomplished. Whether it was due to the lack of facilities in the College of Veterinary Medicine or to some other factor, no work was ever done with farm animals, and Dr. Haterius during his stay at Ohio State worked almost exclusively with albino rats. He resigned in 1938 to become the chairman of the Department of Physiology at the Boston University School of Medicine.

Another brilliant young man, who was brought to Ohio by Dr. Hartman but remained only briefly, was Dr. George W. Thorne. Dr. Thorne worked with Dr. Hartman at the University of Buffalo, where he received his medical degree in 1929. He joined the Physiology Department in 1935 as assistant professor. His research interests were in the field of adrenal physiology, and he worked rather closely with Dr. Hartman. In 1936, he took a leave of absence in order to accept a National Research Council Fellowship and never returned. He had several excellent offers of positions and later became a professor of medicine at Harvard Medical School and physician-in-chief at Peter Bent Brigham Hospital.

In 1936, Dr. James Kenneth Wallace Ferguson, an ardent Scot of Canadian citizenship, joined the Department as assistant professor. He was an outstanding young physiologist whose research interests were in the field of respiration. He had received his medical degree in 1932 at the University of Toronto, where he worked with such men as Dr. Charles H. Best and Dr. Lawrence Irving. He also spent a year at Cambridge University in England working with F. J. W. Roughton and Joseph Barcroft.

While Dr. Ferguson was at Ohio State, he collaborated in this research activities with Dr. Fred Hitchcock with most gratifying results. In 1938, he was offered a post in the Department of Pharmacology at the University of Toronto, which he accepted. Shortly thereafter, he was made chairman of that department and later became director of the Connaught Medical Research Laboratories, as well as a professor of pharmacology. To replace Dr. Ferguson, Dr. Hartman brought to the Department Dr. Gordon C. Ring, who at they time was a teaching fellow in the Department of Physiology at the Harvard Medical School. Dr. Ring's research interests, like those of Dr. Ferguson, were in the field of respiration but leaned toward respiratory metabolism. He had taken his PhD degree at Harvard in 1935, and he came to Ohio State with the rank of assistant professor. In 1942, he was granted a military leave of absence and accepted a commission in the Food and Nutrition Branch of the Sanitary Corps. He returned to the Department after World War II and served for one year (1945-46) before resigning to become associate professor of physiology at Temple University School of Medicine. He later was appointed chairman of the Department of Physiology at the University of Miami School of Medicine in Florida.

Influence of World War II

With the outbreak of World War II, there was considerable change in the orientation of the Physiology Department. Perhaps the most pronounced change was the concerned with the organization of a Laboratory of Aviation Physiology. Early in 1941, Dr. Fred Hitchcock (Figure 4) became active in the establishment of such a laboratory. He conferred with Dean Alpheus W. Smith of The Ohio State University Graduate School and obtained his support for the project. Dr. Smith was able to get an appropriation of \$3,000 for the purchase of a decompression chamber. Negotiations were started for the construction of the chamber, but actual work on it had not begun when the attack on the United States' fleet at Pearl Harbor occurred. Almost at once, the Office of Scientific Research and Development was organized in Washington, and Dr. Hitchcock was asked to act as a responsible investigator on a project involving a study of tolerance to decompression. At first, it was proposed to make this study center around the role of the adrenal gland, since the chairman, Dr. Hartman, held such an eminent place in the field of adrenal physiology. Therefore, Drs. Hitchcock and Hartman were appointed co-investigators on the project. Shortly after the project became active, however, Dr. Hitchcock devised and demonstrated to a representative of the Office of Scientific Research and Development a technique for exposing experimental animals to rapid or explosive decompression. As a result of this, Dr. Hitchcock was asked to drop all other work and devote the



Figure 4 Fred A. Hitchcock standing beside his high-wing monoplane.

resources of the Aviation Physiology Laboratory to a comprehensive study of the physiological effects of explosive decompression. This project, which continued for more than ten years, yielded much information of basic importance to modern aviation physiology.

Another contribution of great and lasting value to physiologists was performed outside the laboratory by Dr. Hitchcock in collaboration with his wife, M. A. Hitchcock. This was the scholarly translation into English of Paul Bert's *La Pression Barometrique* (2). This classic was thus made available for the first time to many readers, since only a few copies of the original work existed in this country.

From the start, the department was extremely fortunate in the caliber of the young men and women who came to carry on the work in aviation physiology. The first person to join the laboratory staff was Dr. William Whitehorn, who had received his MD from the University of Michigan in 1939. After his internship, he spent two years there, as an assistant professor in physiology with Dr. Robert Gesell, and came to Ohio State in 1942 as a research associate in the Laboratory of Aviation Physiology. In 1944, he was made an instructor in physiology and divided his time between research, teaching, and a part-time appointment in the Department of Medicine. In 1946, he was promoted to the rank of assistant professor. The following year, he resigned to accept a place on the staff of the Physiology Department in the College of Medicine of the University of Illinois, where he had a distinguished career. Other distinguished investigators in the Laboratory of Aviation Physiology included Drs. Charles Billings, Earl Carter, John Dines of the RAF, Abe Edelmann, Albert Fasola, John Kemph, George Kydd, Ralph Stacy, and Sid Leverett, who later became editor of Aviation Space and Environmental Medicine. Dr. Leverett recently (1985) was honored by the Air Force Medical School at Brooks Air Force Base by having the Leverett Laboratory Building named for him.

World War II had profound effects on the teaching program of The Ohio State University. The College of Medicine went on the "War Time Accelerated Program" beginning with the summer quarter, 1942. This resulted in a much increased teaching load for the physiology staff and less time for research. Graduate students were being called into the armed services, and only those engaged on research projects considered important to the war effort (therefore, carrying a priority rating) were given the privilege of continuing with their studies and research. This added up to an increased teaching load with a depleted staff. Despite these handicaps, the faculty did an outstanding job in the accelerated teaching program and at the same time kept the research program of the Department going. The detracting factors were further aggravated following the end of the war by the marked increase in enrollments with little expansion in staff.

It should be pointed out that when it was first built (1930-34), Hamilton Hall, where the Physiology Department resides, was somewhat inadequate in providing laboratory facilities for physiology teaching and research. In the quarter of a century since the building was erected, such laboratory facilities as it offered showed marked deterioration. Remodeling of the north wing of Hamilton Hall (1952-1953), which occurred when the Department of Pathology moved into the StarlingLoving Hospital building, gave the Department more floor space but did little in the way of improving the antiquated laboratory apparatus and equipment. During the period of Dr. Eric Ogden's chairmanship (1949-1962), the old smoked drums and inductoria were replaced by modern electronic equipment and the four teaching laboratories were rebuilt and improved.

While Fred Hitchcock was acting chairman of the Department (1947-1949), two additions to the faculty were made. The first was Dr. Ralph W. Stacy, appointed assistant professor in 1949. Dr. Stacy had taken both his MS and PhD degrees in physiology at Ohio State and then served as an assistant professor at the University of Kentucky for one year. He was promoted to the rank of associate professor in 1954 and to professor in 1959. In 1962, he left to take a research professorship at the University of North Carolina. Dr. Stacy's research activities were chiefly in the field of biophysics, and he was largely responsible for the development of this aspect of physiology at The Ohio State University. In 1957, he took the initiative in helping to found the Biophysical Society and served as an officer in that organization for a number of vears.

The second addition was Dr. Charles D. Hendley, who joined the faculty as as assistant professor in 1948. He was a specialist in the field of vision and the physiology of the eye, who had taken his doctorate at Columbia University under Dr. Selig Hecht. Hendley resigned in 1950 to accept a position as associate professor of pharmacology at the University of South Dakota and later became senior pharmacologist for the Schering Corporation at Bloomfield, NJ.

Richard W. Stow (PhD 1953, in biophysics from the University of Minnesota), whose major appointment was in the Department of Physical Medicine, became a part-time assistant professor in physiology in 1962, replacing Ralph Stacy. He took over Dr. Stacy's course in physical instrumentation for biologists and developed it into a popular university-wide course on biomedical instrumentation. Dr. Stow developed a number of biomedical instruments for studying tissue blood flow but is most widely known for his conversion of a pH electrode for the measurement of CO_2 . Dick Stow retired in 1982 and in 1985 was honored by the Biomedical Engineering Society with the Nernst Award in recognition of his accomplishments in physical medicine and the invention of the CO_2 electrode.

The Ogden Years

Dr. Eric Ogden became chairman of the department in 1949 and made several additions to the staff. In 1951, Dr. Milton A. Lessler joined the physiology department as an assistant professor. He was advanced to associate professor in 1957 and to professor in 1963. Dr. Lessler was educated at Cornell University (BS, 1937; MS, 1938) and at New York University (PhD, 1950). He served in five invasions with the 82nd Airborne Division (1942-1945) and, upon being discharged from the Army, spent four years as a pre- and postdoctoral NIH fellow and teaching assistant at New York University. His early research interests were in quantitation of nuclear DNA and the cytophysiology of growth. Later he studied the cellular effects of ioning radiation and worked with the Yellow Springs Instrument Company to develop a practical O2 electrode system for metabolic and biochemical measurements of cells and mitochondria. He also taught

a definitive course in cell physiology and carried on an active research program on the effects of lead, mercury, and dimethyl sulfoxide on cell metabolism. On his retirement in 1985 he became President Elect of the Ohio Academy of Science.

William Graydon Myers, born in Toledo in 1908, received all his degrees from The Ohio State University: AB, 1933; MS, 1937; PhD in physical chemistry, 1939; and MD in 1951. He interned at University Hospital and during this period (1941-42) aided in the use of radionuclides for the treatment of human beings. He later received international recognition for the development of eight radioactive isotopes (cobalt-60, gold-198, chromium-51, iodine-123, iodine-125, strontium-86m and -87m, and carbon-11) for diagnosis and treatment of disease. As a Julius F. Stone Fellow in Medical Research (1945-1949), he represented The Ohio State University College of Medicine as a member of the Radiological Safety Section for both atomic bomb tests during Operation Crossroads at Bikini Atoll, June-August 1946. He was appointed as the Julius F. Stone Research Associate Professor in the Departments of Medicine, Radiology and Physiology (1949-1953) and director of the Division of Medical Physics and Radio-isotopes (1951-1957). He was appointed a professor of physiology in 1953 and had a long-time association with the Department, rarely missing a monthly meeting. Dr. Myers instituted one of the first University courses in radiation biophysics, which he taught in the Physiology Department until his retirement in 1979.

Dr. Norman A. Coulter was appointed to the departmental faculty as an assistant professor in 1952. He completed the MD degree at Harvard Medical School in 1950 and, for the next two years, was a National Research Council Fellow at Johns Hopkins University. His research interests were in the field of the mathematical and biophysical aspects of physiology. He worked with Dr. Stacy in developing the field of biophysics and left in 1964 to become a distinguished professor of physiology at the University of North Carolina.

Dr. Leo A. Sapirstein joined the Department in 1953 (see Figure 5) as an associate professor and was promoted to the rank of professor in 1955. He received both the PhD and MD degrees from the University of California. Before coming to Columbus, he was an instructor in physiology at the University of California (1943– 44) and senior assistant surgeon in the National Cancer



Figure 5

Physiology staff in the department library (May 1953). Sitting (left to right): Nancy Buckley, Katerine Brownell, Frank Hartman, Eric Ogden (Chmn), Fred Hitchcock, Emil Bozler, Robert Grubbs, Clifford Angerer, and Milton Lessler. Standing (left to right): William Myers, Ralph Stacy, Norman Coulter, and Leo Sapirstein.

Institute (1947-1952). His major interests were in the field of cardiovascular and renal physiology.

Further strength was added to the cardiovascular program by Dr. Gerhard Brecher, who was a widely recognized leader in experimental ophthalmology and the physiology of the cardiovascular system. Dr. Brecher was born in Germany and studied at the University of Hamburg, Duke University, and the University of Lausanne, Switzerland. As an exchange student at Duke University, he received an MS in 1930 and then completed his PhD at the University of Hamburg in 1932 and MD at the University of Keil in 1937. Dr. Brecher was an associate professor at Western Reserve University School of Medicine when he was asked in 1955 to come to Ohio State University as the Julius F. Stone Research Professor and director of the Institute for Vision. He was associated with the Physiology Department from 1955 to 1957, when he left to assume the chairmanship in physiology at Emory University. Dr. Brecher was instrumental in recruiting Dr. Heinz P. Pieper for the Department, convincing him that he leave Germany and consider a career at The Ohio State University.

Other additions to the faculty, during Dr. Ogden's chairmanship, included Dr. Margaret T. Nishikawara, as assistant professor, in 1954. She completed BA, MA, and PhD degrees at the University of Toronto and specialized in the field of metabolism and endocrinology. She became an associate professor in 1963, professor in 1972, and acting chairman upon Dr. Pieper's retirement in July 1985. Dr. Larissa Lukin, with degrees from Katowice College in Poland and Heidelberg University in Germany and a PhD from Columbia University, was appointed Assistant Professor in 1957 and, in 1963, went to the University of California. Her research was in the field of respiratory metabolism. Dr. Heinz Pieper, who had an MD magna cum laude from the University of Munich, was appointed assistant professor in 1957 and actively contributed to the field of cardiovascular physiology at The Ohio State University. He was advanced to associate professor in 1960, to professor in 1968, and became chairman of physiology in 1974 when Dr. Robert Little left to become chairman of the Medical College of Georgia at Augusta.

The Graduate Program

Graduate teaching in the Department can be said to have begun in 1923 when W. W. Tuttle came to Ohio State as a National Research Council Fellow in Physiology to do graduate work with Professor Hoskins. He received the PhD degree in 1924, the first such physiology degree granted by The Ohio State University. Dr. Tuttle became a distinguished professor of physiology at the State University of Iowa and was a joint author of a popular text book in this field. After 1924, graduate work in physiology increased at first slowly and then more rapidly. By 1932, nine PhD's in physiology had been awarded and, from 1932 to 1958, 34 such degrees were granted. A large number of master's degrees were also conferred. From 1923 to 1933, 23 master's degrees were awarded, and from 1933 to 1958, 46 MS degrees were awarded.

Most of those who have received advanced graduate degrees from The Ohio State University Department of Physiology have gone on to become outstanding professional physiologists. Many are teaching and doing research in Departments of Physiology at the Universi-
ties of Michigan, Illinois, Iowa, Northwestern, McGill, and Miami (Ohio); others work in research institutes or government laboratories, such as the Argonne National Laboratory, the Aerospace Medical Laboratory at Wright Field, the Army Chemical Center, the Aviation Medical Laboratory at Johnsville, PA, and the Brookhaven National Laboratory on Long Island.

During the final years of Dr. Ogden's tenure as chairman (1959-1962), there were few changes in the staff. One major change, however, did occur in June 1960, when Professor F. A. Hitchcock, who had been a member of the Physiology Department since 1923 and director of the Laboratory of Aviation Medicine since its inception in 1941, reached the retirement age. During his career, he had received many honors. In 1957, he served as president of the Space Medicine Branch of the Aerospace Medical Association, and from 1950 to 1956 he served on the Council of The American Physiological Society. In 1955, he was the recipient of the Tuttle Award in recognition of his outstanding research in aviation medicine and, in 1957, he was elected a Life Member of the Scientific Council of the Brazilian Interplanetary Society. He was a member of some nine International Congresses in Physiology and Astronautics in seven different countries. After his retirement, Fred Hitchcock served as educational director of the American Institute of Biological Sciences in Washington, DC, and in 1963-64, he was appointed adjunct professor of physiology at the University of Pennsylvania and went to Shiraz, Iran, as a visiting professor. On his return to Columbus, he was awarded The Ohio State University Distinguished Service Medal. After Dr. Hitchcock's retirement, Dr. Edwin P. Hiatt (MD, PhD) was appointed professor and director of the Laboratory of Aviation Physiology (now known as the Laboratory of Environmental Physiology). Dr. Hiatt already had a distinguished career in this field, having served for 14 years at Wright-Patterson Air Force Base, first, as Chief of the Acceleration Section and, later, as Chief of the Biophysics Branch.

Joseph A. Lipsky was appointed assistant professor in 1961, after completing his MS degree in the Department with Earl Carter, MD, who left to join the staff of the Mayo Clinic. Joe Lipsky obtained his PhD in a cooperative program between the Department of Physiology and the Cardio-Pulmonary Laboratory of the Division of Respiratory Diseases, under Joseph F. Tomashefski, MD. He was promoted to associate professor in 1967 and professor in 1977 and continues his research interests in respiration and exercise. Joe Lipsky served as director of the Phase II Medical Curriculum from 1976 to 1981 and was instrumental in strengthening the basic sciences in the medical curriculum.

In 1962, Dr. Eric Ogden, after serving for 13 years as chairman of the Department, resigned to accept the position of chief of the Environmental Biology Division at the Ames Research Center in California. A committee was appointed to search the country for an outstanding physiologist to take over the chairmanship of the department. This search lasted for two years and during this time, Dr. Robert C. Grubbs was appointed acting chairman to look after the administrative responsibilities of the department. Dr. Grubbs was well suited for this position, since he had acted as vice chairman during most of Dr. Ogden's tenure.

Dr. Grubbs made few changes in the department during his brief tenure, but in 1963, he brought Dr. Thomas B. Calhoon back to the Department as an associate professor. Tom Calhoon, a former PhD student of Dr. Angerer's, was an assistant professor at the Medical College of South Carolina. Dr. Calhoon became an outstanding member of the department and in 1966 he received the Alumni Award for Distinguished Teaching. He was promoted to professor in 1967 and, in the same year, he resigned to accept the chairmanship of the Department of Physiology at the University of Louisville.

