

## Publishing in Peer-Reviewed Journals Fundamentals for New Investigators

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According to statistics recently compiled by Aldrich et al. (1), in 1989 and in 1990 a total of 406 individuals received their PhD degrees in areas represented by the American Physiological Society. The majority of these individuals have started their careers in the academic, federal, or private sectors and have assumed professional responsibilities that include the communication of their scientific knowledge to students, staffs, colleagues, or superiors. Inherent with these responsibilities is an obligation to the physiology community to share this information to advance and to improve our understanding and awareness of physiological processes and mechanisms. The best way to fulfill this responsibility is to publish in scientific reviewed journals. Publishing in peerreviewed journals is not only altruistic for the advancement of physiology, it is essential for successful grantsmanship, peer recognition, academic or job promotions, prestigious invitations, and for the obtainment of full membership within APS. Unfortunately, few individuals who have recently been awarded their PhD degrees have also received information concerning the fundamentals of publishing in peer-reviewed journals. This article, which was a presenta-

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tion at the 1990 APS fall meeting, incorporates the viewpoints of many APS members who have been successful as authors, reviewers, or editors.

#### Publishable Manuscripts Require Good Questions, Designs, Methodologies, Data, and Presentations

It is very difficult to publish data in peer-reviewed journals from studies that are flawed by their purposes, designs, and methodologies regardless of how well they are presented. In fact, one of the advantages of the review system is to keep such studies from being published in the physiology literature, because they create unnecessary confusion and controversy and they impede the progress of science. It must be also appreciated however that there is no assurance that the completion of a good study will automatically ensure publication by a journal that has been selected by the author.

#### Select the Appropriate Journal

There are now approximately 40,000 scientific and technical journals published throughout the world, and of this number, most of the significant literature is published within 1,000 journals or less (2). The majority of the information that is important to APS members is found in approximately 200 journals (2). Because of the large number of journals published, it should be no surprise that if an author is sufficiently persistent, most submitted articles will eventually be published by a "scientific journal."

As a basic rule, the investigator should first consider the journal of his/her professional society. Most societies have a journal or journals whose editorial boards are represented by its members. The APS has 10 peer-reviewed specialty journals; consequently, the submission process becomes more (continued on p. 278)

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#### **PRESIDENT'S COLUMN**

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As A Matter of Opinion

## **On Writing Abstracts**

I have made this letter longer than usual because I lack the time to make it shorter.

Blaise Pascal Provincial Letters. XVI. 1657

work may have little impact. To write simply and concisely requires development of skill not only in writing clearly but also in distilling the essence of your research. The basis of such skills is planning ahead.

#### Planning the Abstract

## Guideline 1: Write Early and Often

The most serious fault committed by abstract writers is delaying until the last moment. As surely as Pascal's apology is true, the time to begin preparing an abstract is weeks, not a day or a few hours, before the deadline. Surely the central theme must already be in mind, from which the title and introductory sentence follow naturally. With the wide availability of word processors, one can rewrite the abstract frequently as the message becomes more clearly defined in one's mind.

In my laboratory we think nothing of revising an abstract 10 or 20 times with input by several people during the month or 6 weeks before the due date. In that way simplicity and clarity win out over rhetoric or purple prose. Sometimes the submitted abstract bears little resemblance to the original version. None of us is above suspicion. I have written at least 100 abstracts over the years and have read and revised as many more. I still find that others who read my early drafts often detect important errors of omission as well as commission, and they nearly always recommend deletion of my favorite line.

Because the space allotted for APS (FASEB) abstracts is about the smallest permitted by any scientific organiza-

a scientific abstract when he made his famous remark, but 334 years later, his admonition about how difficult it is to write succinctly is still true. Although what I write here is also applicable to full papers and to posters, it is particularly appropriate now that abstractwriting season for the spring physiology meeting is upon us. So let me consider the purpose of an abstract and present a few guidelines by which you can write one effectively.

I don't suppose Pascal was writing

An abstract should be a synopsis of the most important aspect of your research, and clarity should be the main objective for effective communication. The abstract should have a concise, descriptive title, so others will find it, and it should consist of simple declarative statements, so others will comprehend the message. You may have done the best experiment in your field, but if no one can fathom your abstract, your

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

Headquarters phone: 301-530-7164. Fax: 301-571-1814.

tion, it is useful to follow the "one ideaone abstract" concept. In other words, it is not necessary or desirable to put every nuance of an experiment into the abstract.

At the first draft or two, of course, you should include everything you think may be important. If you type with the margins set to the allowed width of the abstract space, you can easily tell when you have exceeded the proper length. Do include the title and all of the author data. However, do not be concerned about fonts, justification, proportional spacing, or lines per inch. All that is easily adjusted for the penultimate draft. Get the message right and the format will take care of itself.

### Abbreviations

# Guideline 2: No Nonstandard Abbreviations

Dare I tread on one of science's most sacred precincts? Yes. Do not use any abbreviations other than those internationally accepted. One possible exception is in a table or a graph. Use of new abbreviations is one way to ensure that others will overlook your abstract. If you think you are saving space, thereby allowing more room for information, forget it. Very little space is saved, what replaces the full words is probably not important, and clarity of communication is lost. I give a double condemnation to those who include abbreviations in abstract titles.

One investigator told me he wrote abbreviations for frequently used terms because he thought readers would become bored by repetition of the complete phrase. More likely, his abstract was inherently boring because of unnecessary repetitions. Most of us automatically think out the full phrase anyway, especially when the abbreviation is a new one, so nothing is gained by using abbreviations. I applaud the APS journal policy of not allowing abbreviations in abstracts to papers. I believe it has already had a salutary effect on abstract writing for our meetings.

# Linear Writing Replaced by Table or Graph

#### Guideline 3: Organize Data Into Tables or Graphs

Nothing is more difficult for me to decipher in an abstract than several lines of linear data. Nearly all data can be presented in a simple table or graph. In my laboratory, nearly every abstract contains a table of data. Because space is limited, one soon learns what is central and what is marginal. All primary relevant data, even if negative, ought to appear in a paper, but in an abstract only the essential positive results are required. It is neither necessary or helpful to cram extraneous information into the abstract.

Table or graph headings are the one place where abbreviations may be re-

quired, but even here their use should be minimal and the terms clearly explained in the text. I am please that the use of tables and graphs in physiology abstracts has increased over the last few years, although such abstracts are still in the minority. If one can't summarize the data in a table or a graph, maybe there's not enough material for an abstract.

Try the following experiment. Begin your next APS abstract one month before the due date and do not use any nonstandard abbreviations during the early drafts. Arrange your data presentation as a table or a graph. I'm certain your abstract will take form more easily, be clearer, and fit the available space, in which case you will have made a positive step toward clear communication.

Norman C. Staub

Future Meetings					
<b>1992</b> FASEB Spring Meeting	April 5-9, Anaheim, CA				
APS Conference: Integrative Biology of Exercise	September 23-26, Colorado Springs, CO				
APS Conference: Cellular and Molecular Biology of Membrane Transport	November 4-7 Orlando, FL				
<b>1993</b> FASEB Spring Meeting	March 28-April 1, New Orleans, LA				
<b>1994</b> FASEB Spring Meeting	April 24-29, Anaheim, CA				

#### An APS Journal Goes Monthly

The Publications Committee is pleased to announce that, effective with the January 1992 issue, the *American Journal of Physiology: Lung Cellular and Molecular Physiology* will begin monthly publication. This change reflects a steady growth in the number of high-quality papers submitted to the Journal and will accelerate the publication process.

#### TIPTON

#### (continued from p. 275)

selective. The simplest approach is for the author to ask the question, "Whom do I want to read and be influenced by my manuscript?" The answer can be found by looking at the names of the editor, associate editors, and the members of the editorial boards of the various journals. If the people the authors know and respect are listed, the problem has been solved. On the other hand, if the intent of the author is to be read in journals that have high impact factors and citation ratings, he/she should first become familiar with the evaluation system described by Salive (2). Quite frankly, few APS members understand these terms or the system because it is primarily used for esoteric, comparative, or financial reasons by librarians, editors, or committees concerned with the reorganization, elimination, justification, or establishment of journals. Moreover, the publishers of the Science Citation Index evaluate all the individual journals of the American Journal of Physiology as one (2).

If for any reason a potential author is uncertain about the types of manuscripts being encouraged by a particular journal, he/she should contact the editor or an associate editor to verify that the journal would be receptive to review the study in question.

#### Understand the Process by Which Reviewers Are Selected

Once the journal has been identified, it is essential that the instructions to authors be read before submitting the desired number of copies to a given address. Most submitted manuscripts go to a central location before being assigned by the editor to an associate editor for reviewer assignment. In some situations the editor keeps the manuscript for processing from his/her office. If authors have a preference for a specific associate editor, they should indicate this fact when they submit the manuscript. With few exceptions, this request is honored. Before the two or three reviewers are selected, the corresponding editor first examines the subject area of the study as well as the title, abstract, text, key words, and references. In addition, they check their files for the names of individuals who have expertise in the areas identified within the manuscript. Because of the large number of manuscripts they receive and their other responsibilities, most corresponding editors do not critically evaluate the manuscript until the reviews are completed. The end result is that the abstract, title, and references become extremely important considerations in the selection of the reviewers.

#### Understand the Rudiments of the Review Process

Once reviewers have been selected, they are forwarded rather detailed instructions on how to undertake the evaluation and the specific critique sheets on which they are to write comments for the corresponding editor as well as a review for the author. In the information returned to the corresponding editor, the reviewer circles one of four ratings: acceptable in its present form, acceptable with suggestions for revision, acceptable only if adequately revised, and unacceptable for publication. Most journals have the reviewer provide a priority rating on the importance of the study to our existing body of knowledge, with 1 being the most and 5 being the least important. In addition, the reviewer provides some commentary on the strong and weak features of the study. This information plus comments on the returned critique form is used by the corresponding editor to inform the author of the "fate" of the manuscript. The crux of this process is that the reviewer is basically instructed by the journal to look for what is new, unique, distinctive, or innovative about the study that will advance our understanding about a physiological process or mechanism. Unless the manuscript can make that point clearly and emphatically, the study faces the possibility of rejection. In 18 years as a section editor, associate editor, or editor for various journals, I have not seen one submitted manuscript that was accepted without a revision. In essence, expect revision but avoid rejection by presenting manuscripts that demonstrate clearly and effectively why the study is worthy of publication.