Expansion in the Sixties

In April 1964, Dr. Robert C. Little was appointed chairman of the department. He, like Dr. Ogden, was a cardiovascular physiologist. Dr. Little completed his MD at Western Reserve University in 1944 and then served as a Captain in the Army Medical Corps (1945– 1947). He was a postdoctoral fellow with Dr. Carl Wiggers in 1947 and continued in this capacity until 1949. After holding a variety of academic and research positions, he was appointed professor of physiology at Seton Hall College of Medicine and Dentistry in 1958 and held this position until coming to Ohio State in 1964.

Under Dr. Little's direction, the Department of Physiology expanded rapidly. The full-time active members of the department with the rank of assistant professor and above rose to 21 as against 16 in 1958 with the following chief additions. Dr. Harold S. Weiss, who originally came to Ohio State as Associate Professor and Research Associate to assist Dr. Hiatt in the Laboratory of Environmental Physiology. He was advanced to the fulltime faculty and raised to the rank of professor in 1967. Dr. Charles W. Smith joined the staff in 1964 as an associate professor and was promoted to professor in 1969. He holds both the masters and PhD degrees from the University of Michigan and was on the teaching staff at the University of Michigan and Seton Hall College of Medicine. His principal interest is in respiratory physiology. Dr. Stephen J. LeBrie, a renal physiologist, was appointed an associate professor in 1966. He holds both the MS and PhD degrees from Princeton University and came to Ohio State from Tulane University School of Medicine. Ten assistant professors joined the department between 1962 and 1969. These are Albert L. Kunz, MD (1962); Lawrence T. Paul, PhD, E. Keith Michal, PhD, and Jim A. Grossie, PhD (1965); Kenneth M. Hanson, PhD (1966); Richard L. Clancy, PhD, and Chester E. Hendrich, PhD (1967); and Marjorie F. Sparkman, PhD (1968). Biographical data on these staff members will be found in the final section of this history.

As has already been pointed out, the Department of Physiology was a University department, although for administrative purposes it is located in the College of Medicine. This meant that all courses in physiology, regardless of the college involved, were taught by the department. (The single exception to this rule is veterinary physiology, which is taught in the College of Veterinary Medicine.) As a result of this arrangement, some 12 separate physiology courses were taught in the Department; about half had little or no connection to the College of Medicine. These included courses for students majoring in physical education, home economics, education, arts and sciences, animal science, and branches of biological sciences other than physiology. Organization of the College of Biological Sciences in July 1966 had a marked effect on the number of courses offered by the Department. According to an agreement with the College of Biological Sciences, the Department of Physiology limited its undergraduate teaching to students in the School of Nursing, School of Allied Medical Professions, College of Optometry, and the College of Pharmacy. As a result of this arrangement, some of the undergraduate courses were taken over by the College of Biological Sciences.

During the years of Dr. Ogden's tenure, as chairman of the department, the teaching of elementary undergraduate courses was rotated among the junior members of the department. This policy gave younger members of the department varied experience in teaching and made it possible for them to keep in touch with the important research developments in the broad field of physiology. On the other hand, professional and graduate courses were taught exclusively by the senior members of the department, who lectured to the students in these courses on their specialities and were responsible only for that portion of the course upon which they had lectured.

When Dr. Little became chairman of the Department in 1964, he undertook a comprehensive study of the undergraduate teaching commitments of the Department and there was a reorganization of the undergraduate program into two levels of instruction. An introductory sequence designed for general college students was offered along with an intermediate level course for professional and other students who had a need for a more intensive course. Senior faculty members were assigned the responsibility for each of these courses on a rotating basis with the help of several junior faculty members. The instruction of professional and graduate students under this regime was carried out by a team of faculty members, with lectures divided so that each individual covered the area of his own special interest. The emphasis was changed to a team effort, where the instructor and the students worked together to collect and interpret physiological data. Demonstration experiments made use of closed-circuit television to give each student a close-up view of the proceedings while the experiment was carried out in the classroom. The graduate students now take the same course as the medical students but are required to do additional laboratory experiments in which the students themselves carry out the experimental procedures with modern electronic equipment.

A six-member graduate committee runs the graduate program and passes on the acceptability of the research and dissertation subjects. Two members of this committee are apointed each year by the chairman of the department and the committee chooses its own chairman. Since 1958, there have been approximately 97 PhD and 113 master's degrees awarded.

The research activities of the department have been extensive and diversified. Almost every aspect of physiological science has been investigated by one or more members of the faculty. For example, during the academic year 1967-68, some 36 separate research projects were under investigation by 20 members of the faculty. The high quality of this research is indicated by the fact that these 36 research projects were supported by 38 grants from various foundations, NIH, and other fund granting organizations. An average of 15 papers a year, based on departmental research, were published in major scientific journals.

During the period 1965-85, major cardiovascular problems being investigated by members of the staff included Dr. Little's studies of stress relaxation and myocardial contraction, Dr. Pieper's investigations with intravascular catheters of myocardial heat production as a measure of cardiac efficiency, as well as Dr. Bozler's research on the physicochemical aspects of cardiac and smooth muscle. Autoregulation of regional blood flow and the effects of hypercapnia on cardiac performance were part of an NIH cooperative project which had the all inclusive title "The Biology of the Heart." This was a joint effort of the Colleges of Medicine and Veterinary Medicine and involved a number of departments including Medicine, Pathology, and Physiology. Work underway included studies on 1) the reaction of heart muscle to injury, 2) biochemical control of energy release in the myocardium, 3) electrical events of the heart, 4) mechanical events of the heart, 5) cardiovascular pharmacology.

Another field in which the Department carried an active research program is that of environmental physiology. Work in this field was started in 1941 when Fred Hitchcock organized the Laboratory of Aviation Physiology with the support of the US Office of Scientific Research and Development. These pioneering investigations in the physiological and pathological effects of rapid decompression, over a period of 10 years, resulted in the publication of some 30 papers. After World War II, the laboratory was supported by contracts with the Office of Naval Research, the Aero-Medical Laboratory, Wright Patterson Air Force Base, and the National Safety Council. The laboratory carried out the first studies of second-to-second changes in O₂ and CO₂ content of expired air, as measured by a specially designed mass spectrometer built in the laboratory under the direction of Dr. Ralph Stacy.

Edwin P. Hiatt joined the faculty in 1960 as a full professor to head the Laboratory of Aviation Physiology and was instrumental in having it renamed the Laboratory of Environmental Physiology. Dr. Hiatt, a PhD from the University of Maryland in 1941, had spent five years at New York University College of Medicine, working with Homer Smith in renal physiology. He completed his MD degree at Duke University in 1951 and served for 15 years as an associate professor of physiology at the University of North Carolina. He was chief of the Acceleration Section and later the Biophysics Branch of the aerospace Medical Laboratory at Wright Patterson Air Force Base in Dayton, Ohio (1957-60). Under his direction, the Laboratory of Environmental Physiology carried out investigations on the effects of prolonged exposure to pure O₂ atmospheres at reduced pressure and the physiological effects of several so-called inert gases as part of artificial capsule environments. Dr. Hiatt took leave from The Ohio State University in 1965–66 to work with the CIA in Washington to evaluate the bioastronautic intelligence that became available as the United States and Russia probed vehicular space travel.

On his return from Washington, Ed Hiatt spent several years in collaboration with Dr. Helmut Engeles of the Engineering Department on a US Department of Highway Safety project of physiological factors involved in severe highway accidents. In 1970, Dr. Hiatt was relieved of his regular teaching duties to represent physiology on the faculty committee designing the first independent study curriculum at The Ohio State College of Medicine. A small separate faculty was assigned to set up and teach the preclinical part of medical education with computer assisted and self-examination programs that they wrote. This was the first such program in the United States and with some modification provides the preclinical education of approximately one-third of each entering medical class. Dr. Hiatt retired in 1977, and he was subsequently elected the Clinton County coroner and practices industrial medicine as a factory physician while carrying on a beef cattle breeding at the Hiatt Farms near Wilmington, Ohio.

Dr. Harold S. Weiss (MS, 1949; PhD, 1950, from Rutgers University) became director of the Environmental Physiology Laboratory in 1965, when Ed Hiatt left for his tour of duty with the CIA. Harold Weiss served as a Captain and meteorologist with the US Air Force in the China-Burma-India Theater during World War II and after his discharge remained in the Reserves until called back to active duty during the Korean conflict. It was during that period (1951-53) that he gained considerable experience in aerospace and environmental physiology. Dr. Weiss was appointed research and development officer of the Biophysics Branch of the Aero-Medical Acceleration Laboratory in Johnsville, Pennsylvania. In 1954, he returned to Rutgers University as an assistant professor and was advanced to associate professor (1957) before joining the staff at Ohio State University in 1962. Harold Weiss became a professor in 1967 with his major research publications in the field of O_2 toxicity and artificial gaseous environments. He was also known as an excellent teacher and graduate student advisor. During the period 1973-1974, Harold Weiss, as director of the Environmental Physiology Laboratory, was instrumental in moving the specialized environmental and altitude equipment from The Ohio State University Research Founcation into the former animal quarters on the fifth floor of Hamilton Hall. The laboratory, with support from NIOSH, EPA, and NASA, continued studies on problems related to the environment including carcinogenesis and inhalation toxicology. Some of the original equipment used by Dr. Hitchcock for his early experiments on explosive decompression are still used in connection with the environmental chambers in the Hamilton Hall laboratories.

Further examples of cooperative research by the Physiology Department were joint efforts with the Departments of Preventive Medicine and Physical Education. When William Ashe, MD, became chairman of the Department of Preventive Medicine in 1954, he obtained a substantial NIH grant for a large-scale study of the physiological effects of vibration. Preventive Medicine did not have adequate research space for the project so an agreement was reached with Dr. Hitchcock to share the OSU Research Foundation space assigned to the Laboratory of Aviation Physiology. This space sharing resulted in many years of close cooperation between the two departments. A similar effort was launched when Donald Mathews, PhD, a student of Peter Karpovitch, professor of physiology, Springfield (Massachusetts) College, was hired in 1959 by the Department of Physical Education to set up a research program in exercise physiology. There was some delay in setting up the Exercise Physiology Laboratory; so Don Mathews spent much of his time helping out in the Laboratory of Environmental Physiology. He developed a close working relationship with the Environmental Physiology Laboratory, which continued for many years, to the benefit of both physiology and physical education.

Albert L. Kunz, an MD from Indiana University (1956), joined the physiology staff in 1962 as an instructor and NIH postdoctoral fellow. He worked closely with Dr. Art Coulter in the cardiovascular program and was awarded an MS degree in 1965. Bob Little, then chairman, appointed him as assistant professor in 1965 and associate professor in 1969. Dr. Kunz became a full professor in 1976. He developed a program in respiratory control physiology which has produced five PhD's and attracted six postdoctoral investigators to date. In 1981, Dr. Kunz, with the aid of the NIH, Fogarty International Center, and the College of Medicine, organized an International Symposium on "The Comparative Physiology of Respiration." The symposium was dedicated to the late Fred Hitchcock as a pioneer in respiratory and aviation physiology and is published in the Journal of Applied Physiology (vol. 53, 1982).

Academic year 1965 saw additional faculty expansion with the appointment of Lawrence T. Paul (MS, 1960 and PhD, 1963 from Ohio State) as assistant professor along with E. Keith Michal (PhD, University of Illinois, 1965) and Jim A. Grossie (PhD, University of Missouri, 1963). Dr. Paul became an associate professor in 1972 and divides his time between the cardiovascular program and teaching the basic physiology courses. Dr. Michal, who was a pilot in the USAF from 1954 to 1959, became an associate professor in 1972 and devotes his efforts to teaching and the Neuro-Respiratory Control Program. Jim A. Grossie became an associate professor in 1971 and developed a program on the effect of endocrines on neuromuscular activity. He also is active in graduate level instruction in both lecture and lab.

Dr. Kenneth M. Hanson was born and educated in Sioux Falls, South Dakota (BS, Sioux Falls, College, 1951). He took a job at the University of Minnesota in the Physiology Department then headed by Dr. Maurice Visscher, who at that time had graduate students such as Frances J. Haddy and Norman Shumway. The University of Minnesota personnel encouraged him to take additional courses in science and math. He then enrolled at the University of Indiana, where he came under the influence of Paul C. Johnson and Sidney Ochs, and became involved in some of the pioneer work on autoregulation of blood flow done by Dr. Johnson. He completed his MS in 1963 and PhD in 1965 at Indiana University Medical Center. He came to Ohio State as an assistant professor in 1966 to set up an independent research program in factors affecting the splanchnic blood flow. His teaching duties involved gastrointestinal physiology, where he expanded the medical lectures and regularly taught a graduate course in GI physiology that generated campus-wide interest. He was promoted to associate professor in 1971 and to professor in 1976 and continues his studies on the physiology and pharmacology of splanchnic blood flow.

Richard L. Clancy, a PhD from the University of Kansas, was appointed an Assistant Professor in 1967. He had been a staff fellow at the NIH Cardiology Branch and actively participated in the cardiovascular program. Dick returned to Kansas after two years, where he continued his work in cardiology, later becoming a professor at The University of Kansas Medical Center.

Chairman Bob Little added Chester F. Hendrich to the staff because of the need for more strength in endocrinology with the retirement of Katharine Brownell-Hartman. He received his PhD from the University of Missouri with postdoctorates at Emory University (1964-65) and Dartmouth (1965-67). He left when Dr. Little assumed the physiology chair at the Medical College of Georgia at Augusta in 1973 and later became a professor at that institution. Marjorie Sparkman, who finished her PhD under Charles Smith, briefly joined the physiology staff in 1968-69 to assist with teaching the basic physiology courses to students from the School of Nursing. She left to organize and teach similar classes at Florida State University.

Gregory R. Nicolosi, after completing his PhD on aortic smooth muscle response with Dr. Pieper in 1971, was appointed as an assistant professor in the department. He served for one year before joining the faculty of the University of South Florida Medical School at Tampa. He continued his cardiovascular research there and later was appointed associate dean of the Medical School.

David H. Noyes, who had his BEE from Rensselaer Polytechnic Institute, Physicum from the University of Heidelberg, Germany, and a PhD (1969) from the University of Alabama, was appointed an assistant professor in 1969 to add strength in the area of biomedical engineering. He has been a biomedical electronics supervisor at the University of Alabama (1962-66) and later (1966-69) a consulting engineer in the design of biomedical instruments at the same institution. He became an associate professor in 1975 and has contributed to studies of human and animal tooth mobility and bioelectrocal activity of epithelial tissue and is an active participant in The Ohio State Spinal Cord Injury Program.

Jean F. Delahayes, who had all his training in France with a Doctor of Science from the University of Paris, was appointed an assistant professor in 1970. He soon showed his expertise as a teacher and collaborated with Emil Bozler on studies of calcium movement in cardiac tissue. He joined the faculty of the Medical College of Georgia when Bob Little assumed the chairmanship and later returned to France.

Heinz Pieper Years

After a nationwide search for a new chairman, Heinz P. Pieper, MD, was appointed in 1973 because of his outstanding contributions as a teacher and his leadership in cardiovascular research. At this time, the physiology staff recognized a weakness in neurophysiology and Dr. Pieper decided to provide at least two new staff positions oriented toward developmental and neurophysiology. This resulted in the appointments of John J. Curry II and Bradford T. Stokes as assistant professors in 1973 and Robert P. Fiorindo as assistant professor in 1974. Dr. Fiorindo had his PhD (1969) from the University of California, Berkeley, and had been an assistant professor at Notre Dame. His principal interests were in endocrinology. He left in 1981 to join the faculty of the College of Osteopathic Medicine of the Pacific, Pomona, California.

John J. Curry (MS, Adelphi University) completed his PhD in 1969 with Paola Timeras at the University of 500 California, Berkeley, and became an instructor, then assistant professor in physiology, at Boston University School of Medicine. His major interests were in gonadotrophins, reproductive behavior, and the developing nervous system. He was advanced to associate professor in 1977 and developed a joint program with obstetrics and gynecology on the mechanisms of pregnancy induced hypertension. Drs. Curry and Stokes developed the first course in neurophysiology at Ohio State and were instrumental in introducing neurophysiology into the medical curriculum.

Brad Stokes, who had served 35 months as a commissioned officer of the US Army in Vietnam, joined the faculty soon after completing his PhD in 1973 at the University of Rochester with Keith E. Bignall. He became an associate professor in 1979 and, in recognition of his research and administrative abilities, professor in 1985. Brad Stokes was associate director of the Independent Study Program from 1975 to 1978 and since 1982 has been director and co-principal investigator of the Spinal Cord Injury Program (funded by the NIH) at Ohio State.

Jack A. Rall, who completed his PhD in physiology in 1972 at the University of Iowa and a two-year postdoctoral with W. F. Mommaerts at UCLA, was appointed an assistant professor in 1974. He brought new techniques for the study of muscle physiology to the department. He cooperated with Emil Bozler (during his retirement years) in muscle research, while developing his own program. He was awarded a five-year NIH career development award (1978-1983) and spent the year 1981-82 in England, as an honorary fellow of the University College London, participating in research on single muscle fibers. Jack Rall became an associate professor in 1979 and professor in 1985 in recognition of his outstanding contributions to the energetics of muscle contraction.

Jean-Pierre L. Dujardin, who completed his PhD in cardiovascular physiology with Dr. Pieper in 1976, was appointed an assistant professor in 1976 and advanced to associate professor in 1982. Jean-Pierre has a unique biomedical engineering background with a Burgerlijk Ingenieur cum laude in electrical engineering from the University of Ghent, Belgium. He later worked at the J. F. and C. Heymans Institute under Professor A. L. Delaunois before coming to Ohio State. Dr. Djuardin's expertise in mathematics and biomedical engineering made him a valuable addition to the cardiovascular research and teaching program of the department.