Until recently, very few institutions or professional societies offered sessions or workshops on reviewing manuscripts. Although it is not the intent of this article to cover the topic of why manuscripts are rejected, reviewers are inclined not to be receptive to manuscripts that are vague, poorly written, contain numerous misspellings, have references that are wrong or are not in the style required by APS (usually interpreted as a manuscript rejected by another journal), or combinations thereof.

## Expect to Have Interactions With the Corresponding Editor

It is most unlikely that any submitted manuscripts will be accepted for publication without revision. Within APS journals, the acceptance rate ranges from 52% to 72%, with the average around 60%. Although situations vary among journals, many manuscripts require two revisions and some three before they are accepted for publication. To me, these revisions provide the quality control that enables APS journals to achieve premier ratings in their specialty areas. It also means that authors have considerable interaction(s) with the corresponding editors of these journals.

As the intermediary between the author and the publisher, the corresponding editor must balance the rigors of science, the purposes of the journal, the viewpoints of the reviewers, and the integrity of the data with the convictions of the investigators. This is a difficult task that requires good faith and effective communication by all parties. When hard decisions must be made, they favor science rather than personalities. In the main, reviewer's opinions are upheld, although all corresponding editors are sensitive to the opinions of authors and receptive to appeals or requests for expert input. If impasses are reached, authors have the prerogative to withdraw and resubmit without prejudice. Authors can also appeal their rejections, but usually this process involves only the editor. As a general rule, authors of rejected manuscripts should reflect on the reasons for at least four weeks before accepting the generalization that editors and reviewers are ignorant, insensitive, and prejudiced against them and their research area.

#### The Peer Review System Is Not Perfect

Any process that requires the use of human judgment is imperfect and subject to criticism, and the peer review system is no exception. However, the system has enabled the APS to publish journals that have achieved premier status in their scientific specialties. This achievement did not occur by chance; rather it occurred because of the scientific integrity of dedicated and knowledgeable reviewers and their corresponding editors who placed the welfare of the journal over their personal biases and convictions. The young investigators of today will be reviewers and editors of tomorrow. Hopefully the fundamentals listed will assist them in assuming these responsibilities in the days ahead.

#### References

- Aldrich, L. M., D. G. Stuart, and R. Alison. Association of chairman of departments of physiology annual questionnaire results. *Physiologist* 34: 72, 1991.
- 2. Salive, J. E. APS journals and the science citation index. *Physiologist* 32: 249, 1989.

### APS Conference Integrative Biology of Exercise

#### September 23–26, 1992 Colorado Springs, CO

Wednesday, September 23	Thursday, September 24	Friday, September 25	Saturday, September 26
Symposium 3:00-6:00 pm Limiting factors for maximum performance: how do we define and test them?	Tutorial 8:00-9:00 am Exercise in the diabetic. Lecturer: E. Horton	Tutorial 8:00-9:00 am Protein polymorphism and muscle function. Lecturer: Richard L. Moss	Tutorial 8:00-9:00 am Metabolic integration during exercise. Lecturer: B. Saltin
Chair: Stan Lindstedt Symposium 3:00-6:00 pm Body fluid homeostasis during exercise. Chairs: Ethan Nadel/ Carl Gisolfi	Tutorial 8:00-9:00 am Control of glycolysis in contracting muscle. Lecturer: R. Connett	Minisymposium 8:00-9:00 am Theories for the decreased maximal blood lactate level in chronic hypoxia. Chair: Paulo Cerretelli	Tutorial 8:00-9:00 am Evolution of olympic performance. Lecturer: P.O. Astrand
	Symposium 9:00 am-Noon The lung at the limit of its function during exercise. Chair: Brian J. Whipp	Symposium 9:00 am-Noon The PO2 gradient from hemoglobin to cytochromes. Chair: Peter Wagner	Symposium 9:00 am-Noon Neural control of the cardiorespiratory systems during exercise. Chair: Jere H. Mitchell
	Symposium 9:00 am-Noon Control of lipid oxidation in contracting muscle. Chair: Jeanie McMillin	Symposium 9:00 am-Noon Cellular bases of muscle adaptation. Chair: K. Baldwin	Symposium 9:00 am-Noon Human versus nonhuman models of exercise: what can we learn from animals? Chair: James H. Jones
	Symposium 3:00-6:00 pm Microvascular function in contracting skeletal muscle. Chair: Brian Duling	Symposium 3:00-6:00 pm Cellular bases of skeletal muscle fatigue. Chair: Robert Godt	Symposium 3:00-6:00 pm Regulation of respiration in striated muscle. Chair: M. Kushmerick
	Symposium 3:00-6:00 pm Muscle mechanics: from molecular cross-bridges to intact animals. Chair: Richard Taylor	Symposium 3:00-6:00 pm Effects of exercise training on the coronary circulation. Chair: M. Harold Laughlin	Symposium 3:00-6:00 pm Exercise during physiological and pathophysiological states.
	Flying W Ranch 6:30 pm Dinner and Entertainment	Banquet Lecture and Award Presentations 7:30 pm Featuring: Sir Roger Bannister	Chair: C. Gunnar Blomqvist

## Preview APS/FASEB 1992 Spring Meeting Symposia

### Anaheim, California April 5–9, 1992

# Immunomodulation of Smooth Muscle in the Gut

Sponsor: APS Gastrointestinal Section. Chair: S. Collins. Participants: J. Gauldie, P. Libby, F. Cominelli, W. Snape Jr., S. Collins, and M. Graham.