Jack A. Boulant joined the department as an associate professor in 1977 in order to further strengthen the area of neurophysiology. He has a PhD (1971) from the University of Rochester, where he worked with Keith E. Bignall. There he became friends with Brad Stokes, who was instrumental in bringing him to Ohio State. Jack Boulant had been a NIH predoctoral fellow (1967-71) at the University of Rochester then a postdoctoral fellow (1971-1974) at Yale University, working in environmental physiology at the John B. Pierce Foundation Laboratory in New Haven. There he gained considerable experience and expertise in the use of microelectrodes for the study of temperature regulation in the hypothalamus. Dr. Boulant served as an assistant professor of physiology at the University of South Florida, Tampa (1974-1977), before joining the faculty of Ohio State University in the fall of 1977. At Ohio State, he set up a laboratory for the study of temperature regulation, which has attracted several outstanding students and postdoctural fellows to the neurophysiology program. In recognition of his outstanding work in temperature regulation, he was appointed in 1984 to the Fred A. Hitchcock Endowed Chair as professor of environmental physiology.

The most recent additions to the Department of Physiology are Evangelyn W. Kanabus, Bruce A. Biagi, and George E. Billman. Dr. Kanabus, a PhD in 1977 from the University of California, Los Angeles, joined the staff as an assistant profesor in 1979. Her prime interests are in blood flow and O_2 transport in muscle. She had postdoctoral experience at UCLA and then as a research associate at St. Vincent Charity Hospital in Cleveland. Ohio, where she worked with W. J. Whalen on O₂ measurements in tissue with microelectrodes. Bruce Biagi joined the faculty in 1982 bringing to the department expertise in renal tubule research. After completing his PhD at the University of Rochester in 1974, he took a postdoctoral appointment at Yale University. There he worked with Dr. Gerhard Giebisch (1974-1982) and completed a number of published studies on kidney tubule transport. Dr. Biagi spent the 1981-82 year as a visiting research scientist at the Department of Physiology and Medical Physics at Uppsala University in Sweden before accepting an assistant professorship at

The Ohio State University, where he continues his work on kidney tubule transport. George Billman completed his PhD at the University of Kentucky in 1980 and became a research associate in physiology and biophysics at the University of Oklahoma Health Sciences Center in Oklahoma City. He was appointed an assistant professor of research (1982-1984) and continued his studies on myocardial factors involved in sudden cardiac death with Dr. H. L. Stone and P. J. Schwartz. Dr. Billman joined the Department at The Ohio State University in the summer of 1984 and continues his studies on the mechanisms involved in and the prevention of sudden death.

This history was prepared with the dedicated assistance of Doris Ranft, secretary of the Department of Physiology from 1969 to present.

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Short History of the Election Process

As the members of APS consider changes in the procedure for election of President-Elect and Council, it is useful to look back and recall how the present system has evolved. In 1887 when the Society was founded, the Council was elected by the membership, but the Council, once elected, selected the President and other officers. This lasted until 1904, when the members voted to elect the officers directly. Elections took place at the annual meeting, although members could also cast their vote ahead of time by a proxy mail ballot. In 1914, as part of a series of major Constitutional changes, rotating terms for Council members were instituted and the ballot by proxy was eliminated. From 1914 through 1975, the entire election process from nomination to final election took place by secret ballots at the business meetings. The procedure was long and cumbersome, frequently requiring several ballots to narrow down the range of candidates, and usually taking up a large portion of the business meetings. On several occasions, attempts were made to change the system, especially the method of nomination, but nothing was done. It was generally felt that the members who attended the business meeting were those who held a real stake in the Society and that they should therefore elect the officers and Council. Nominating committees were repeatedly rejected because it was thought that they might lead to rule by a clique.

In 1970 Robert Berne conducted a mail survey of the membership on the matter of the Society's election procedures. The vote was heavily in favor of election by mail. But instituting a mail ballot required a change in the Bylaws and that change had to be approved by the members present at a business meeting. It took five years to get a change in the Bylaws passed. The only acceptable form of mail balloting was found to be one that duplicated as closely as possible the successive balloting that took place at the business meetings. Therefore, separate nominating and election ballots were required, as well as a system that would enable members to rankorder the candidates. Such a system seemed to be more democratic than a simpler system because it allowed for a fuller expression of opinion. When the mail ballot began in 1976, the top ten candidates nominated for President and for Councillor were placed on the election ballot. It was soon found that a great many ballots had to be discarded because they were improperly cast. The present system, in which the election ballots contain four candidates for President-Elect and eight for Councillor(s), resulted from a Bylaw change in 1981.

O. E. Reynolds

America	an Physiological Society.
Members desi	ring to vote by proxy are requested to return
the attached ballot,	, properly prepared and enclosed in a signed
envelope, to the Sec	retary, 25th and E Streets, N. W., Washington,
D. C.	
The member	s of the existing Council are:
Presi	ident-WILLIAM H. HOWELL
Secre	atary-REID HUNT
Treas	surer—WALTER B. CANNON
Addi	tional Members-
	GRAHAM LUSK
	DI ALLA LO
Americ	an Physiological Society.
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CURRENT APPLICATION FORMS

Most issues of <u>The Physiologist</u> routinely carry one copy of the current application form (following). This form will serve for all categories of membership. Any member desiring to sponsor more than one applicant may use a Xerox copy of this form. Any application submitted on an out-dated form will be redone on the acceptable form.

One application form serves all membership categories. There are, however, specific sets of instructions for each category. Therefore it is essential that sponsors and applicants carefully attend to those instructions specific to their desired category.

GENERAL INSTRUCTIONS

FOR ALL CATEGORIES:

Use only the current application form. Check the box indicating the category of membership for which you are applying. Use the <u>SPECIAL INSTRUCTIONS</u> for that category when filling out the form. Type the Application. Fill out all applicable spaces. Only completed applications will be reviewed.

Alien Residents. Alien residents of the U.S. must enter the Alien Registration Receipt Card number under the address block on the application. Canadian residents should furnish a copy of "Landed Immigrant Status" form. Mexican residents should furnish a copy of their form FM-2.

<u>The Bibliography</u> must be submitted in the form found in the Society's journals. An example of the current form is:

JONES, A. B., and C. D. Smith. Effect of organic ions on the neuromuscular junction in the frog. Am. J. Physiol. 220:110-115, 1974.

DO NOT INCLUDE A CURRICULUM VITAE

Send no reprints.

<u>Deadline Dates</u>: Completed applications received between February 1 and July 1 are considered for nomination by the Council at the Fall Meeting. Applications received between July 1 and February 1 are considered for nomination by the Council at the Spring Meeting. Applications are not complete until all materials, including sponsor's letters, are received.

QUALIFICATIONS (Except Students):

The Membership Advisory Committee uses the following five categories in evaluating an application:

- 1. <u>Educational History</u>. Academic degree and postdoctoral training are evaluated and assessed with regard to how closely the applicant's training has been tied to physiology.
- 2. Occupational History. Particular emphasis is given to those applicants who have a full time position in a department of physiology, or are responsible for physiology in another department. Relatively high ratings are given to people with positions in clinical departments and to people functioning as independent investigators in commercial or government laboratories.

- 3. Contributions to the Physiological Literature. This category is of major importance. The applicant's bibliography is evaluated on the basis of publications in major, refereed journals which are concerned with problems judged to be primarily physiological in nature. Emphasis is given to papers published as the result of independent research. Special note is taken of publications on which the applicant is sole author or first author.
- Interest in and Commitment to Teaching Physiology. This evaluation is based on: (1) the fraction of the applicant's time devoted to teaching, (2) publications related to activities as a teacher including production of educational materials, and (3) special awards or other recognition the applicant has received for outstanding teaching effectiveness.
- 5. <u>Special Considerations</u>. This category permits the Membership Advisory Committee to acknowledge unique accomplishments of an applicant. These might be excellence in a specific area, or unusual contributions to Physiology resulting from talents, interest or a background substantially different from the average.

In general, persons who qualify for regular membership will have a doctoral degree in physiology or related area and will have published several papers in refereed journals. It should be clear that they have played a major role in some of this research. They should have a position in physiological research, teaching, administration or related area, other than a training position (Council, April 1984).

In general, applicants will be considered for associate membership if they have an advanced degree in physiology or related area and are doing research and/or teaching of physiology (Council, April 1984).

In April 1984, Council adopted: "any student who is actively engaged in physiological work which should lead to an advanced degree in physiology or related area, as attested by two regular members of the Society and who is a resident of North America, can qualify as a student member. No individual may remain in this category for more than five years, without reapplying."

SPONSORS:

Primary responsibility for membership rests with the two sponsors who must be regular members of the Society. Sponsors should discuss the appropriateness of the selected category of membership in this Society with prospective applicants.

Each sponsor should write an independent confidential letter about the candidate using the five categories listed above to evaluate the candidate. Furnish an original and seven copies to the Membership Secretary.

CHECK LIST:

- 1. Original copy of application signed by both sponsors.
- 2. Application on a current form, including the bibliography (1 original and 7 copies).
- 3. Mail the original, which has been signed by the two sponsors, plus 7 copies to:

Membership Secretary American Physiological Society 9650 Rockville Pike Bethesda, Maryland 20814

SPECIAL INFORMATION AND INSTRUCTIONS

FOR REGULAR MEMBERSHIP

Bylaws of the Society:

Article III, Section 2 - Regular Members. Any person who has conducted and published meritorious original research in physiology and who is a resident of North America shall be eligible for proposal for regular membership in the Society.

Duties and Privileges:

- 1. Hold Elective Office.
- 2. Vote at Society Meetings.
- 3. Serve on Committees, Boards and task forces.
- 4. Serve on Federation Boards and Committees.
- 5. Sponsor New Members.
- Can present orally <u>only one</u> contributed paper, but, may coauthor and/or sponsor <u>more than one</u> contributed paper by a non-member at the Spring (FASEB) and the Fall Meetings of the Society.
- 7. Receive The Physiologist.
- 8. Receive Federation Proceedings, Public Affairs Newsletters and annual Membership Directory.
- 9. Subscribe to handbooks and periodicals published by the Society at membership rates.
- 10. Register to attend scientific meetings of the Federation and the APS Fall meeting at membership rates.
- 11. Participate in FASEB Member's Life Insurance Program, Disability Program and in Hospital Protection Plan. (For Residents of the United States, its territories or possessions).
- 12. Eligible to receive the Daggs Award.
- Eligible to be selected as Bowditch Lecturer (Members under 40 years of age).

FOR CORRESPONDING MEMBERSHIP

Bylaws of the Society:

Article III, Section 3 - Corresponding Members. Any person who has conducted and published meritorious research in physiology, who is presently engaged in physiological work and who resides outside of North America shall be eligible for proposal for corresponding membership in the Society.

Duties and Privileges:

- 1. Serve on Society Committees, Boards and Task Forces.
- 2. Serve as one sponsor of new Corresponding Members (One regular member must be the other sponsor of a new Corresponding Member).
- Can present orally <u>only one</u> contributed paper, but, may coauthor and/or sponsor <u>more than one</u> contributed paper by a non-member at the Spring (FASEB) and the Fall Meetings of the Society.

- 4. Receive The Physiologist.
- 5. Receive Federation Proceedings, and annual Membership Directory.
- 6. Subscribe to handbooks and periodicals published by the Society at membership rates.
- 7. Register to attend scientific meetings of the Federation and the APS Fall meeting at membership rates.

FOR ASSOCIATE MEMBERSHIP

Bylaws of the Society:

Article III, Section 5 - Associate Members. Persons who are engaged in research in physiology or related fields and/or teaching physiology shall be eligible for proposal for associate membership in the Society provided they are residents of North America. Associate members may later be proposed for regular membership.

Duties and Privileges:

Same as for Regular Members except for the privileges of:

- 1. Holding Executive Office, or membership on certain committees.
- 2. Voting at Society Meetings.
- 3. Sponsoring New Members.
- 4. Eligibility for receiving the Daggs Award.
- 5. Privilege of selection as Bowditch Lecturer.
- 6. May sponsor only those abstracts on which they are listed as first author or co-author.

FOR STUDENT MEMBERSHIP

Not all questions on the application form may be appropriate – Please place NA next to any such questions.

Bylaws of the Society:

Article III, Section 7 - Student Members. Any student who is actively engaged in physiological work as attested by two regular members of the Society and who is a resident of North America. No individual may remain in this category for more than five years, without reapplying.

Duties and Privileges:

- 1. Present one contributed paper at the Spring (FASEB) and the Fall scientific meeting with the endorsement of the student's advisor.
- 2. Receive The Physiologist.
- 3. Subscribe to handbooks and periodicals at member rates.
- 4. Register to attend scientific meetings of the Federation and the APS Fall meeting at student rates.

Submit original	and 7 copies of	applicatio	n and supporting	documents.	
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Pathophysiology of Temperature Regulation

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The human body is equipped with a sensory system capable of detecting whether body temperature has risen or fallen. Information from temperature receptors, which are distributed widely in many tissues, is transmitted to the hypothalamus, where autonomic responses are coordinated, and to the cerebral cortex, where behavioral responses are coordinated. When body temperature tends to rise, the typical responses are seeking a cooler environment, shedding clothes, peripheral vasodilatation, and sweating; these responses reduce heat load or enhance heat loss. Conversely, when body temperature tends to fall, the typical responses are seeking warmth, putting on more clothing, peripheral vasoconstriction, and shivering, all responses that reduce heat loss or increase internal heat generation. In either case the responses act to prevent or reverse the temperature changes that initiate them; the system operates as a negative-feedback control mechanism. Detailed accounts of the physiology of normal human thermoregulation may be found in general textbooks of physiology (14) or in specialist books on thermal physiology (7, 51, 85, 97, 109).

The outcome of normal thermoregulatory function is that, over a wide range of ambient temperatures, body core temperature is controlled at a relatively stable level: early morning rectal temperature is generally within 0.5° C of 37° C. There is a circadian rhythm, such that rectal temperature tends to be $0.5-1^{\circ}$ C higher in the evening than in the early morning (24). The ambient temperature range over which normal body temperature is achieved with minimal activation of metabolic and evaporative processes is called the thermoneutral zone. For a naked adult this zone is between 27 and 33° C approximately.

There are circumstances in which body temperature deviates from its usual stable level. Some of these deviations are physiologically normal; others reflect pathophysiology. In this review we plan to discuss normal and pathophysiological deviations of body temperature. The review is intended primarily as a resource for teachers of medical students.

Deviations of body temperature may take three forms. Heat gain can exceed heat loss despite the compensatory reactions and body temperature will rise: hyperthermia occurs. Heat loss can exceed heat gain and body temperature will fall: hypothermia occurs. Finally, the control mechanisms may break down and temperature will rise or fall according to whether the balance of metabolic heat production and heat transfer with the environment constitutes a net heat gain or loss: the body temperature is abnormally labile. If the rectal temperature rises above 40° C or falls lower than 35°C, there is increasing malfunction and risk of tissue damage and ultimately death.

Before discussing particular examples of hyperthermia, hypothermia, and abnormal lability, we need to consider how body temperature should be measured. We also need to describe how temperature regulation differs in the very young and very old from that of the adult and to draw attention to the situation in which temperature deviates from its normal level in the absence of any pathology.

Measurement of Body Temperature

Many doctors have a blind faith in clinical thermometry. How sure can one be that clinical thermometers indicate temperature correctly? We have come across clinical thermometers available through retail outlets that are in error by more than 1°C. Unless the manufacturer has an impeccable reputation, all clinical thermometers for hospital use should be calibrated on purchase.

Assuming that the thermometer reads correctly, what physiological information can it convey? If one were to seek a single representative body temperature, then the best would be the temperature of mixed venous blood; it would reflect the general thermal status of the body tissues. Since very little heat transfer takes place in the human lung, arterial blood temperature will be close to mixed venous blood temperature. The best approximation to blood temperature is the esophageal temperature at the level of the heart (9, 20). Only the most heroic of conscious patients will tolerate the nasoesophageal catheter necessary to monitor esophageal temperature, but in anesthetized or comatose patients it is the best temperature to measure (19).

The next best temperature is rectal temperature, which is usually a few tenths of a degree higher than arterial blood temperature (75). Since the temperature varies a few tenths of a degree with position in the rectum, it is important that the thermometer always should be inserted to the same depth. Vaginal temperature is virtually identical to rectal temperature (1). Rectal temperatures should always be employed in neonates and infants (carefully, so as not to puncture the rectum), and in adults if there is any suspicion of heat-induced disease, hypothermia, or factitious fever (see below).

Oral temperature is a poor reflection of blood temperature (113). Its widespread use results entirely from the convenience of the mouth as a body orifice. Oral temperature cannot be measured in patients who are vomiting or unconscious. It is very dependent on the breathing pattern and on ambient temperature. Its relationship with other body temperatures is variable, but it tends to be $0.5-1.5^{\circ}$ C below the prevailing rectal temperature. It is a credit to clinicians, who use oral temperature almost exclusively, that they can make good diagnostic and therapeutic decisions on the basis of such poor information.

Other body sites, for example, the external auditory meatus and the axilla, have been used for measuring body temperature. There is little evidence that they are physiologically appropriate or clinically useful (75). Skin temperature does not reflect the prevailing blood temperature: it can be anywhere between the environmental wet-bulb temperature¹ and the blood temperature, depending on the state of dilatation of the peripheral vasculature. When the vasculature is maximally dilated, skin temperature in the area approaches body core temperature; when vessels are maximally constricted skin temperature approaches that of ambient air. A comfortable mean body surface temperature for adults is $\sim 33^{\circ}$ C (61). The laying of a hand on the forehead may well be a useful therapeutic procedure, but it is no substitute for thermometry.

If a clinical thermometer is used to measure body temperature, whatever the site, it must be used correctly. A common fault is to leave the thermometer in position for too short a time. Even though clinical thermometers often are marked as 0.5 min instruments, they need 3 min to stabilize properly. The standard clinical thermometer reads from 35 to 42°C; it is therefore useless for a patient with profound hypothermia. Low-reading clinical thermometers are available but every emergency room and/or casualty department should now have a portable electronic thermocouple or thermistor thermometer.

Normal Deviations from Normal Body Temperature

Exercise

The metabolic heat load resulting from strenuous exercise is far greater than the heat load imposed by any environmental heat stress. At rest, a 70-kg man will generate heat at an average rate of 100 W over several hours. During short bouts of heavy exercise he can generate heat at a rate of 1,000 W and a champion athlete at more than 1,500 W, which is about the same as a domestic heater.

Muscle temperature rises rapidly over the first few minutes after the onset of steady exercise and can soon exceed 40°C (100). Heat from the muscles is picked up by the blood, and blood temperature consequently rises too. The rise in temperature initiates autonomic heat loss mechanisms (peripheral vasodilatation and sweating) that dissipate the heat to the environment. Over a wide range of environmental temperatures, the body temperature elevation depends mainly on the intensity of the exercise (74); the rectal temperature stabilizes at an elevated level at which the heat loss mechanisms are activated sufficiently to balance the metabolic heat load. At the end of a game, rugby players commonly have rectal temperatures above 39°C (16) and temperatures of 42 or 43°C have been recorded in runners finishing a marathon or shorter distance events (117). Body temperature remains elevated for many hours after the end of the exercise (123).

In environments in which the wet-bulb temperature is above $\sim 25^{\circ}$ C, the equilibrium rectal temperature no longer depends on exercise intensity alone but rises with increasing environmental heat stress. If strenuous exercise is attempted at high wet-bulb temperatures, the body temperature may not reach equilibrium at all.

Man is perhaps the only large terrestrial vertebrate capable of exercising for more than a few hours, an attribute derived from the very high capacity to produce sweat (44). Evaporation of sweat is by far the most powerful autonomic heat loss mechanism: evaporating 1 g/min dissipates about 40 W; so evaporating 2.5 g/min dissipates the entire resting metabolic heat production. However, sweating dehydrates the body, and during strenuous exercise the water loss can exceed 2 l/h (79). Dehydration severely compromises body function and, among other effects, results in a further elevation of body temperature. Acclimatization to heat improves sweating capacity and cardiovascular function and reduces the body temperature rise that occurs during exercise (79, 103, 124).

Sleep

During sleep the metabolic heat generation is only slightly less than it is in an awake resting person (8), and in most sleep stages thermoregulation proceeds normally (47). However, evidence is accumulating that during rapid-eye-movement (REM) sleep, thermoregulation, along with other functions controlled by the hypothalamus, loses precision and may even cease. Sweating has been reported to decline markedly during the REM stage of sleep in a warm environment (50, 104).

The Menstrual Cycle

About 80% of ovulating women have a biphasic cycle of body core temperature related to the menstrual cycle. The early-morning resting core temperature rises $\sim 0.5^{\circ}$ C on a day near that of ovulation. However, there is no rigorous coincidence between the body temperature rise and changes in any of the hormones associated with the menstrual cycle (82). Considering this lack of coincidence, the problems of measuring temperature properly, and the other factors that influence temperature, attempting to predict the day of ovulation from temperature recordings is not reliable (54, 72, 81). It is not even possible to distinguish consistently an ovulatory from a nonovulatory cycle on the basis of body temperature measurements (81).

The Very Young and the Very Old

The Very Young

The fetus has a very efficient heat exchanger in the placenta and can rely totally on the mother for thermoregulation. Fetal body temperature is generally $\sim 0.6^{\circ}$ C above maternal body temperature. Birth precipitates the baby into a harshly cold environment. The newborn baby does not thermoregulate as well as the adult, and the social rituals surrounding birth and infant care often place a thermoregulatory stress on the baby unnecessarily.

Since the ability to generate heat depends on body mass and heat loss to the environment on the surface area, neonates, who have a surface area-to-mass ratio about 3 times higher than that of adults (13, 57), have difficulty thermoregulating in cold environments, simply by virtue of their size. Low-mass babies are

¹ Wet-bulb temperature, the temperature indicated by a ventilated thermometer with a film of evaporating water, depends on air temperature and humidity. A saturated environment with a temperature of 25°C has a wet-bulb temperature of 25°C; so does an environment in which the air temperature is 39°C and the relative humidity 30% (5).

particularly susceptible. Although full-term babies are born with control over the peripheral vasculature equal to that of an adult, their autonomic thermoregulatory responses are not fully developed (53). Healthy babies can increase their basal heat production ($\sim 1.5-2$ W/kg) ~ 2.5 times, in response to cold, within 1 or 2 days of birth, though less so on the first day. They rarely shiver (76): the increased heat derives from the noradrenergic lipolysis of the brown fat deposits characteristic of the neonate, and activation of specially adapted mitochondria in the brown fat to produce heat (43, 84, 88). The sweating capacity, per unit skin area, of neonates is less than that of adults, possibly because the cholinergic receptors on the sweat glands are immature. Sweating on the first few days of life is localized mainly to the skin of the head (98). Such sweat mechanisms that are active develop late in gestation, so that babies born 3 wk before term sweat very little and those born more than 8 wk before term not at all (53).

When the baby is born, evaporation of amniotic fluid and water from superficial skin layers exacerbates the heat loss, and body core temperature falls rapidly, by $2-3^{\circ}$ C in the usual delivery room conditions (84). Swabbing or washing the baby after birth increases the temperature drop and has no known physiological advantages (107). Indeed, the appropriate action is to prevent evaporation by drying and wrapping the baby in warm blankets.

If the thermal environment of the delivery room is comfortable for the mother and medical staff, it is much too cold for the new arrival, who should be removed as soon as possible, now that social sophistication seems to have abolished the practices of swaddling, cuddling, and sleeping with the baby (98). Keeping a baby in the delivery room but under radiant heaters is fraught with danger (12, 13, 107). If the baby is kept warmly wrapped, the desirable ambient temperature in the nursery should be $\sim 25-27^{\circ}$ C (probably too high for the nurse). The minimum safe environmental temperature is $\sim 21^{\circ}$ C (53). Higher ambient temperatures are required for lowbirth-weight babies and for those with low caloric intake (11, 39).

Premature babies, or full-term babies who are unhealthy at birth, have a high mortality unless maintained in an incubator. If the baby is kept virtually naked, the incubator will need to be high (32–35°C). Heat transfer from the baby in the incubator depends on much more than air temperature; it is particularly hazardous to place incubators with plastic tops near open windows, air conditioners, or phototherapy lamps, because of the uncontrolled radiant heat transfer (53). Indeed, how to control the environment in an incubator is a problem far from resolved.

Mortality rises in small babies if they are kept in an environment as little as 1° C below their neutral temperature (53). Hypothermia in babies tends to result in metabolic acidosis, hypoglycemia, and increased risk of kernicterus (29, 94). Many babies whose body temperatures fall below $27-32^{\circ}$ C will not survive (110).

The most usual thermal hazard facing a newborn baby is that of hypothermia. In hot conditions hyperthermia can also occur and in extreme conditions is a common cause of death in neonates in the first 24 h after birth (10). Probably because of their immature sweating, neonates cannot endure temperatures higher than their body temperature. There has been a report of fatal heatstroke in a 4-mo-old baby in temperate England, simply because too many blankets (eight) were applied (41).

The Very Old

Thermoregulatory competence declines with age, and particularly after the age of 70. Both autonomic and behavioral responses are impaired. Whereas young adults will detect a change in air temperature of the order of 1°C, old people can detect a rise or fall of temperature only if it exceeds $\sim 2.5^{\circ}$ C (98). Thus old people are less able to detect that they are under thermal stress and consequently do not take appropriate compensatory actions. In a study of old people in the United Kingdom, about one-fourth of the people investigated lived in dwellings considered cold by younger people and had oral temperatures of <35.5°C (36). Nevertheless, many of these old people did not report that they felt cold. Experiments have shown that the preferred ambient temperature of 75 yr olds is actually the same as that of 27 yr olds, but the old people show less inclination to alter environments (17).

In addition to the impairment of thermoregulatory behavior, old people have a reduced ability to vasoconstrict, and hence to conserve heat, have reduced metabolic rate, and probably also have reduced shivering (91). Sweating also declines with age; the number of active glands does not decline, but the sweat output per gland is reduced (98).

The consequence of the impaired thermoregulation is that cold winters and summer heat waves take an enormous toll in the elderly, not only as a direct consequence of hypothermia and hyperthermia but also because their inability to thermoregulate properly is associated with increased mortality from respiratory tract infections, ischemic heart disease, and cerebrovascular disease, to which old people are prone (10, 33, 73).

Abnormal Lability of Thermoregulation

Hypothalamic Malfunction

The anterior/preoptic area of the hypothalamus is the principal site of integration of efferent activity responsible for the autonomic responses that compensate for both rises and falls in body temperature. One expects that hypothalamic lesions would result in excessive lability of temperature in both heat and cold stress, and indeed this is the case (35). Since in most natural environments heat loss tends to exceed generation in resting people, the lability usually presents as hypothermia.

Hypothalamic lesions are fortunately rare, and when they occur they usually result in widespread physiological malfunction of which inability to thermoregulate properly is a relatively minor part.

The Surgical Patient

The surgeon sees more aberrations of temperature regulation then any other medical practitioner (99). The principal aberration arises from the fact that all known general anesthetics inactivate the thermoregulatory system; man becomes poikilothermic under general anesthesia. Spinal anesthesia also disrupts thermoregulation, probably by interrupting afferent fiber activity from thermoreceptors. As was the case with hypothalamic malfunction, body temperature under anesthesia may rise or fall. Operating rooms are generally kept at a

temperature such that the patient tends to lose heat (otherwise they would be unbearably hot for the surgical team), so that unless proper precautions are taken, hypothermia is a risk of anesthesia, even when the room temperature is as high as 29°C (22, 28). The tendency to hypothermia is exacerbated by neuromuscular blockers. which inhibit shivering, by those inhalation anesthetics that increase peripheral blood flow, and by surgical procedures such as laparotomies, which expose a large internal surface area from which water evaporates (45). The hypothermia compromises the patient by reducing liver function, tending to precipitate cardiac arrhythmias, and tending to depress respiration, thus causing respiratory acidosis. Moreover, hypothermia enhances the anesthesia, so the patient tends to become too deeply anesthetized.

In the postoperative period, as thermoregulation recovers, there is often violent shivering, which increases the O_2 consumption up to 500% and also increases cardiac work (92). Care must be exercised in artificially rewarming postoperative patients, because peripheral vasodilation in a patient who has lost blood precipitates hypotension.

Although hypothermia is more common, hyperthermia resulting from heat stress can occur during anesthesia, particularly if high doses of atropine are used for premedication and nonpermeable drapes are employed, both of which block sweating (37). Hyperthermia can also result from the overzealous use of heating pads to prevent hypothermia (46). Very rarely, malignant hyperthermia can occur, a completely different thermal aberration (see below).

Apart from the aberrations resulting from anesthesia, the surgical patient is at risk of suffering other thermoregulatory pathophysiology. Postoperative fevers are common (96). Some result from sepsis or atelectasis, but others have no detectable origin. Hyperthermia often follows blood transfusions, even when the donor blood is properly matched and sterile (99).

The abnormal lability of body temperature under anesthesia is used with advantage in deep hypothermia surgery. Deliberately lowering body temperature to $\sim 20^{\circ}$ C depresses tissue energy demand profoundly and so facilitates cardiac surgery and neurosurgery (114).

Drug-Induced Lability

Many drugs (in addition to anesthetics) impair thermoregulatory function and so induce abnormal lability of body temperature. Two examples are chlorpromazine and alcohol, and in both cases temperature may rise or fall (87). Alcohol causes increased heat loss, impaired perception of thermal comfort, and depressed blood glucose levels even in moderate doses (42) and is a frequent prediposing factor in accidental hypothermia (see below).

Paraplegia

Thermoregulation, both behavioral and autonomic, is severely compromised in paraplegic and quadriplegic patients (25, 26). The thermosensory pathways are disrupted and so are the motor pathways responsible for shivering. In the case of high spinal lesions, the sympathetic pathways responsible for vasoconstriction and sweating also may not function. Responsibility for the thermoregulation of the whole body has to be assumed by the residual sentient area above the lesion.

Hyperthermia

Fever vs. Hyperthermia

Many clinicians bestow the title of fever on any rise in body temperature. There is a fundamental physiological difference between fever and other hyperthermias. Failure to appreciate the difference can result in mismanagement of fever or other hyperthermias, or both (111). In all hyperthermias body core temperature rises. Only in fever, however, is there no tendency for compensatory mechanisms to attempt to restore body temperature to a normal level. Indeed, body temperature is actively defended at the febrile level; exposure of a febrile patient to a cold environment will excite vasoconstriction and shivering even though body temperature is elevated. Moreover, the febrile patient consciously prefers a high body temperature and so feels cold when exposed to a cold environment, even though the thermometer shows him clearly to be hot.

Physical cooling is an appropriate therapy in other hyperthermias, but during fever cooling will be resisted physiologically and will distress the patient (75, 111).

Heat-Induced Disease

The International Classification of Diseases (106) recognizes several heat-induced diseases. With hindsight, the classification lacks a rational basis and needs to be reviewed. Some of the conditions listed may not exist, and the distinction between others is obscure.

One of the listed conditions that may not exist is heat cramp (N 992.2) (68, 106). The etiology of muscle cramps is still unknown, but cramp is likely to be related to microcirculatory failure (63); if so, heat-induced dehydration may be a predisposing factor. Although salt ingestion seems to relieve cramp (63), there is little evidence that cramp results from salt deficit. Deliberate attempts to induce cramps in volunteers on salt-free diets, exposed to exercise in the heat, have failed (108). Also, clinical conditions that cause hyponatremia seldom elicit muscle cramp (68). In any event, heat exposure tends to produce hypernatremia rather than hyponatremia, because sweat is hypotonic with respect to plasma. Finally, most diets provide salt far in excess of physiological requirements (112); therefore salt replacement during acute heat exposure is seldom, if ever, necessary, and salt tablets are always contraindicated (3).

Heat exhaustion (N 992.3, 4, 5) is generally taken to be a condition in which dehydration results in an inability to tolerate a hot environment, and collapse from heat exhaustion can then occur without appreciable hyperthermia. Heat syncope (N 992.1) is a mild condition in which reduced peripheral resistance in skin and muscle causes transient hypotension. The term sunstroke used to be used synonymously with heatstroke (N 922.0) because it was thought that heatstroke was caused only by the sun, but the term should be avoided. Lethal sunburn is a disorder of metabolism caused by the release of kinins and other toxins from the skin (83) and is quite distinct from heatstroke.

Serious heat-induced disease occurs typically in military operations, in sports events, in hot industries, and in situations that cause physiologically inappropriate behavior-hundreds die during the annual pilgrimage to Mecca (65). The victims are often highly motivated healthy young people. The noxious agent is the heat itself, and the heat can arise from the environment or from metabolic heat production, or both. The risk of heatstroke is highest during exercise in a hot environment or in circumstances in which heat loss to the environment is obstructed, for example, by impermeable clothing (117).

Obesity, old age, lack of acclimatization, fever, lack of sleep, and particularly dehydration increase the risk of heat-induced disease. Several drugs also do so. Examples are anticholinergics, monoamine oxidase inhibitors, and other drugs that affect sympathetic nervous system activity, or drugs such as alcohol and antidepressants that interfere with central nervous system function (75). Patients who have recovered from extensive skin burns and whose skin is irreparably damaged also show a predisposition to hyperthermia because their capacity to sweat is severely decreased (49, 105).

The most severe form of heat-induced disease is heatstroke in which body temperature rises so high that tissue is seriously damaged. How high the temperature needs to be for such damage to occur is unknown, but the risk of heatstroke increases precipitously when rectal temperature exceeds 40°C, and temperatures of 43°C disrupt brain and liver function. The severity of tissue damage, and hence the mortality, depends on the duration as well as the level of hyperthermia.

The thermal damage to tissues affects many organs. The central nervous system is affected early, and abnormal behavior, often dismissed as malingering or insolence, is often the only warning of an incipient crisis. Coma, tremor, and incontinence are common, though not invariable, signs of heatstroke. There are disruptions of hemostasis resulting in disseminated intravascular coagulation, renal damage resulting in proteinuria and hematuria, gastrointestinal malfunction, liver failure, and spasm. Minor myocardial injury occurs but heart failure is rare. The acid-base status of patients with heatstroke is one of profound metabolic acidosis (66). One would expect the patients to hyperventilate: indeed this is the case, and in addition the temperature rise itself causes hyperventilation. One also would expect hyperkalemia caused by widespread necrosis. Earlier in the episode, however, patients may exhibit hypokalemia despite the acidosis, and it is thought that potassium is withheld in cells or is lost via the gut (106).

The onset of heatstroke is sudden and the mortality high. Diagnosis is not easy. Whenever a patient who may have been exposed to heat or exercise presents with central nervous system disturbances of any form, rectal temperatures should be measured. However, the temperature may have fallen by the time the measurement is made. A hot dry skin, resulting from failure of the sweat glands, was once considered an essential feature of heatstroke, but there are now many reported cases of heatstroke in patients who continued to sweat profusely (106). Serum transaminase and lactate dehydrogenase concentrations are always massively raised within 24 h of the onset of heatstroke, and measurements of those enzyme concentrations is obligatory in suspected heatstroke (62).

The successful treatment of heatstroke depends on early recognition and the immediate application of body cooling. Figure 1 shows the pamphlet issued to all supervisors as part of the anti-heatstroke campaign in the South African gold mines, a campaign that has reduced heatstroke morbidity and mortality significantly (122). Note that cooling should be instituted at the site of the

HEAT STROKE

SYMPTOMS

One or more of the following symptoms may be exhibited:

- Skin always very hot to the touch, mostly dry but often still wet from sweating. Body temperature invariably excessively high.
- Quarrelsomeness, aggressiveness, hysterical running about the patient may act as if he is insane.
- Spasms of the limb muscles like shivering this may be mistaken for a "fit".
- Vacant staring of the eyes the pupils are dilated.
 Loss of control over bladder and bowels.
- Collapse and unconsciousness.