This symposium will examine the response of smooth muscle to immune activation, with a particular interest in the impact of intestinal inflammation on muscle function. The main objectives are to update our understanding of the inflammatory process and to conceptualize the role of muscle in the inflamed gut. The program will address current concepts of the inflammatory responses, with special emphasis on the roles of cytokines. Changes in smooth muscle function following immune activation will then be discussed at a variety of levels, ranging from clinically relevant changes in motility observed in humans with Inflammatory Bowel Disease, to those at the level of the muscle cell. The issue of whether muscle responds to immune stimulation simply as an "innocent by-stander" or as an active participant will be discussed, and examples are drawn from work done in vascular smooth muscle. The symposium will conclude with reviews of changes in smooth muscle from the inflamed intestine of animals and humans.

# Genome Mapping and Sequencing: Role in Cell Physiology

Sponsor: APS Cell & General Physiology Section. Chair: R. A. Frizzell. Participants: R. A. Frizzell, D. R. Cox, R. L. White, D. Schlessinger, and D. K. Granner.

Gene organization and regulation of gene expression have emerged as topics of central importance in developmental biology, molecular endocrinology, and cell physiology. The Human Genome Initiative (NIH and DOE) is now sponsoring a concerted effort to generate complete physical and genetic linkage maps of the human, mouse, yeast, and selected invertebrate genomes within 10 years. The technologies, under development, the indexed sites, and repositories of overlapping DNA fragments and cell hybrids that are the products of the HGI should accelerate substantially the application of genetics to physiology. The symposium will cover five main topics: 1) cystic fibrosis: a paradigm of the genetics-cell physiology connection; 2) the power of somatic cell genetics in mapping DNA sequences and genes to chromosomal sites; 3) the use of polymorphisms in constructing global genetic linkage maps of chromosomes; 4) the incorporation of mammalian and other large heterologous DNA fragments into yeast artificial chromosomes (YACs) and the generation of complete libraries of overlapping segments; and 5) the exploitation of mapping and sequencing technologies and reagents in physiological research.

# Effects of Hypoxia on Cellular Protein and Gene Expression

Sponsor: APS Hypoxia Interest Group. Chairs: H. W. Farber and P. W. Hochachka. Participants: P. W. Hochachka, H. W. Farber, H. F. Bunn, G. R. Anderson, and R. S. Zitomer.

Exposure to acute and chronic hypoxia alters the metabolic function of most cell types studied. Although many of these alterations have been described and investigated, the basic protein and genetic effects of hypoxia are not well understood. Yet, these basic responses likely protect the cell against the potentially toxic effects of hypoxia, cause release of factors that influence surrounding and potentially distant milieus, and possibly alter the phenotype of the cell. In this symposium, we will examine the established effects of hypoxia on both cellular proteins and gene expression. We will address the basic cellular mechanisms by which organisms and their resident tissues and cells might develop tolerance to acute or chronic hypoxia. We will also discuss the role of hypoxia in regulation of gene transcription and possibly in inducing malignant phenotypes. Each presentation will summarize the existant knowledge in the field, emphasizing the speaker's contribution, and will identify areas of controversy and areas where data are lacking. The discussion provoked by these presentations will provide better understanding of current concepts of hypoxic regulation of cell function and should help direct future research in this growing and important area.

### Integrative Thyroid Physiology in Conventional and Comparative Animal Models

Sponsor: APS Comparative Section. Chair: H. B. John-Alder. Participants: F. Ismail-Beigi, H. B. John-Alder, R. Denver, C. Brown, and J. G. Eales.

Basic research on thyroid physiology is an area of widespread interest and active research among comparative physiologists as well as more classical physiologists who utilize conventional animal models. Too often, however, "conventional" research and comparative research proceed along nearly independent courses. This symposium will survey current research on thyroid physiology in a conventional mammalian model system as well as in ectothermic vertebrates of particular interest to comparative physiologists. The symposium will draw attention to unifying functional themes in vertebrate thyroid physiology even while focusing on features that have restricted taxonomic distribution. Central goals of this symposium are *1*) to illustrate the usefulness of an integrative, organimal perspective for establishing the interpretational context of mechanistic research and *2*) to emphasize the role that conventional thyroid research can serve in guiding reductionist, mechanistic investigations