TREATMENT

- Start treatment immediately and send for a trained person.
- Remove all the patient's clothing and let him lie down.
- Keep his naked body wet by splashing water onto him by hand and gently spreading it over his skin. Do not spray water directly onto him from a hose.
- Blow compressed air over him from a distance of one metre. Temporarily stop splashing water onto him when goose pimples are noticed.
- Give small amounts of water to drink occasionally if the patient is conscious.
- Apply artificial respiration if breathing fails.
- Continue cooling until trained help arrives or until two hours have elapsed.
- After two hours of cooling place the patient on a stretcher, cover lightly with a blanket and remove him to hospital.

This method whereby the water is splashed and spread over the skin by hand, rather than being sprayed on by hosepipe, is applicable regardless of the temperature of the water. The colder the water, the smaller the quantity of water that should be used. Ice blocks may only be used under medical supervision.

It must be emphasised that the purpose of using water is to keep the skin wet, so that the man is cooled by evaporation with the aid of the compressed air. **REMEMBER** — WHEN IN DOUBT TREAT AS FOR HEAT

REMEMBER — WHEN IN DOUBT TREAT AS FOR HEAT STROKE, I.E. PROMPTLY COOL THE PATIENT WITH WATER AND COMPRESSED AIR.

Figure 1

Guidelines for treatment and identification of heatstroke, issued by the Mine Safety Division, Chamber of Mines of South Africa.

incident and should continue until the rectal temperature has fallen to safe levels ($<38.5^{\circ}$ C), which may take up to 2 h. Ice baths are contraindicated unless the patient is comatose or anesthetized and vasodilatation can be maintained pharmacologically in the face of skin cooling (125). Where suitable facilities are available, more aggressive cooling, for example by peritoneal dialysis, can be undertaken. Sophisticated water sprays have been installed to treat heatstroke victims during the annual pilgrimage to Mecca (65).

Drug-Induced Hyperthermia

Drugs that induce hyperthermia can act either by obstructing the normal heat loss pathways (64) or by inducing excess metabolic heat generation. Atropine, which blocks the cholinergic innervation of sweat glands, falls into the first category. There are several kinds of drugs that will increase metabolic rate. In the case of monoamine oxidase inhibitors, the drugs act by exciting inappropriate muscle contraction centrally, and they also cause peripheral vasoconstriction (119). The mechanism of action of some other drugs, like aspirin in large doses, is unknown.

A serious, though fortunately rare, form of druginduced hyperthermia is malignant hyperthermia, in which a genetic defect predisposes to catastrophic hyperthermia surgical patients given succinylcholine and/or gaseous anesthetics, particularly halothane. The incidence of malignant hyperthermia is $\sim 1:20,000$ anesthetics, and the underlying pathophysiology is similar to that which prevails in porcine stress syndrome in pigs and capture myopathy in wild animals (80). Within a few minutes of induction of halothane anesthesia, susceptible patients show tachycardia, hyperventilation, peripheral vasoconstriction, and widespread muscle rigidity. Body core temperature rises at $\sim 1^{\circ}$ C/min, gross lactacidosis and hyperkalemia ensue, and the episode is usually fatal. An alert anesthetist sometimes can save the patient by stopping the anesthesia and initiating aggressive cooling. The drug dantrolene reverses malignant hyperthermia, probably by inhibiting calcium release from the sarcotubular system (56), if given before body core temperature rises above 42°C.

The precise nature of the cellular defect responsible for the syndrome remains unknown. The muscle rigidity results from a rapid rise in intracellular calcium (80). Mitochondrial malfunction causes a massive lactacidosis. The origin of heat is an enigma; 25-50% results from aerobic metabolism, the balance from an unidentified nonoxidative mechanism and from reduced heat loss (80).

Hypermetabolic Disorders

Some endocrinological disorders, such as thyrotoxicosis and pheochromocytoma, result in hyperthermia, primarily because the hormones activate metabolic heat production; some reduce heat dissipation too (111).

Genetic Defects and Teratogenic Heat

Apart from the defect involved in malignant hyperthermia, other genetic defects also predispose to hyperthermia. Two examples are the defects resulting in ectodermal dysplasia and in cystic fibrosis. In the first sweat glands are absent, and in the second sweat contains abnormally high electrolyte concentrations that do not diminish with acclimation to heat (90).

Not only do genetic defects predispose to hyperthermia; during pregnancy, hyperthermia, especially lasting 1 or more days, predisposes to resorption of the fetus, abortion, and congenital defects (27, 93). The evidence, so far confined to experimental animals and retrospective studies on humans, points to damage to chromosomes of mitotic cells and to chromatin of interphase cells. The evidence is sufficiently strong for clinicians to advise against very hot baths, saunas, and strenuous jogging or other strenuous exercise in the first 16 wk of gestation, when the pregnancy itself presents no obstacle to exercise.

Hyperthermia Therapy for Neoplastic Disease

Heat has been employed since antiquity to "appease aches and pains and ward off demons" (101), purposes for which it is still employed by physiotherapists. Induced hyperthermia, for many years the standard treatment for syphilis, is enjoying a revival as a means for treating neoplastic disease, alone or in combination with more conventional antineoplastic therapy. Hyperthermia appears to be particularly deleterious to cells undergoing DNA synthesis (101) so that hyperthermia does relatively more damage to neoplastic tissue than to normal tissue (115).

In the case of a localized tumor, localized heating can be applied, and the risks of adverse reactions are not great. However, if the neoplasm is diffuse, then wholebody hyperthermia is required, and the risks are appreciable, since temperatures are raised well into the heatstroke range. Typically, anesthetized patients will be kept at body core temperatures of $41-42^{\circ}$ C for 2–4 h (101). There have been several fatalities reported. If such hyperthermia is to become a more widely used therapy for cancer, then a great deal of research will have to be done to devise ways of preventing thermal damage to the normal tissues.

Fever

Thermoregulation in Fever

Fever is a particular form of hyperthermia in which body temperature rises above normal levels in a regulated way. The rise is accompanied by appropriate activation of normal thermoregulatory mechanisms. Although fever is such a common sign of disease, thermoregulation in fever is apparently as normal as it is in health.

During fever, the thermoregulation proceeds as if the set-point temperature were reset upward. The patient seeks heat and may undergo a rise in metabolic rate, vasoconstriction, and a reduction in sweating, all of which serve to raise body temperature. When fever ultimately resolves, the opposite thermoregulatory mechanisms will be invoked, such as behavior that avoids warmth, vasodilatation, and an increase in sweat rate. Exactly which mechanisms are employed depends on the prevailing environmental temperature. During the stable plateau phase of fever, thermoregulation proceeds, in the face of exercise or variations of ambient temperature, as it would in the afebrile state, except in that metabolic rate may be raised slightly.

Interleukin 1

Fever accompanies some trivial and some very serious clinical conditions (see Table 1). Whatever the etiology, the pathophysiology of fever appears to be the same whenever fever occurs. Some of the body's phagocytic cells are stimulated to synthesize and release into the circulation a protein called "interleukin 1" (IL-1), which then acts on the hypothalamus to modulate thermoregulation as we have described. Agents that may act on the phagocytic cells are the endotoxins of Gram-negative

Table 1Examples of Clinical ConditiThat May Be Accompanied b	ons by Fever
Disease Category	Examples
Infection Bacterial Viral Protozoal Spirochetal Fungal Chlamydial Rickettsial	Septicemia; abscesses Measles; mumps; influenza Malaria Syphilis Candidiasis Atypical pneumonia Q fever; tick bite fever
Malignancy	Hodgkin's disease; rectal carcinoma; acute leukemia; hepatoma; bone sarcoma; atrial myxoma; visceral carcinoma
Nonspecific and immunological conditions	Systemic lupus erythematosus rheumatoid arthritis; acute rheumatic fever; drug allergies; incompatible blood transfusion
Noninfective inflammation	Postoperative inflammation; pancreatitis; gout; crush inju- ries; acute hepatic necrosis; familial Mediterranean fever; myocardial infarction; throm- bophlebitis
Modified from Hellon and Pergamon Press.	Townsend (48), by permission of

bacteria, Gram-positive bacteria, viruses, fungi, and protozoa (4). Antibody-antigen reactions and some tumors may also induce IL-1 production.

Of the phagocytic cells, only blood monocytes and tissue macrophages appear to produce IL-1 in vivo. Lymphocytes produce a lymphokine, which acts on the monocytes and macrophages to enhance IL-1 production, and large granular lymphocytes (natural killer cells) produce IL-1 themselves (52).

Interleukin 1 is a hormone with multiple actions (4). It used to be called endogenous pyrogen, leukocyte pyrogen, leukocyte endogenous mediator, or lymphocyteactivating factor. IL-1 in vitro is a protein of molecular weight of \sim 15,000, though it may circulate as a larger molecule.

We suspect that IL-1 acts via at least two intermediates to exert its effects on the hypothalamus (see Figure 2). The first of these intermediates is a protein synthesized in the brain in response to IL-1 and not yet identified. The second intermediate is a prostanoid, one of the derivatives of arachidonic acid. During fever, arachidonic acid is released from brain phospholipids. metabolized by cyclooxygenase enzymes to prostaglandin endoperoxides, and then converted to prostaglandin, prostacyclin, and thromboxane. Prostaglandin E injected into the brain in many animal species induces a feverlike rise in body temperature. However, there is some evidence that a prostanoid other than prostaglandin also may be involved in fever (71). Blocking the action of cyclooxygenase will prevent arachidonic acid breakdown into any of the putative pyrogenic derivatives, and this is the action of the nonsteroidal antiinflammatory drugs such as aspirin, the classical antipyretics. Steroid drugs such as cortisone also reduce fever (21, 40), and they have the property of preventing arachidonic acid release from brain phospholipids.

Basis of Fever Management

In adults, the body temperature rise in fever rarely exceeds 2.5°C; so there is little risk that the high temperature itself will cause tissue damage. In children, the situation is more complicated. There is a suggestion, based on work in sheep and guinea pigs, that the neonate may not be able to develop fever within the first few hours of birth (58), although human neonates can produce IL-1 to the same extent as adults unless delivered by cesarean section (23). From the second day



Figure 2

Pathway involved in temperature rise of fever. Phagocyte products act on the brain to cause the characteristic temperature rise and on reticuloendothelial system and liver to produce other features of fever.

after birth, at least, human infants develop fevers. Moreover, babies and young children can develop much higher fevers than adults (>41°C) when infected. About 5% of children with fever of >40°C will have convulsions (116), though it is not clear whether the high temperature itself causes them.

Because of the nature of thermoregulation in fever, any attempt to cool a febrile patient physically will be resisted by the thermoregulatory system. The first line of action, and the only one necesseary in adults and most children, is to restore the thermoregulatory system to its afebrile state by use of antipyretic drugs. In children with very high temperatures, the cooling that will occur spontaneously after the drug is administered can be assisted by tepid sponging or other physical means. Except for the case of children with very high temperatures (75, 77), there appears to be no good physiological reason to drop the temperature in fever (see below), other than by treating the cause. The attraction of the antipyretic drugs, especially to the parents of sick children, is that they also resolve the malaise of fever, which is not the consequence of the high temperature per se (32).

Fever and Survival

The ubiquitous nature of fever – it extends to some of the most primitive of vertebrates – has given rise to the idea that fever has some survival or adaptive value (67, 70). Some of the body's defense mechanisms, for example, phagocyte mobility and bacteriocidal activity, may be enhanced by increased temperature. Serum iron concentration falls in fever, and the combination of high temperature and low serum iron concentration inhibits the proliferation of some bacteria (67).

Direct evidence for the role of increased body temperature in the survival value of fever arises from observations on a group of hypothermic children suffering from infections. Mortality was decreased among the children whose body temperatures rose above the hypothermic level during the infection in contrast to those children whose temperatures remained low (29).

The arguments in favor of the survival value of fever, however, are unlikely to convince the febrile patient, feeling miserable, to refrain from taking antipyretic drugs.

Pyrexias of Unknown Origin

In most cases, establishing the origin of a fever constitutes no great diagnostic problem, but sometimes a patient presents with a persistent fever the origin of which is not obvious. Such fevers are classified as pyrexias (fevers) of unknown origin (PUO) when extensive routine investigations into the known causes of fever fail to elucidate the origin of the pyrexia. Most patients with PUO do not have rare diseases. Rather, the diseases they have are the ones notoriously difficult to diagnose, or the diseases have presented in an atypical way. About one-third of patients with PUO are found subsequently to have had infections, one-fifth malignancies, one-fifth collagen-vascular diseases, and the remainder miscellaneous problems such as abscesses, adverse drug reactions, and pulmonary embolism. A small percentage of PUO cases remain undiagnosed (30). Unfortunately, the pattern of the temperature rise in PUO, and indeed in other fevers, is no great help in diagnosis (86).

Among the most difficult PUOs to diagnose is that of factitous fever, in which the patient contrives the high

temperature (2). The patients are almost always young women with paramedical training. The body temperature recordings are falsified by manipulation of the thermometer or by alteration of the temperature charts. Some patients achieve a fever by self-innoculation with pyrogenic substances. Diagnosis may be achieved by close supervision of the temperature measurements, measuring oral and rectal temperatures simultaneously, and intensive observation of the patient.

Hypothermia

Etiology

Hypothermia is not a medical curiosity. It is a commonplace condition. Only in the United Kingdom has a serious attempt been made to estimate the mortality from hypothermia, and it is thought to be about 20,000 per year (78).

Hypothermia is usually defined as a condition in which the body core temperature is $<35^{\circ}$ C. A survey in the UK has shown that $\sim 4\%$ of old people admitted to hospital, for whatever cause, have a rectal temperature $<35^{\circ}$ C (31). A similar incidence probably prevails in other temperate and cold countries. Most of these hypothermias remain undetected, first because low-reading thermometers generally are not used and second because standard clinical thermometers seldom are shaken down to the 35°C mark: if the mercury is left, as usual, just below the "normal" mark, it will not fall further in the hypothermic patient, so that the temperature will be recorded as "low normal." The patients may not complain of hypothermia.

Apart from the hypothermia that is induced deliberately in surgical patients, there are two categories of pathological hypothermia. In both, the elderly account for the majority of the victims. The first is accidental hypothermia, in which an otherwise healthy person is exposed to a cold environment in a situation in which the thermoregulatory system cannot compensate adequately. Typical examples are the old person living alone who falls on the floor on a cold night [postural hypotension occurs in 14% of the elderly (31)], the hiker immobilized in the open as a result of injury or exhaustion, young boys (mainly) after accidental water immersion (59), or the shipwreck victim. The environment does not have to be particularly cold to induce hypothermia: there have been cases from indoor environments in which the temperature has been 18°C (6), and recent deaths in North Sea divers have brought to light the risk of fatal hypothermia in divers wearing suits heated with water at 29°C (60).

The second category of pathological hypothermia is secondary hypothermia, in which some condition predisposes to thermoregulatory failure under cold stress (69). Examples are conditions that reduce metabolic energy production, such as hypothyroidism, hypoglycemia, hypopituitarism, ketoacidosis (38), and malnutrition; conditions that disrupt the neural control of body temperature, such as cerebrovascular disease, head trauma, or drug overdose, particularly of alcohol (34); and conditions that accelerate heat loss from the skin, such as burns.

The mortality from accidental hypothermia can be low (<10%) if the patient is managed properly. In the case of secondary hypothermia the mortality may be 75-90% (69) and is particularly high in elderly men (38).



Pathophysiology

The extent and nature of physiological malfunction in hypothermia depends on the level to which body core temperature falls (see Figure 3). As was the case with heatstroke, the first signs of hypothermia result from disruption, by the abnormal temperature, of central nervous system function: ataxia, amnesia, slurred speech, and irrational behavior, including paradoxical undressing (120) and hallucinations. Most patients are unconscious at body temperatures below $28^{\circ}C$ (91).

Shivering ceases at a body core temperature of $\sim 33^{\circ}$ C, and recovery cannot occur spontaneously beyond this point. Metabolic rate then drops progressively with temperature, falling to 50% of normal at $\sim 28^{\circ}$ C (95).

Loss of plasma leads to increased hematocrit and sludging (18). One of the reasons for the loss of fluid is an initial "cold diuresis," which is followed at lower kidney temperatures by oliguria and decreased renal enzyme function, resulting in decreased reabsorption (especially of glucose) and decreased secretion (18). Disturbances in acid-base balance are common but do not follow any consistent pattern. Blood samples taken from a hypothermic patient and then analyzed at 37°C give spuriously low values of pH; when a real acidosis exists it usually resolves spontaneously on rewarming.

Reduced enzyme activity also retards the detoxifying and conjugating function of the liver. Hyperglycemia may result from decreased glucose uptake and oxidation. Pancreatitis and gastric hemorrhages are invariable accompaniments to hypothermia (91).

The effects of low temperature on the heart are particularly important. As temperature falls, heart rate and cardiac output fall progressively. Blood pressure rises initially and then falls, and it becomes increasingly difficult to detect a pulse. The myocardium becomes increasingly irritable despite hypokalemia (15). Atrial fibrillation is common, and at temperatures of < 28- 30° C there is a high risk of ventricular fibrillation (121), which is often the terminal event. The J wave of the electrocardiogram, a positive-negative deflection immediately following the QRS complex, occurs in only one in three patients but, when it does occur, is suggestive of hypothermia.

At postmortem examination the most common findings are a purple skin, edema of the face, stomach erosion, and multiple infarcts in many organs, all consistent with shock or hypoxia (55).

Basis of Management

There is no general agreement on the management of hypothermia, and the problem would benefit from more extensive physiological research. The subject has been extensively reviewed recently (91).

Clearly the best intervention is prevention. In the case of the young and healthy potential victim of accidental hypothermia, what is required primarily is education about the risks, nutrition, clothing, and early recognition based on high suspicion of aberrant behavior. In the case of the elderly victim, prevention is a huge social problem, because the important predisposing factors are poverty and loneliness.

Rewarming the mildly hypothermic patient, particularly one who is young and still conscious, is no great problem. Immersing the patient in a warm bath is the method most widely used in hospitals. In the field, the victim should be moved to a warm dry shelter when possible, wet garments should be removed, and the victim should be wrapped in a dry sleeping bag or similar cladding. Direct body contact with a normothermic person is a valuable form of emergency rewarming.

How to rewarm the profoundly hypothermic patient is much more controversial. Rewarming should not be attempted in the field, even if the patient is apparently in extremis; it requires intensive care facilities. The two major problems are the "afterdrop," an additional fall in core temperature that occurs at the onset of rewarming, and myocardial irritability. The mechanism of the afterdrop is not yet clear (102). As a consequence of the myocardial irritability, any attempt to intubate the patient or pass an esophageal thermometer, attempts at cardiopulmonary resuscitation, or indeed anything but the gentlest of handling is likely to precipitate ventricular fibrillation. Once ventricular fibrillation occurs, sinus rhythm usually cannot be restored until the patient is warmed to $>28^{\circ}$ C. There is no agreement as to the relative merits of surface rewarming vs. core rewarming using techniques such as peritoneal dialysis or extracorporeal blood warming (6, 95). Rapidly administered warm saline, intravenously or via enemas or gastric washings, significantly decreases mortality in hypothermic infants (94).

No one is dead until warm and dead. The body is remarkably well preserved at low temperatures. Metabolism is suppressed and O_2 stores are maintained. The electroencephalogram is flat at body temperatures of $<20^{\circ}$ C, pupils are commonly fixed and dilated at body temperatures of $<30^{\circ}$ C, and deep tendon reflexes may be absent, so the profoundly hypothermic patient may appear dead. Several such patients have been resuscitated successfully, without any sequelae, particularly young children who have fallen below the ice of a frozen river (18). Cardiac arrest and apnea of several hours' duration should not preclude attempts to resuscitate a profoundly hypothermic patient (89, 118).

We thank the South African Medical Research Council and the Council of the University of the Witwatersrand for financial support and Dr. L. C. Senay and Dr. K. E. Cooper for their help in revising the manuscript.

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Laboratory Exercise on Active Transport

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The exercise on active transport described here, unlike others we have tried to perfect, consistently produces reliable results when performed by students in an undergraduate anatomy and physiology course. The exercise demonstrates qualitatively the specificity of the transport mechanism, including a consideration of competitive inhibition, and the role of ATP in active transport.

Before performing the exercise students should be familiar with the processes by which materials move across membranes, both passive and active, as well as factors that will determine whether a molecule will be actively transported.

We developed this laboratory exercise from a research report on transport mechanisms by Nijout (1). The procedures can be successfully performed by groups of four introductory-level students in a 2- or 3-hour laboratory period. A complete description of the protocol we provide to the student follows.

Introduction

In this exercise, you and your partners will observe active transport of a dye, chlorophenol red, by cells of Malpighian tubules in caterpillars (called tobacco hornworms) of a moth, Manduca sexta. Active transport is one mechanism by which organisms move certain molecules from their body fluids into excretory structures (such as Malpighian tubules or nephrons) that eliminate them from the body. A metabolic inhibitor, 2,4-dinitrophenol (DNP), which prevents the formation of ATP, will be added to determine if transport of the dye by cells of the Malpighian tubules is energy dependent. Another colorful dye of similar size, gentian (crystal) violet, will be used to demonstrate that substances exist that cannot be actively transported by the Malpighian tubules. Molecules of a dye not transported by the tubules differ from chlorophenol red molecules in charge, three-dimensional shape, or some other feature that makes the transport mechanism unable to bind to and/or move them.

A given transport mechanism is able to transport only a few specific types of molecules. If two different types of molecules that can use the same sites on the transport mechanism are present, they will compete for the transport sites. Thus the rate of transport of either molecule is slower than if just one molecule is present. A decreased rate of transport due to competition between different types of molecules for a carrier is called competitive inhibition. In this exercise, a putative competitor of chlorophenol red, hippuric acid, which is colorless, will be added along with chlorophenol red to illustrate competitive inhibition.

Exercise

You and your partners will do four tests. Obtain all of the materials required for the four tests so that you can efficiently perform them at 5-min intervals: a dissecting microscope, a light, four wax-bottom dissecting dishes, 24 straight pins, forceps, a pair of dissecting scissors, a 600-ml beaker of tap water (about 24°C), four 1-ml syringes, and four caterpillars.

Before doing each test, fill a syringe with 0.15 ml of the solution appropriate for the test you are doing, mark a caterpillar on its cuticle (surface) with a permanent-ink marker so that you can identify it, and anesthetize the marked caterpillar by completely submerging it in tap water for 10 min. After beginning to anesthetize this caterpillar used for *test 1*, you will begin to anesthetize the second, third, and fourth caterpillars in 5, 10, and 15 min, respectively.

Test 1. Active Transport Solution: Chlorophenol red dve

a) Inject 0.15 ml of chlorophenol red solution into the base of a "leg" (termed a proleg) near the **tail end** of an anesthetized animal. (The tail has a horn.) Inject carefully at an acute angle to the body wall so that you inject just under the body wall into the hemocoele or blood compartment – **don't go too deep.** Record the time of injection in Results. Because this insect has an open circulatory system, its blood moves freely about the tissues in a blood compartment and bathes internal structures such as the Malpighian tubules. The dye will be dispersed throughout the blood and come into contact with the cells of the tubules. Put the caterpillar in the dissection dish for 10 min to allow diffusion of the dye into the blood and then into the beaker of water for an additional 10 min.

b) Now put the anesthetized animal into the dissecting dish. Stretch the animal tautly and pin the head and tail of the animal so that the row of air openings or spiracles (brownish dots) along either side of the animal is up. With a scissors, make a long shallow incision above one row of spiracles. At both the head and tail ends, make shallow transverse incisions perpendicular to and across your first incision. Pull the body wall away from the viscera and pin it to the dissecting dish so that the internal organs can be seen. As you open the animal, cut the tracheal tubes (numerous, whitish air-conducting tubes) close to the body wall. Put the animal under the dissecting microscope and focus on the long thin Malpighian tubules located on the gut. Many of the tubules have bumps along their surface, although some of them appear smooth. Observe the Malpighian tubules nearest to the tail end of the animal. (Do not confuse Malpighian tubules with the smooth silvery tracheal tubes, which do not transport chlorophenol red.) Look to see if the Malpighian tubules on the gut are red, and if so, what shade of red? If the tubules are not red, what color are they? Record the time and your observations in Results.

Test 2. ATP and Active Transport Solution: DNP and chlorophenol red dye

a) Adhering to the procedures and precautions described for *test la*, inject 0.15 ml of DNP and chlorophenol red mixture into the base of a "leg" near the **tail end** of another animal. This animal should be injected 5 min after injection of the animal used in *test l*.

b) Same as test 1b. Compare results of tests 1 and 2. Test 3. Is Another Dye Actively Transported? Solution: Gentian (crystal) violet dye

a) Inject 0.15 ml of gentian violet into the base of a "leg" near the **tail end** of a third animal. This animal 518

should be injected 5 min after injection of the animal used in *test 2*. For details of procedure, see *test 1a*.

b) Same as test 1b. Compare results of tests 1 and 3.

Test 4. Competitive Inhibition

Solution: Hippuric acid and chlorophenol red dye

a) Inject 0.15 ml of hippuric acid and chlorophenol red mixture into the base of a "leg" near the **tail end** of a fourth animal. This animal should be injected 5 min after injection of the animal used in *test 3*. For details of procedure, see *test la*.

b) Same as test 1b. Compare results of tests 1 and 4.

Results

Record your data and the data from other class groups in the chart below.

				Results From
			Results	Other Groups
			(color &	(color and
			degree of	degree of
	Time	Time	color in	color in
	Injected	Checked	tubules)	tubules)
Test 1 Chlorophenol red				
<i>Test 2</i> DNP & chlorophenol red				
Test 3 Gentian violet				
Test 4 Hippuric acid and chlorophenol red				

Questions

- 1. How do you know that chlorophenol red was actively transported into the Malpighian tubules and did not passively enter the tubules? Give evidence from your experimental results.
- 2. What are the differences between active transport and passive processes?
- **3.** Cite several examples of active transport in your body. List both the location in your body and the substances that are transported.
- 4. Why is it advantageous for cells to have active transport mechanisms?
- 5. Is active transport energy-dependent? Give evidence from your experimental results.
- 6. Does the active transport mechanism studied here transport all molecules that come in contact with it? What is the specificity of the carrier? Give evidence from your experimental results.

Comments

A group of students performing this exercise typically obtains results similar to the following. In *test 1*, in which only chlorophenol red is injected, the Malpighian tubules are red to dark pink after 20 min. Occasionally, the color is orange since chlorophenol red is a pH indicator. In contrast, when chlorophenol red is injected with either DNP or hippuic acid, the color in the tubules is less intense, indicating slower transport of chlorophenol red due to a lack of ATP or competitive inhibition, respectively. When gentian violet is injected, the tubules remain colorless or whitish, indicating no transport of dye into them. Individual variation may exist among the four animals used by a group of students. To partially control for this, we pool the data from the entire class by having each group record the results from the four tests in a chart on the chalkboard. This large sample size consistently produces the results described above.

The procedure that is most difficult for students is dissection of the animals. We display a sample dissection under a dissecting microscope and encourage students to observe it before attempting the dissection. Teaching assistants are present to assist students with dissections and to answer questions.

A crucial factor in the success of this exercise is the size of the animals. The caterpillars develop in five instars; only larvae in the fifth instar – usually 2-3 inches long and weighing 7-9 g – are large enough to permit the experimental manipulations. However, the efficiency of the transport mechanism is decreased on the day preceding pupation. Because an animal remains in the fifth instar for only a few days before beginning to pupate, care must be taken when ordering animals from a supply company so that they are 1-3 days from pupation on the day the exercise is to be performed.

The vehicle for delivery of the injected substances is a physiological saline containing 25 mM NaCl, 33 mM MgCl₂, 4 mM CaCl₂, 25 mM potassium methanesulfonate, and 50 mM Tris methanesulfonate. The saline is adjusted to pH 7.0 with 2.5 M methanesulfonic acid (see Rheuben and Kammer, 2). For an alternate saline using bicarbonate and phosphate buffers, see Weevers (3). In the saline is dissolved 2×10^{-2} M chlorophenol red, 2×10^{-2} M chlorophenol red plus 8×10^{-2} M 2,4-dinitrophenol, 2×10^{-2} M gentian violet, or 2×10^{-2} M chlorophenol red plus 10^{-1} M sodium hippurate.

Supplies

Caterpillars (tobacco hornworm eggs or larvae) are available from Carolina Biological Supply, Burlington, NC. Methanesulfonic acid stock solution (2.5 M), made by adding 100 g methanesulfonic acid contained in 69.8 ml (Aldrich Chemical, catalog no. M860-6) to 346.4 ml distilled water.

Tris • OH stock solution (2 M), made by adding 242.2 g Tris (hydroxymethyl)aminomethane (Aldrich Chemical, catalog no. T8, 760-2) to distilled water to make 1 liter.

KOH stock solution (2 M), made by adding 112.2 g potassium hydroxide (Aldrich Chemical, catalog no. 22, 147-3) to distilled water to make 1 liter.

Potassium methanesulfonate stock solution (25 mM), made by adding 100 ml of 2 M KOH to 80 ml of 2.5 M methanesulfonic acid.

Tris methanesulfonate stock solution (50 mM), made by adding 100 ml of 2 M Tris \cdot OH to 80 ml of 2.5 M methanesulfonic acid.

Chlorophenol red solution, made by adding 0.84 g chlorophenol red (Aldrich Chemical, catalog no. 19,952-4) to 100 ml saline.

Gentian violet solution, made by adding 0.82 g gentian violet (Aldrich Chemical, catalog no. 86,099-9) to 100 ml saline.

Chlorophenol red plus DNP solution, made by adding 0.84 g chlorophenol red and 1.47 g 2,4-dinitrophenol (Aldrich Chemical, catalog no. D19,850-1) to 100 ml saline.

Chlorophenol red plus hippuric acid solution, made by adding 0.84 g chlorophenol red and 1.79 g hippuric acid (sodium salt hydrate) (Aldrich Chemical, catalog no. 27,164-0) to 100 ml saline.

We thank Ann E. Kammer, Lynn Schanker, and Fred Wilson for critical reviews of the manuscript.

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Muscle Atrophy During Space Flight: Research Needs and Opportunities

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Numerous observations of United States and Soviet space crews, animals flown in space, and subjects exposed to simulated weightlessness have demonstrated skeletal muscle atrophy. The muscle atrophy experienced to date, in missions from a few weeks to 6 months, has apparently not compromised crew effectiveness in flight and seems to be reversible following mission completion. Daily vigorous exercises of the major muscle groups appear to retard the muscle deconditioning; however, the reliability and effectiveness of exercises have not been adequately demonstrated from a scientific standpoint. Although the muscle atrophy experienced to date by U.S. astronauts appears to have been innocuous in flight, it may have interfered to an unknown degree with the physiological efficiency of astronauts engaged in extravehicular activity (EVA), including exploration of the lunar surface. Postflight, it contributes to a temporarily reduced state of physical fitness and orthostatic intolerance. In addition, leg volumes of astronauts are diminished upon return to Earth. Thus space-related muscle atrophy represents a significant biomedical problem.

The National Aeronautics and Space Administration (NASA) supports intra- and extramural research ranging from basic studies to applied technology.¹ As a part of the process of program assessment and planning, NASA requested that the Life Sciences Research Office (LSRO) of the Federation of American Societies for Experimental Biology (FASEB) review and evaluate available knowledge and ongoing research and provide additional scientific input for future research programming in muscle atrophy.² This has been done with the assistance of an ad hoc Working Group of outstanding investigators.³

Objectives and Scope of the Study

The objectives of the study of the problem of muscle atrophy associated with space flight were 1) to review extant knowledge of the subject; 2) to examine NASA's current and projected research program; 3) to identify all significant gaps in essential knowledge; 4) to formulate additional suggestions for future research consideration by NASA; and 5) to produce a documented report of the foregoing items that can be used for NASA research program planning.

The scope of topics that were reviewed covers the basic biologic disciplines, certain clinical aspects, possible means of intervention, and the areas of models, methods, and equipment. The major portion of the report is devoted to the observations of the ad hoc Working Group during their meeting at FASEB and their followup contributions including critiques of the report. It includes background information on muscle biology and atrophy, a review of muscle atrophy associated with actual and simulated space flight, and the findings of the ad hoc group with respect to important gaps in knowledge, desirable research approaches, and the present NASA research program on muscle atrophy.

The purpose of this synopsis is to acquaint potentially interested scientists with the problem of space-related muscle atrophy in the hope of stimulating new research on critical questions.

Background Information

Normal muscle

Function. The sliding-filament model is generally accepted as the basic contractile system of striated muscle, and the sarcoplasmic reticulum and transverse tubular system, in concert with calcium ions, link neuro-muscular excitation and muscle contraction. The complex process of muscle contraction was outlined by Fuchs (33).

Metabolism. The energy required for muscular activity is ultimately derived from carbohydrates, whose

¹ The NASA Biomedical Research Program is conducted intramurally by NASA Research Centers and by means of extramural grants and contracts. Qualified scientists interested in learning more about the program and in submitting research proposals should write to Chief, Space Medicine Branch/EBM, Life Sciences Division, NASA Headquarters, Washington, DC 20546.

²This paper is a synopsis of a report prepared for the National Aeronautics and Space Administration (NASA) by the Life Sciences Research Office (LSRO) of the Federation of American Societies for Experimental Biology (FASEB). Single copies of the report are available gratis from: Chief, Space Medicine Branch/EBM, Life Sciences Division, NASA Headquarters, Washington, DC 20546. Copies are also available from the Special Publication Office, FASEB, 9650 Rockville Pike, Bethesda, MD 20814 at \$8.00 each (prepaid) or from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, VA 22161 [PBN84-20135 or PBN84-27416].

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oxidative breakdown provides for highest muscular efficiency and endurance (10), and from free fatty acids (35, 48). For brief intensive activity, muscle can use energy supplied anaerobically via ATP and creatine phosphate and by anaerobic glycolysis, during which the muscle incurs an "oxygen debt."

Excitation-contraction. The process by which the muscle action potential starts the contraction derives its energy from the interaction of ATP with muscle proteins (124). Anaerobic metabolism yields sufficient energy for only a few seconds of sustained maximal muscle contraction (54); aerobic reactions yield the greatest amount of energy. Small amounts of energy are needed to restore the regulatory calcium ions from the sarcoplasm to the sarcoplasmic reticulum and to pump sodium and potassium ions through the membranes of muscle fibers (54).

Clinical Atrophies

According to Stewart (105), atrophy may be considered as a decrease in size or wasting away of a body tissue or, in growing organisms, as arrested development. In this report, skeletal muscle atrophy associated with space flight is classed as a type of "disuse" atrophy, with acknowledgement of the lack of a completely satisfactory definition of the term. The term disuse atrophy is widely used in the scientific and clinical literature; however, its appropriateness with regard to muscle changes associated with space flight is questionable. Abramson (1) noted difficulties in defining the atrophy of disuse; he suggested that decrease in size of tissues resulting from their inability to develop full function might be a general definition. Robbins and Cotran (91) list decreased work load as one of the apparent causes of muscle atrophy, and Saltin and Gollnick (93) note that, with disuse or inadequate nutrition, there is a loss of muscle mass associated with a decrease in cross-sectional area. The LSRO ad hoc Working Group on Muscle Atrophy suggested that an acceptable basic definition might be a reduction in muscle size or mass in contrast to hypertrophy, with implications for associated physiological and functional effects.