on comparative models. In the latter context, the symposium will illustrate the utility of ectothermic models for integrated research on organismal roles and molecular actions of thyroid hormones. Ismail-Beigi will discuss the molecular basis of thermogenic actions of thyroid hormones in mammals, with particular emphasis on the nuclear events underlying responses of the Na\*-pump. The juxtaposition of Ismail-Beigi's "classical" research with presentations on ectothermic physiology will enhance the general attractiveness of the symposium and will draw attention to the less well-known areas of research. John-Alder will describe organismal correlates of thyroid hormonal stimulation of resting metabolism in reptiles, animals that do not use metabolic heat for temperature control, and will demonstrate the importance of experimental studies on free-living animals in natural populations. Denver will illustrate broad similarities between endotherms and ectotherms in the molecular control of the pituitary-thyroid axis, despite fundamental differences between these groups in their hypothalamic responses to environmental temperature. Brown will describe thyroid hormonal roles during embryonic, larval, and postlarval development in fishes and will thus extend this well-known functional context that is deeply entrenched in the amphibian literature. Eales will discuss the regulation of thyroxine deiodination in fishes and will present evidence of particular dietary components that modulate cellular autoregulation via deiodination pathways. Eale's presentation will have considerable general appeal, because clinical interest in the regulation of thyroid function has focused increasingly on cellular autoregulation through control of peripheral deiodination of thyroxine.

### Mechanisms of Hyperpnea-Induced Airflow Obstruction

Sponsor: APS Respiratory Section. Chairs: J. Solway and P. M. Vanhoutte. Participants: P. M. Vanhoutte, J. M. Drazen, J. Solway, E. R. McFadden, Jr., P. D. Pare, Jr., A. R. Leff, and P. T. Macklem.

Hyperpnea-induced bronchoconstriction (HIB) is a cardinal feature of exercise-induced asthma. Although it seems clear that airway heat and water exchange play a key role in provoking HIB in human asthma, the precise mechanism by which this occurs remains a matter of controversy. Recent mechanistic studies, conducted in human subjects and in novel animal models of hyperpnea-induced airway responses, have focused on three interrelated facets of the pathogenesis of HIB. 1) The nature of airflow obstruction: the longheld notion that airway smooth muscle constriction leads directly and quantitatively to airflow obstruction has been questioned. Rather, it may be that bronchial hyperemia, with or without edema, narrows the airway lumen directly or potentiates lumenal obstruction caused by smooth muscle constriction. 2) The physical stimulus that precipitates HIB: both heat and water losses occur during dry gas hyperpnea, and their local effects on airway temperature and hydration are axially distributed along the airways. The nature of the provocative stimulus is a central yet unsolved issue, as is the mechanism by which the physical stimulus is transduced and by what airway wall cellular constituents. 3) The biochemical pathways involved: a variety of mediators (including tachykinins and eicosanoids) are released by cool, dry gas hyperpnea under various experimental conditions. These compounds can increase bronchial blood flow and vascular permeability and can lead to airway smooth muscle constriction. It also seems likely that release of one compound may itself elicit the secretion of others. Thus HIB may be provoked by complex, distributed physical stimuli (heat and water loss) that may act through a variety of interacting biochemical mediators capable of causing airflow obstruction by alterations in bronchial blood flow, accumulation of edema, or airway smooth muscle contriction. To sort out these controversies, five well-known investigators will present relevant studies briefly and then will adress these issues in a round-table discussion lead by two additional international authorities on this topic.

### Pericyte and Mesangial Mechanisms and Microvascular Function

Sponsor: APS Cardiovascular Section. Chair: D. Shepro. Participants: D. Shepro, I. Herman, P. D'Amore, N. Morel, H. E. Abboud, B. Ballerman, and K. F. Badr.

Endothelial cells constitute the primary physical barrier between blood and tissues in the microvasculature. The other microvessel wall cell is the pericyte (PC), which is termed the mesangial cell (MC) in the renal microcirculation. In contrast to endothelium, amidst much speculation, little is known about the biology of PC/MC and their roles in the microvasculature. The symposium has three objectives: 1) to demonstrate the importance of phenotypic biochemical markers as they relate to the physiological characteristics of specific tissue microcirculation, 2) to show that PC/MC affect endothelial differentiation; and 3) to show that paracrine communication between PC/MC and endothelial cells in part autoregulates microvascular perfusion and permeability.



### New Maps of Flow for the Lung: Fractal, Statistical and Anatomic Descriptions

Sponsor: APS Respiratory Section. Chair: H. T. Robertson. Participants: H. T. Robertson, K. C. Beck, R. W. Glenny, T. A. Wilson, E. A. Hoffman, J. B. West, J. B. Bassingthwaighte, J. C. Hogg, and J. R. Rodarte.

Almost three decades have passed since the formulation of the gravitational gradient hypothesis to explain the heterogeneity of both ventilation and perfusion in the lung. However, even the original studies that supported the gravitational hypothesis recognized nongravitational variability, which at the time was attributed to random biological noise. Recent studies utilizing several different methodologies have vielded progressively higher resolution maps of regional blood and gas flow in the lung, and it is now apparent that this nongravitational variability has patterns that are not random. While there is continuing debate as to the extent of the variability, it now appears to be at least as large as the gravitational influence in horizontally oriented lungs. New information on lung function in weightlessness from the spacelab mission has confirmed the existence of nongravitation heterogeneity in the lung. In addition to providing more accurate maps, these new data sets permit the application of analytic techniques that offer a new perspective on the concept of physiological heterogeneity. The distribution of blood flow in the lung can be described as a fractal structure. This mathematical approach to the description of regional flow heterogeneity has the intuitively appealing property of being linked to the bifurcating structure of the lung. Now that high-resolution blood flow and ventilation data sets are available, it is an appropriate time to discuss both the advantages and weaknesses of the various measurement techniques and to discuss the insights pitfalls of the fract and local correlation techniques used to analyze these new maps of flow.

# How is Urine Concentrated by the Renal Inner Medulla?

Sponsor: APS Renal Physiology Section. Chairs: J. L. Stephenson and D. J. Marsh. Participants: M. A. Knepper, L. Bankir, M. Imai, H. Layton, D. J. Marsh, and J. L. Stephenson.

Hypertonic urine is formed in the mammalian kidney by extraction of water in excess of solute from the collecting duct fluid as it traverses the medullary osmolality gradient, which in the concentrating kidney rises steadily from cortical-medullary junction to papilla. In the outer medulla, the underlying process generating the gradient is well understood to be countercurrent multiplication driven by active NaCl absorption from the thick ascending limb of Henle's loop. Here there is quantitative agreement between models and data. In the inner medulla, there are no thick limbs and no demonstrable active transport of any significance from thin limbs; consequently, the underlying process generating the gradient must necessarily differ from that in the outer medulla. Earlier models proposing that the gradient is generated by urea diffusing in from the collecting duct mixing with salt diffusing out of thin ascending limb have failed when tested quantitatively with computer simulations. Consequently several investigators have recently offered new models to explain concentration in the renal inner medulla. The purpose of the symposium is to present these models and so to address the specific question asked by its title. Whatever the model, it must satisfy mass balance requirements, which will

be outlined by Knepper. The model must also meet the architectural constraints imposed by the medullary anatomy; these will be addressed by Bankir. Finally, the model must incorporate the transport characteristics of the various nephron segments as determined by perfusion studies; these will be described by Imai. The new models themselves embody two general directions. In one, exemplified by March and Imai, more account is taken of the detailed architecture of the inner medulla. In the other, exemplified by Layton and Stephenson, the possible effect of previously unconsidered forces driving multiplication is analyzed. The symposium will bring together individuals who have taken a predominantly experimental approach (Bankir, Imai, and Knepper), individuals who have taken a predominantly theoretical approach (Layton and Stephenson), and an investigator who has used both methodologies (Marsh). In addition, Layton will present experimental data from animal studies and isolated perfused tubule studies gained in his collaboration with Knepper. The symposium will bring the audience an update on ongoing studies of the concentrating mechanism, previously published in diverse journals, some of which are unlikely to be available to the general audience. The symposium should also provide the audience with the conceptual basis for teaching the urinary concentrating mechanism.

# Imaging Techniques for Assessing Cell Function

Sponsor: APS Education Committee. Chair: F. S. Fay and L. J. Heller. Participants: L. J. Heller, D. L. Taylor, R. Y. Tsien, S. Block, and F. S. Fay.

In recent years, new methods for visualizing cellular structure and function have greatly increased our understanding of basic cellular processes. Because of extensive interest in these techniques, the APS Education Committee is presenting this symposium aimed at providing basic information and broad descriptions of several current imaging techniques. The presentations will include descriptions of the use of fluorescent analogs, fluorescent indicators, caged compounds, optical traps, and the digital imaging microscope for imaging cytoskeletal structures, signal transduction mechanisms, and cellular function. The use of these techniques in a variety of cell and tissue types will be presented with special emphasis on vascular smooth muscle and blood vessels.

#### Renal Responses to Altered Sodium Intake

Sponsor: APS Water & Electrolyte Homeostasis Section. Chairs: J. L. Osborn and R. J. Roman. Participants: J. P. Granger, J. L. Osborn, E. G. Schnieder, R. J. Roman, and O. Carretero.

This symposium is designed to provide current viewpoints regarding the regulation of sodium and water balance following changes in sodium and water intake. It is well known that plasma sodium concentration remains constant during large fluctuations in sodium intake. The route of administration of the sodium load, the volume of sodium load, and the relative sodium concentration all may induce alterations in humoral, neural, and physical factor controllers of urinary sodium excretion. The signal sensed by the kidneys, the cardiovascular system, or the neural systems has recently been studied with several experimental approaches. This symposium will explore each of these factors and provides a current discussion of the mechanisms underlying the regulation of sodium balance and extracellular fluid volume homeostasis.

### Reconstructive Therapies for Muscle Deficits: From Direct Gene Transfer to Whole Muscle Transplantation

Sponsor: APS Myo-Bio (Muscle) Group. Chair: J. A. Faulkner. Participants: E. J. Schultz, B. M. Carlson, J. A. Faulkner, G. K. Pavlath, and G. Karpati.

Structural and functional deficits in skeletal muscles may result from denervation, inherited and acquired diseases, and direct trauma. The question addressed by this symposium is, "To what degree can structural and functional deficits be reversed by the appropriate selection of transplantation of whole skeletal muscles, with or without immediate neurovascular repair; of myoblast transplantation; or of direct gene transfer?" In addition, underlying mechanisms will be addressed. The number of satellite cells and their ability to migrate within muscles will be related to the growth and regeneration of skeletal muscle fibers. In free whole skeletal muscle grafts, the influence of factors inherent to host organisms of different ages will be contrasted to factors intrinsic to the muscles grafted. The structural and functional deficits observed in whole muscle grafts made with neurovascular repair will be identified and the underlying mechanisms discussed. The rationale for and research observations on myoblast transplantation and introduction of normal genes into muscles of animals with inherited muscle disease will be presented. In addition, progress in the clinical trials of myoblast transplantation will be presented.