Pathophysiological features of disuse muscle atrophy include a shrinkage in the size of muscle cells by partial losses of structural components and organelles such as mitochondria, myofilaments, and endoplasmic reticulum (91). Atrophic cells are not dead; eventually, however, with marked degrees of disuse, muscle cell death may occur, giving way to replacement by fibrous tissue (16, 90). Underuse of the skeletal musculature by space travelers affects mainly the antigravity muscles, is only a partial or relative type of disuse, and has not resulted in marked degrees of atrophy during space missions lasting up to 6 months.

Causes

A decrease or lack of function of living tissues results in their shrinkage or wasting away (1, 91, 105). Clinical causes and types of muscle atrophy include I) denervation of the musculature as a result of trauma or disease of the spinal cord or motor roots; 2) the spinal musculature atrophies; 3) the peripheral neuropathies; 4) certain stages of the progressive muscular dystrophies; 5) the inflammatory myopathies; and 6) certain myopathies that are associated with metabolic or endocrine disorders (114). Investigative models for study of disuse atrophy in laboratory animals are, for example, surgical denervation or pharmacological block of nerve conduction, chronic tenotomy, spinal cord transection or isolation, joint immobilization, and suspension of rats to produce a head-down body tilt with unloading of the hindlegs (27, 32, 52, 58, 75, 78, 104, 113).

Prevention

Except for countermeasures against muscle atrophy in simulated or actual space flight, studies of prevention of disuse atrophy have concerned clinical problems that are complicated by atrophy. The following are experimental and clinical approaches to prevention of muscle atrophy.

1) Reinnervation. Reinnervation of denervated muscle following trauma reverses atrophy and restores physiological function. Nerve impairment from trauma varies from transient blockage without disruption of the axon to complete division of the nerve. If reinnervation occurs before atrophy becomes irreversible, nerve regeneration is an optimal type of prevention of irreversible muscle atrophy following nerve damage. Nerve regeneration within 3-4 mo of injury may restore muscle function fully, whereas reinnervation after 2 yr rarely restores any muscle function (54).

2) Electrical stimulation. Prevention or retardation of atrophy of denervated muscle by electrical stimulation has been demonstrated in the rat (30, 50, 51, 57, 62, 63, 97, 108, 115), the rabbit (53), and the dog (64). It is well established that current intensities must be high enough to produce vigorous muscle contractions to prevent or retard atrophy in denervated muscles (30, 57, 115).

3) Exercise. Physical exercise by voluntary contraction of muscle groups has long been used to restore atrophied muscle following injury and disease (21).

4) Biochemical control. Alternative approaches to preventing or retarding disuse atrophy have been suggested by certain lines of investigation, for instance, the use of aids to muscle protein synthesis such as supplemental leucine (11, 34, 44), substances that reduce muscle protein degradation in vitro such as leucine and α -ketoisocaproate (44), and substances that reduce muscle protein degradation in vivo such as mixtures of the branchedchain amino acids (BCAA) (106).

5) Pharmacological control. Another possible means for preventing or controlling muscle atrophy involves methods of inhibiting the factors that mediate muscle proteolysis. For example, cyclooxygenase inhibitors such as aspirin and indomethacin block muscle proteolysis associated with the release of interleukin-1 in patients with sepsis or trauma (3, 4). However, from a clinical point of view, this appears somewhat controversial (13, 14, 74); nevertheless, if similar proteolytic factors should be discovered in the search for mechanisms of disuse atrophy, the concept may have merit. Further elaboration of the roles of the proteases and their inhibitors found in skeletal muscle (5) might lead to practical means of pharmacological or biochemical intervention. Beneficial effects of the protease inhibitor, pepstatin, in a mouse model of muscular dystrophy were reported by Schorr et al. (95); however, Enomoto and Bradley (25) observed no benefit of treatment with pepstatin, antipain, or leupeptin in mice with hereditary muscular dystrophy.

6) Hormonal control. The influence of anabolic hormones on muscle is also of interest. Goldberg and Goodman (43), for example, reported that growth hormone reduced weight loss and induced growth in denervated muscles in hypophysectomized rats. In another study, restoration of muscle weight, electrical activity, contractile capacity, and work performance of the gastrocnemii of immobilized hindlimbs of rats treated with human growth hormone was reported by Apostolakis et al. (2).

Rehabilitation

Experience in rehabilitating atrophic muscles has been largely in the clinical setting following immobilization of limbs as a result of injury or disease. The basis of muscular rehabilitation is voluntary exercise with regimens chosen to suit individual needs (20, 21, 61, 71, 77, 99). Restoration of the musculature to its preatrophic bulk and power appears to be difficult in many cases and perhaps impossible in some. Stillwell and colleagues (107) noted that, with the best available techniques, 3–8 wk were required to restore the quadriceps muscle to its normal strength, and Karpovich (61) observed that, often, definitive treatment ends and rehabilitation starts only after a long period of time. Among patients recovering from disuse atrophy, tcenagers are more likely to recover muscle bulk than young or mature adults.

Space-Related Muscle Atrophy

In the weightlessness of space flight, the functional load on the musculoskeletal system is insufficient to maintain normal physiological status of the musculature. There is no need for active opposition to gravity or to maintain customary terrestrial posture, and the effort required to move the body and its appendages is remarkably reduced (85, 101).

Primary interest is in the atrophy of the antigravity muscles, whose customary roles in maintaining body posture on Earth are drastically modified in weightless flight. Included are most of the muscles of the lower extremities, the gluteal muscles, the trunk muscles, extensors of back and neck, and their antagonists. Unloading of the musculoskeletal system in zero-G results in a unique form of underuse.

Oganov et al. (82) defined the changes in skeletal muscle associated with long-term space flights as "functional atrophy" and noted that they included loss of muscle mass, decline of muscle "tone," strength, and endurance, primarily of the muscles of the legs and torso. Increased protein catabolism including breakdown of skeletal muscle has been a consistent finding in space flight. A reduction of the volume of the lower extremities and a persistent rise in urinary nitrogen, phosphorus, amino acids, and 3-methylhistidine are some of the typical associated findings (80, 118). Whether these changes are caused by zero-G or other factors in the space flight environment has not been fully established, but weightlessness is generally thought to be the main etiologic factor (9, 38).

U.S. astronauts and Soviet cosmonauts have typically developed negative potassium balance during flight, manifested postflight by decreased values of serum and urinary postassium, total body content of potassium-40, and exchangeable potassium (39, 68, 69). This negative balance has been ascribed to a reduction of the intracellular potassium depot as a result of a decrease in cell mass, particularly in skeletal muscle. The negative potassium balance has persisted for as long as 6 days postflight (39).

Soviet scientists reported moderate functional and anatomic degradation of certain muscle groups in

cosmonauts, including atrophy and postflight reduction of strength in the gastrocnemii, tibialis anticus, and neck muscles. The decrements in muscle performance capability apparently persisted for 6 wk or longer, postflight (65). The range of reduction of leg volume during the Skylab missions averaged from ~ 7 to 11% of the preflight values. More than half the loss in leg volume probably resulted from the cephalad shift of blood and tissue fluids that accompanies exposure to zero G; the remainder is considered a loss of muscle mass (111). Postflight stereometric analysis of the Skylab astronauts by means of a stereophotogrammetric method showed major losses in volume of the abdomen, buttocks, and calves, and less pronounced losses in the thighs (119, 121). From these studies, Whittle (120) estimated that eight of the nine Skylab astronauts probably lost muscle from the legs, the largest amount being 1.43 kg and the average amount 0.52 kg.

Studies in the rat. Rats exposed to zero-G in Cosmos biosatellites for ~ 20 days showed gross, microscopic, and biochemical evidence of atrophy and a decline of contractile force and work capacity of such antigravity muscles as the soleus and triceps brachii (38, 81). Myofibrillar and sarcoplasmic proteins were decreased in the soleus, but not in other muscles examined (37). Muscle glycogen content and activities of glycogen phosphorylase, adenylate cyclase, and phosphodiesterase of the space-flown rats did not differ from controls (79). Whole muscle demonstrated accelerated rates of contraction (soleus) and a decrease in strength, elasticity, and endurance (soleus and extensor digitorum longus). These changes in functional properties were consistent with those observed in intact space-flown rats, for example, a reduced tolerance to static loads (38). All observed changes in the rats' musculature disappeared by the 25th postflight day.

Simulated weightlessness. Methods of partial simulation of weightlessness have been employed in muscle studies such as bed rest or water immersion for human subjects and head-down body suspension for rats. Atrophy of muscles of the legs and thighs was reported in human volunteers kept at strict bed rest while wearing removable lower body plaster casts for 6-7 wk (19). Similar effects were reported from other medium- to long-term bedrest studies (12, 60, 66, 83, 84, 87, 92, 112). Human subjects exposed to simulated weightlessness for 7 days be means of immersion in water demonstrated a 30-40% decrease in maximum dynamic and isokinetic strength of the leg extensors and in the isokinetic strength of the tibial muscles (49). For simulating the effects of microgravity on rat skeletal muscle, the tailsuspension model of hypokinesia/hypodynamia has shown considerable promise (28, 58, 75, 78).

Other Experimental Approaches

Mechanical immobilization of joints leads to weakening and atrophy of the associated musculature in human subjects (17, 72, 94, 107, 122, 123) and in animals (7, 15, 32, 47, 55, 109, 110). The term disuse atrophy in a model with an intact nerve supply is obviously inaccurate; however, the practical advantages of mechanical immobilization have made it popular as an investigational method. True disuse atrophy of muscle occurs, for example, during certain intervals following spinal cord injury or after pharmacological blockade of motor nerves with tetrodotoxin (22, 23).

Table 1 Factors Related to Muscle Biology

- Decreased rates of muscle protein synthesis, appearing within 6 h in immobilized rat limbs (7) return to normal rates within 6 h after remobilization (8)
- Insulin responsiveness for 2-deoxyglucose uptake at the 24th hour decreases in the same model (7, 96)
- Insulin appears to be an important hormonal factor for short-term regulation and maintenance of positive protein balance in skeletal muscle (45)
- Marked differences occur in rates of atrophy of stretched immobilized muscle versus muscle immobilized in the resting or shortened positions (6, 7, 100, 102, 110)
- When muscle is denervated, strong electrical stimulation may retard atrophy (61)
- In vivo, sarcolemmal resting membrane potentials have been shown to decrease in denervated muscles (103) and, in muscles of immobilized limbs, to decrease (73) or to remain unchanged (29, 46)
- Elevated blood cortisone levels have been reported during limb immobilization (36) and space flight (69)
- Tissue concentrations of alkaline serine proteinases increase dramatically in the muscular dystrophies, starvation, and endocrine imbalances (5)
- Intracellular Ca²⁺-activated proteinases may offer approaches to investigating the regulation of muscle protein turnover (18, 89)
- Cathepsins B, D, H, and L and associated inhibitors such as pepstatin and leupeptin may be involved in myofibrillar protein degradation of disuse atrophy (5)
- An apparent increase has been reported in glucocorticoid receptors in the cytosol of immobilized gastrocnemius muscle cells (24)
- The somatomedins stimulate both proliferation and differentiation of muscle cells in vitro. Insulin is active only at grossly supraphysiological concentrations, and probably cross-reacts with the somatomedin receptors (26)
- Passive tension or repetitive stimulation retards protein degradation in isolated muscle preparations (40, 42)
- Muscle protein degradation may be induced by thyroid hormones (45). Increased postflight levels of thyroxine in the Apollo (98) and Skylab (69) astronauts suggest heightened thyroid gland activity during missions
- Intracellular leucine concentrations may influence the rate of protein synthesis in disused muscle (76)
- Inactivity of skeletal muscle induced by joint immobilization or by pharmacologic or surgical denervation is associated with an increase in extrajunctional acetylcholine receptors (29, 67, 86)

Other models that are considered useful for investigation of muscle atrophy involve tissue culture, organ culture, and partial-body perfusion techniques such as hemiperfusion and isolated perfused muscle preparations. While no model is ideal, valuable data have resulted from muscle studies involving tissue culture (26, 31) and organ culture or hemicorpus perfusion (41, 45, 59, 70).

Etiology and Mechanisms

Opinions of the ad hoc Working Group varied as to the probable cause(s) of muscle atrophy in space flight. Of the several prevalent environmental influences such as weightlessness and the relative hypodynamia and hypokinesia imposed by the spacecraft dimensions and types of crew activities, all agreed that the unloading of the antigravity parts of the musculoskeletal system is the primary cause. Again, at the level of the whole organism, a majority believed the lack of production of customary muscular force may be a causal factor. Probably related to this are clinical observations that a stimulus for muscle growth is pull across the corresponding joints. Production of muscle force-velocity in space probably requires activation of fewer motor units than are needed for the same level of contraction on Earth.

It is generally acknowledged that the exact biologic mechanisms that induce muscle atrophy are unknown and that this is true of muscle hypertrophy as well. Table 1 lists examples of known and hypothetical factors in muscle biology, some of which may suggest research approaches to the mechanisms of muscle atrophy.

In summary, exposure to weightlessness as well as hypokinesia/hypodynamia, leads to decreases in muscle strength and work (exercise) capacity (85). Full recovery of muscular strength, especially in the legs, following space flights of medium (weeks) to long (months) duration requires from several days to several weeks, and data are not available to show conclusively whether full recovery of muscle bulk takes place. However, the average leg volumes of the Skylab 3 astronauts reached preflight values by postflight day 10 (111). Certain characteristics of muscle atrophy associated with space flight are listed in Table 2.

Countermeasures

Most evidence suggests that, despite attempts at intervention such as diet and exercise, skeletal muscle atrophy continues to some extent throughout orbital flight. manifesting progressive muscle loss and negative nitrogen balance (68, 80, 88, 117, 118). The primary means of intervention upon which both the U.S. and Soviet space flyers rely for preventing or minimizing muscular deconditioning of space flight is vigorous physical exercise, mainly of the dynamic type. Operational experience with long-term space missions suggests that carefully designed exercise regimens scrupulously carried out by spacecrews are partially effective. However, studies of nitrogen and mineral balances suggest that muscle atrophy continues to progress during exposure to weightlessness regardless of the use of available countermeasures.

NASA's Research Program in Muscle Atrophy

Although scientific knowledge about the physiological and pathological effects of use and "disuse" of skeletal muscle is abundant, there is still much to be learned. Lack of data on the basic biologic mechanisms of muscle atrophy and hypertrophy hampers the quest for a solution to the problem of muscle atrophy in space. Consequently, NASA supports research on the basic mechanisms of muscle atrophy and efficient methods of

Table 2

Some Features of Muscle Atrophy Associated with Space Flight

- Decrease in muscle volume and mass
- Loss of muscle nitrogen
- Decrease in exercise tolerance
- Decline of muscle strength and endurance
- Increased protein catabolism
- Rise in urinary nitrogen, phosphorus, amino acids and 3-methylhistidine
- Decreased serum and urinary potassium postflight
- Reduction of intracellular potassium depot

prevention or control. Short titles of some of the applicable research are listed in Table 3.

Examination of NASA's research on muscle atrophy indicates that it is an evolving program based on expert guidance received from multiple sources including formal scientific advisory groups. Most studies in the Biomedical Research Program on Muscle Atrophy are consistent with the governing program documents. The overall program appears well conceived to embrace the key objectives and research approaches needed for ultimate solution to the operational problem of muscle atrophy. However, future program planning should include refinement, if possible, of the research objectives and approaches and closer matching of these with ongoing and planned research. The Biomedical Research

Table 3

Examples of NASA-Sponsored Research on Muscle Atrophy

Short titles:

A. NASA Biomedical Research in Muscle Atrophy

- Proteolysis in muscle atrophy
- · Growth factors and muscle atrophy
- Role of bioassayable growth hormone in protein balance
- Gonadal steroids and muscle atrophy
- Muscle fiber type distribution relative to muscle weakness: a new method
- Mechanisms and control of disuse atrophy in skeletal muscle
- Biochemical adaptations of antigravity muscle fibers to disuse atrophy
- Alterations in skeletal muscle with disuse atrophy
- Immobilization/remobilization and the regulation of muscle mass
- The combined influence of stretch and mobility on muscle atrophy caused by immobilization

Table 4

Research Needs and Opportunities

Biochemistry, Endocrinology, and Metabolism

- Genetic engineering to induce muscle protein synthesis
- Role of lysosomes in muscle metabolism
- Effects on muscle of altered levels of hormones and their receptor sensitivities
- Regulatory roles of hormones in muscle physiology; e.g., growth hormones, somatomedins, insulin, corticosteroids, and anabolic steroids
- Endocrinologic effects of weightlessness combined with hypokinesia/hypodynamia

Inflight metabolic balance studies

Neurophysiology and kinesiology

- Astronaut activity: measurement of joint movements and muscle contractions; e.g., electromyography
- Neuromuscular output of astronauts: (1) measure maximum force at zero velocity of selected muscle groups; (2) maximum or a target force at a selected velocity
- Inflight neuromuscular fatigability; e.g., maximum force over 2 min with a maximal contraction every second
- In a model of hypokinesia/hypodynamia, measure resting membrane potential, extrajunctional acetylcholine receptors, and isometric strength of antigravity and non-postural muscles
- In a model of hypokinesia/hypodynamia, study the influence of neuronal circuits proximal to the motor unit on muscle integrity and strength

Models, Methodology, and Equipment

• Electromyogram, force, and velocity of selected muscles in rat models of "disuse" atrophy to help identify research models for muscle atrophy Program on Muscle Atrophy is complemented by other valuable ground-based studies in the Space Biology Program and by muscle studies scheduled for Spacelab 4. Finally, the ad hoc Working Group on Muscle Atrophy concluded that the research suggestions in the basic report (56) offer opportunities for future planning that would enhance the likelihood of achieving NASA's objectives in muscle atrophy research (see Suggestions for Research, below).