#### The Origins of Molecular Biology

Sponsor: APS History Group. Participants: To be announced.

In recent years, molecular-biological concepts and methods have so pervaded all aspects of life science research that molecular biology is about to lose its identity as an identifiable research specialty. In this symposium, five speakers who participated in the early development of molecular biology 30 or more years ago will trace the origins of their discipline. Each speaker will focus on an aspect of that development – bacteriophage, replication, mutation, genetic recombination, genetic code, animal viruses, and cancer – to which he has made substantial contributions and outline its relevance for current and future life-science research.

### Epithelial Protein Secretion and Trafficking: Mechanisms and Function

Sponsors: APS Cell & General Physiology Section and Epithelial Transport Group. *Chair:* S. A. Lewis. *Participants:* S. A. Lewis, G. Bacallo, G. Ojakian, J. Larkin, and J. D. Jamieson.

An epithelium is a sheet of polarized cells whose function is twofold. First is to act as a barrier to restrict the movement of water, electrolytes, and nonelectrolytes between the two compartments; second is the selectively move (transport) electrolytes and nonelectrolytes between the compartments. The mechanism by which epithelia transport ions from one compartment to another follows a simple two-step paradigm that involves the movement of an electrolyte from the first compartment across that cell membrane into the cell, followed by the transport of the substance from the cell interior across the opposing cell membrane into the second compartment. The judicious placement of transport proteins can allow such an ionic movement to occur against both an electrical and a chemical gradient. In addition to the transport of electrolytes, nonelectrolytes, and water, epithelial cells are known to synthesize and secrete proteins in a vectorial manner. The purpose of this symposium is to determine the cellular strategies used by epithelia for protein export or secretion. Four mechanisms will be addressed: 1) enzyme trafficking in the pancreatic acinar cells by cellular synthesis and regulated protein exocytosis; 2) transepithelial protein transport by hepatocytes using a transcytotic pathway; 3) vectorial renal protease secretion, in which enzyme secretion occurs by the release of the enzymes from a membrane bound pool; and 4) protein targeting and trafficking in the formation of epithelial polarity.

#### Approaches to Cloning Renal Transporters

Sponsors: APS Renal Physiology Section and Epithelial Transport Group. Chair: S. C. Hebert. Participants: S. C. Hebert, D. J. Benos, S. L. Gluck, M. A. Hediger, J. J. Gargus, G. V. Desir, and P. Igarashi.

This symposium focuses on the strategies for cloning the cDNAs for renal transporters. Each speaker will cover both the approach(s) utilized in their cloning work and the present state of their cloning effort. In addition, speakers will emphasize basic requirements for their approach(s) to be used successfully to clone transporter proteins (e.g., How easy/difficult is the approach? What are the pitfalls? How generally applicable is the approach?). The approaches include utilizing antibodies against protein(s) purified to homogeneity to screen cDNA libraries, expression cloning utilizing Xenopus oocytes, use of classical genetic concepts as an approach to cloning the RBC urea transporter, and the approach of cloning by homology, which has been used extensively in other fields, to clone renal potassium channels and the renal Na<sup>+</sup>:H<sup>+</sup> exchanger(s). The information presented in this symposium should be of great interest to all epithelial and cell physiologists. The approaches used to clone renal transporters should also be of interest to investigators (both new and seasoned) in many fields. Each speaker will close with information regarding future directions or approaches relevant to their work.

# Leukocyte-Mediated Ischemic Injury in Muscle

Sponsor: Biomedical Engineering Society. Chairs: B. R. Ito and R. J. Korthuis. Participants: C. W. Smith, D. N. Granger, R. J. Korthuis, M. L. Entman, K. M. Mullane, and B. R. Ito.

It is now clear that leukocyte-mediated tissue injury is involved in a wide variety of inflammatory disorders and is a common factor in numerous models of organ dysfunction. Indeed, the cellular dysfunction that occurs when ischemic tissues are reperfused is becoming increasingly recognized as one form of acute inflammation involving the generation of chemotactic agents, the accumulation and activation of leukocytes, and cytotoxic mediator release. The purpose of this symposium is to summarize our current understanding of the mechanisms involved in the production of leukocyte-mediated postischemic cellular dysfunction. The symposium will begin with a review of recent data on leukocyte and endothelial cell adhesion molecules and their cellular regulation during inflammation, followed by an overview of the mechanisms involved in the modulatoin of leukocyte adherence to, and emigration across, postcapillary venules during ischemia and reperfusion. The next several presentations will focus on the role of leukocytes in the genesis of postischemic tissue injury, beginning with an examination of the mechanisms involved in the production of cellular dysfunction in vascular endothelium. This will be followed by presentations on the role of adherence molecule expression in myocardial ischemic injury, specific neutrophil-derived agents that mediate muscle injury, and the involvement of tissue-resident leukocytes in the myocardial ischemia induced by activated complement.