Suggestions for Research

The essential importance of acquiring, as soon as possible, human data on muscle physiology during all inflight opportunities and of experiments that could be

- B. Space Biology Program
- Weightlessness simulation: physiological changes in fast and slow muscle
- Renal function, water and electrolyte balance, and intestinal transport in hypokinetic animals
- Effects of muscle atrophy on motor control
- Influence of suspension-hypokinesis on skeletal muscle
- Skeletal muscle metabolism in hypokinetic rats
- C. Spacelab 4
- Effect of zero-gravity on biochemical and metabolic properties of skeletal muscle
- Electron microscopy, electromyography, and protease activity of rat hind-limb muscles
- Skeletal myosin iso-enzymes in rats exposed to zero-gravity
- Protein metabolism during space flight

Models, Methodology, and Equipment (continued)

- Utility of 3-methylhistidine as a marker of protein degradation
- Use of patients with spinal-cord-damage as models for electrically-induced exercise studies
- An animal model of pure disuse atrophy may result from motor nerve blockage by pharmacologic agents, e.g., tetrodotoxin
- A possibly useful model for studying mechanisms involves the process of reversion to pretraining status of exercised, hypertrophic muscle

Countermeasures

- Establish a data base on pre- and postflight maximal voluntary contractions of arm and leg muscles for use in improving inflight exercise regimens
- Determine minimum amounts of exercise to prevent muscle atrophy in a human model of hypokinesia/hypodynamia
- Investigate possible protective effects of dietary supplements of leucine, valine, and isoleucine, and their ketoanalogues
- Analyze effectiveness of eccentric muscular contraction in physical fitness and rehabilitation
- Determine biochemical, neurophysiologic and other parameters of muscle during adaptation to eccentric loading
- Investigate the possible preventive value against disuse atrophy of inhibitors of myofibrillar and other proteases involved in muscle protein turnover
- Determine the effects of preflight physical fitness training on preserving inflight neuromuscular function and retarding muscular deconditioning
- Investigate the effect of altered sensory perception of voluntary muscle contraction and optimal muscular contractions during inflight exercises

done with minimal encroachment upon the schedules of the spacecrews was strongly emphasized. Such measurements should be representative of a typical day's activities. They would be practical, designed not to interfere with crew duties, and would assess muscle strength, velocity of contraction, levels of electrical activity, and fatigability. The data would be compared with results of measurements of the same parameters in the same individuals in a typical day of ground activity. The suggestions of the ad hoc Group are summarized in Table 4. Each of the four groups of topics shown in Table 4 is presented in detail in the LSRO report to NASA (56).⁴

Conclusions

The skeletal muscle atrophy that has occurred inflight has apparently not compromised crew function during missions (except, possibly, during EVA and lunar surface EVA in Apollo 15), nor has it proved markedly disabling postflight. Nevertheless, recovery of normal muscular strength, bulk, and exercise tolerance has, in some cases, required from several days to several weeks. In missions lasting from ~ 3 wk to 6 mo, crew members who engaged in vigorous leg exercises have demonstrated an ability to maintain inflight aerobic exercise capacity as measured by bicycle ergometry. However, a postflight decrement in muscle strength and endurance has been universally observed, albeit to varying degrees.

In view of the fact that crew effectiveness has apparently not been compromised significantly by the muscle atrophy, one might conclude that it is of no practical consequence. However, this position would be fundamentally inconsistent with good preventive medical care of flight crews, the goal of which is to take all necessary precautions against any adaptive responses to space flight unless they are shown to be beneficial. Thus muscle atrophy is a significant biomedical problem of space flight. It justifies sufficient investigative effort to determine the exact causes and mechanisms involved, and, ultimately, some practical efficient means of prevention or control that will cause minimal interference with the astronaut's demanding schedules before, during, and after space missions.

NASA's current and planned research in this field, perhaps modified and augmented by adoption of some of the suggested research approaches in this report, should provide the necessary knowledge for solution of the problem. However, shortcuts to discovery of the basic mechanisms of space-related muscle atrophy are unlikely to emerge. Therefore, muscle atrophy, which is a significant biomedical problem of space flight, justifies a sustained, vigorous program of research, including long-term studies, as a part of NASA's major enterprises in space.

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⁴Since completion of the LSRO report (56) several pertinent papers have been published (27, 48, 52, 58, 113, 116).

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Satellite Symposia, XXX International Congress of Physiological Sciences

Second International Symposium on Excitation-Contraction Coupling in Muscle

The Second International Symposium on Excitation-Contraction Coupling in Muscle will be held in Edmonton, Alberta, Canada, 7–9 July 1986. This is a satellite symposium to the XXX International Congress of Physiological Sciences to be held in Vancouver, 12–18 July 1986. *Information:* Dr. George B. Frank, Department of Pharmacology, University of Alberta, 9-70 Basic Medical Sciences Building, Edmonton, Alberta T6G 2H7, Canada.

Interstitial-Lymphatic System Symposium

The Interstitial-Lymphatic System Symposium (in relation to liquid and solute movement) will be held 21-24 July 1986 at the Empress Hotel, Victoria, Vancouver Island, British Columbia, Canada. There will be six keynote speakers, eighteen invited discussants, and sixty abstracts will be accepted for posters. No registration fee. *Information:* Dr. N. C. Staub, Cardiovascular Research Institute, 1315-M, University of California, San Francisco, CA 94143.

Smooth Muscle Contraction Symposium

The Smooth Muscle Contraction Symposium is scheduled for 22-26 July 1986 at the Minaki Lodge, Minaki, Ontario, Canada. The main topics are ultrastructural organization of contractile machinery, mechanical properties (crossbridge mechanisms), biochemistry and regulation of contraction, regulatory mechanisms in skinned and intact muscle models, pathophysiological aberrations, and pharmacological modulation of intracellular regulatory mechanisms. *Organizers:* M. J. Siegman, A. P. Somlyo, and N. L. Stephens. *Information:* Dr. N. L. Stephens, Department of Physiology, University of Manitoba, 770 Banatyne, Winnipeg, Manitoba R3E OW3, Canada.

Travel Plans to Vancouver for the XXX International Congress of Physiological Sciences, 13–18 July 1986

- 1. Air Travel at discount prices with special bonuses, via Air Canada or United Airlines
- 2. A selection of Hotels in Vancouver
- 3. Pre-Congress motorcoach tour of the glorious Rockies, including Banff & Lake Louise, \$655.00
- 4. Post Congress 7-Day Cruise of Alaska aboard the magnificent Princess Cruises, \$1,475.00 (a very special price!)
- 5. Two week Tour of China including Beijing, Xian and Shanghai, plus Hong Kong, approx. \$1,400.00

1986 Lita Annenberg Hazen Award

Nominations of candidates of international stature for the 1986 Lita Annenberg Hazen Awards for Excellence in Clinical Research are being accepted. The award totaling \$100,000 honors physician-investigators whose accomplishments have changed our understanding of disease and encourages future research advances. Half of the prize is awarded to a young investigator chosen by the award winner to participate in current research. *Nomination deadline:* 28 February 1986. *Information:* James F. Glenn, Chairman, The Lita Annenberg Hazen Awards, Mount Sinai School of Medicine, 1 Gustave Levy Place, New York, NY 10029. Phone: 212/650-6588.

David Starr Jordan Prize for Innovative Contributions to the Study of Evolution, Ecology, Population, or Organismal Biology

Cornell, Indiana, and Stanford Universities have established a joint endowment to fund a prize in honor of David Starr Jordan, a scientist, educator, and institution builder with important ties to each of these institutions. The prize is international is scope and presented approximately every three years to a young scientist (less than 40 years of age) who is making novel, innovative contributions in one or more of the areas of Jordan's interest: evolution, ecology, population or organismal biology. The intent of the prize is to recognize young scientists who are making research contributions likely to redirect the principal focus of their fields. In addition to a cash award, the recipient receives a specially designed commemorative medal and is required to attend an awards ceremony, visit each of the institutions, and give scholarly presentations of her/his work. The selection of the prize winner is made by a committee composed of representatives from each of the three institutions. The first David Starr Jordan Award carries a prize of \$15,000 and will be announced in late 1986. Nomination forms: Dr. Rollin C. Richmond, Department of Biology, Indiana University, Bloomington, IN 47405. Nomination deadline: 1 April 1986.

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National Research Council Senior and Postdoctoral Research Associateships

The National Research Council announces the 1986 Resident, Cooperative, and Postdoctoral Research Associateship Programs for research in the sciences and engineering to be conducted in behalf of 25 federal agencies or research institutions whose laboratories are located throughout the US. The programs provide PhD scientists and engineers of unusual promise and ability with opportunities to perform research on problems largely of their own choosing yet compatible with the research interests of the supporting laboratory. Awards are made for one or two years; senior applicants who have held the doctorate at least five years may request shorter tenure. Stipends for the 1986 program year will begin at \$26.350 a year for recent PhDs and be appropriately higher for senior Associates. A stipend supplement approximately \$5,000 may be available to regular (not senior) awardees holding recognized doctoral degrees in those disciplines wherein the number of degrees conferred by US graduate schools is significantly below the current demand.

Applications must be postmarked no later than 15 January 1986 (15 April and 15 August 1986). Initial awards will be announced in March and April (July and November for the two later competitions) followed by awards to alternates later. *Information:* The Associateship Programs, Office of Scientific and Engineering Personnel, JH 608-D2, National Research Council, 2101 Constitution Ave., N.W., Washington, DC 20418. Phone: 202/334-2760.

Sixth International Symposium on Intensive Care and Emergency Medicine

The Sixth International Symposium on Intensive Care and Emergency Medicine will be held 15-18 April 1986 at the Brussels Convention Center. Sponsored by the European Society of Intensive Care, the symposium will include plenary lectures, minisymposium, found tables, and tutorials. Scientific contributions will also be selected for presentation as posters. *Information:* Dr. J. L. Vincent, Department of Intensive Care, Erasme University Hospital, Route de Lennik 808, 1070 Brussels, Belgium.

VI International Congress on Neuromuscular Diseases

The VI International Congress on Neuromuscular Diseases sponsored by the Muscular Dystrophy Association will be held 6-11 July 1986 at Century Plaza Hotel, Los Angeles, CA 90067. *Information:* NMD VI, KAM 318, USC School of Medicine, 2025 Zonal Ave., Los Angeles, CA 90033.

Books Received

Everest: The Testing Place. High adventure, medical science, and the thrill of mountaineering become one in *Everest: The Testing Place* by John B. West, MD, with a foreword by Sir Edmund Hillary (McGraw-Hill, \$18.95; publication date: 22 July 1985). This fascinating account of the American Medical Research Expedition to Everest (cosponsored by The American Physiological Society) in the fall of 1981 tells how five people reached the summit and, in spite of oxygen deprivation, treacherous weather conditions, and near tragedy, all returned.

Calcitonin 1984. Chemistry, Physiology, Pharmacology and Clinical Aspects. A. Pecile (Editor). Amsterdam: Elsevier, 1985, 498 pp., illus., index, \$92.50.

Directed Drug Delivery: A Multidisciplinary Approach. R. T. Borchardt, A. J. Repta, and V. J. Stella (Editors). Clifton, NJ: Humana, 1985, 384 pp., illus., index, \$59.50.

Exercise and Sport Sciences Reviews. Vol. 13. R. L. Terjung (Editor). New York: Macmillan, 1985, vol. 13, 596 pp., illus., index.

Fish Endocrinology. A. J. Matty. Portland, OR: Timber Press, 1985, 279 pp., illus., index, \$27.95.

Frontiers in Physiological Research. D. G. Garlick and P. I. Korner (Editors). Canberra: Australian Acad. Sci., 1984, 391 pp., illus., index, \$100.00.

Homeostatic Function and Aging. B. Davis and W. G.

Wood (Editors). New York: Raven, 1985, vol. 30, 222 pp., illus., index, \$35.00.

Human Genetics: An Introduction to the Principles of Heredity (2nd ed.). S. Singer. New York: Freeman, 1985, 198 pp., illus., index, \$13.95.

Inositol and Phosphoinositides: Metabolism and Regulation. J. E. Bleasdale, J. Eichberg, and G. Hauser (Editors). New York: Humana, 1985. 720 pp., illus., index, \$69.50.

Lecture Notes on Nephrology. D. B. Evans and R. G. Henderson. Boston: Blackwell, 1985, 240 pp., illus., index.

Membrane Protein Biosynthesis and Turnover. P. A. Knauf and J. S. Cook (Editors). Orlando, FL: Academic, 1985, vol. 24, 531 pp., illus., index, \$89.00.

Oxytocin: Clinical and Laboratory Studies. J. A. Amico and A. G. Robinson (Editors). Amsterdam: Elsevier, 1985, 448 pp., illus., index, \$111.00.

The Physiological Ecology of Seaweeds. C. S. Lobban, P. J. Harrison, and M. J. Duncan. New York: Cambridge, 1985, 242 pp., illus., index.

Resistance Vessels: Physiology, Pharmacology and Hypertensive Pathology. M. J. Mulvany, S. Strandgaard, and F. Hammersen (Editors). Basel: Karger, 1985, 236 pp., illus., index, \$59.75 (soft cover).

Barbara C. Hansen, Ph.D., has moved to Baltimore, Maryland, to become Vice-Chancellor for Graduate Studies and Research at the University of Maryland at Baltimore. Dr. Hansen, former Associate Vice President at Southern Illinois University at Carbondale, has been an APS member since 1978. . . . Jackie D. Wood, Ph.D., former Professor and Chairman of Physiology at the University of Nevada Medical School has moved to Columbus, Ohio, to become Chairman and Professor of Physiology at Ohio State University, School of Medicine. In addition, Helen J. Cooke, Ph.D., has also moved from the University of Nevada to become Professor of Physiology at Ohio State University. Dr. Wood is a member of the Society's Finance Committee and Dr. Cooke chairs the Committee on Women in Physiology. . . . APS member Peter K. Lauf, M.D., former Professor of Physiology at Duke University School of Medicine has moved to Dayton, Ohio, to become Chairman and Professor of Physiology and Biophysics at Wright State University, School of Medicine. . . .

At the October 16-17 Institute of Medicine (IOM) annual meeting, APS member Samuel O. Thier, M.D.,

Department Chairman. The Louisiana State University School of Medicine, Shreveport, invites nominations and applications for the Chairmanship of an expanding Department of Physiology and Biophysics. Candidates must have an outstanding record of research, strong commitment to medical and graduate teaching, and the vision and experience to establish and lead a department of excellence. Applicants must provide a curriculum vitae, names of three references and statement of research interests to Dennis J. O'Callaghan, Chairman, Physiology Search Committee, Louisiana State University Medical Center, 1501 Kings Highway, Shreveport, LA 71130. [EOAAE.]

There is a \$25 charge per issue for each position listed. A check or money order payable to the American Physiological Society must accompany the copy. Purchase orders not accepted unless accompanied by payment. Ads not prepaid will not be printed. Copy must be typed double-spaced and limited to 150 words. All copy is subject to the editorial policy of *The Physiologist*. EOAAE indicates Equal Opportunity/Affirmative Action Employer and appears only where given on original copy. Copy deadline: copy must reach the APS office before the 15th of the month 2 months preceding the month of issue (e.g., before 15 December for the February 1986 issue). Mail copy to APS, 9650 Rockville Pike, Bethesda, MD 20814. was selected to become the fifth president of IOM succeeding Dr. Frederick C. Robbins. Dr. Thier is currently Sterling Professor and Chairman of the Department of Internal Medicine at Yale University. Dr. Thier is the author of numerous research papers, as well as coauthor of a medical textbook. His main research interest is the study of inherited disorders affecting kidney function.

Four APS members were among the 870 academics receiving awards under the Fulbright Scholar Program to travel, lecture, consults, and conduct advanced research abroad in 1985-86. The APS awardees include **Robert L**. **Hazelwood**, Professor of Physiology at the University of Houston for study in India; Leonard B. Kirschner, Professor of Zoology at Washington State University for study in Denmark; Stephen L. Lipsius, Associate Professor of Physiology at Loyola University Stritch School of Medicine for study in Belgium; and Michael V. L. Bennett, Professor and Chairman of the Department of Neuroscience at Albert Einstein College of Medicine for study in Yugoslavia.

Positions Available

Research Associate. A two- to three-year position at the rank of Postdoctoral Research Associate is available at the University of Tennessee, Memphis, to work with Dr. William R. Crowley (Dept. of Pharmacology) and Dr. C. E. Grosvenor (Dept. of Physiology) on research dealing with neurochemical and cellular mechanisms regulating luteinizing hormone, prolactin, and oxytocin secretion. Candidates should have a PhD or MD degree. Send a curriculum vitae, brief statement of research interests, and the names of three references to either Dr. Clark Grosvenor, Professor, Department of Physiology and Biophysics or Dr. William R. Crowley, Associate Professor of Pharmacology, University of Tennessee, Memphis, TN 38163. [EOAAE]

Space Biology Research Associate Awards. The advent of the Shuttle Program has produced a new era for Space Biology that offers exceptional opportunities for research. NASA is offering several Research Associate Awards for scientists to work in laboratories capable of providing scientific advice and facilities relevant to Space Biology. The awards vary from \$18,000 to \$22,000 based on experience. They are for a 12-month period with the possibility of renewal. Proposals are due February 1. The funding will begin anytime from June 1 to October 1. Eligible are postdoctoral US citizens. Information and application forms: Dr. X. J. Musacchia, Chairman, NASA Award Committee, Graduate Programs & Research, University of Louisville, Louisville, Kentucky 40292 or Dr. Thora W. Halstead, Research Associates Program, Life Sciences Division, NASA Headquarters, Washington, DC 20546.

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