# Advances in Understanding Cerebral Ischemia/Reperfusion Damage

Sponsor: APS Cardiovascular Section. Chair: R. J. Traystman. Participants: R. J. Traystman, G. W. Goldstein, T. Nowak, Jr., R. Kraig, P. H. Chan, F. A. Welsh, and R. C. Koehler.

In recent years much effort has been focused toward understanding mechanisms of cerebral ischemia/reperfusion damage. The endothelial cell, stress proteins (genetic aspects), calcium, free radicals, and various metabolites have all been implicated in this damage. It is becoming clear that no one mechanism can completely account for the damage produced as a result of ischemia/reperfusion. This symposium is intended to review and highlight recent advances into some potential mechanisms by which ischemia/reperfusion damage is produced. Each of the participants of the symposium has made major contributions in this area in recent years and each has a reputation for excellent and balanced presentations. This symposium will emphasize the continuing vitality of integrative cardiovascular physiology as applied to disease states, in this case, stroke.

### Quantitative Studies of Cardiovascular Function With Magnetic Resonance Imaging

Sponsor: Biomedical Engineering Society. Chair: L. Axel. Participants: L. Axel, N. Reichek, C. Dumoulin, and D. Le Bihan.

The symposium will discuss the new capabilities for quantitative study of the cardiovascular system provided by magnetic resonance imaging (MRI). The noninvasive nature of MRI, coupled with its controllable sensitivity to motion, makes it a potentially very useful tool for studying physiological motions of the blood and heart. The specific adaptations of MRI to adapt it for measurement of motion are different in the cases of heart wall motion, blood flow in large vessels, and motion in the microcirculation; the best way to organize and analyze the data in these different areas is still controversial and the subject of active investigation. The papers in this symposium will present the ways in which MRI can be adapted to measure cardiovascular motions and will illustrate its potential with representative recent results. The potential for further future improvement of these techniques with the ongoing technical development of MRI will also be discussed. The speakers will represent both technical and clinical orientations and will consider application to both basic research and more applied pathophysiology.

# The Rheology of Cell Attachment and Adhesion

Sponsor: North American Society of Biorheology. Chair: H. L. Goldsmith and D. A. Hammer. Participants: H. L. Goldsmith, E. A. Evans, T. G. M. van de Ven, D. A. Hammer, D. A. Lauffenburger, L. V. McIntire, and A. Tozeren.

Cell-cell and cell-substrate interactions play a key role in the regulation of physiological responses such as cell growth, blood homeostasis, vascular repair, cell motility, and cell-cell killing. Considerable progress has been made in elucidating cell behavior by understanding the relationship between chemical and physical forces acting on cells during surface interaction. Chemical factors arise from binding between complementary cell surface molecules of high affinity; physical factors affecting cell adhesion are hydrodynamic, colloidal, or mechanical in nature. This symposium will pay special attention to the dynamics of cell adhesion, in particular the fact that for reactions between complementary molecules to be successful they must occur on a time scale short even compared to physical times such as the fluid shear rate. The presentations will attempt to quantitate the fundamental factors that control cell adhesion, thus allowing a true understanding of how physiological systems behave, and provide an intelligent means of comparing one system to the next.

# The Rheology of Cellular Deformation and Activation

Sponsor: North American Society of Biorheology. Chairs: R. Hochmuth and E. Elson. Participants: P. A. Janney, R. M. Hochmuth, S. H. Zigmond, C. Zhu, E. Evans, and E. Elson.

Over the last several years it has been demonstrated that a variety of cells experience substantial mechanical changes as they respond to different types of passive deformations and activating stimuli. For example, when a neutrophil responds to a chemoattractant, its shape becomes polarized along the direction of locomotion, its microfilaments are increased in number and reorganized. and its viscoelastic resistance to deformation increases. The purpose of this symposium is to consider the response of the cell and its cytoskeleton to mechanical deformation, chemical stimulation and cellular adhesion. Of major interest is the role of the structural proteins (microtubules, microfilaments, intermediate filaments) in controlling cellular response. An understanding of the basic processes of cellular deformation and activation can only be obtained by an interdisciplinary approach. Thus this symposium will bring together individuals with backgrounds in cell biology, polymer rheology, biochemistry, and biophysics.

### Molecular Approaches to Motile Systems

Sponsor: APS Myo-Bio (Muscle) Group. Chair: D. M. Warshaw. Participants: J. Howard, S. Block, K. Trybus, J. Sellers, J. Haeberle, and D. M. Warshaw.

Motility is a biological phenomenon that is most commonly observed during muscle contraction, mitosis, and cytokinesis, for example. The ability of a muscle fiber to generate force or shortening as well as the ability for intracellular organelles to be shuttled throughout the cell are properties related to a class of proteins called molecular motors. These proteins have the ability to convert chemical energy into mechanical work. In the past, most of our understanding of the basic contractile mechanism was obtained from skeletal muscle mechanical studies. These studies provided significant insight into the contractile process; however, recent technological advances have allowed questions to be asked at the single protein filament level. The development of the in vitro motility assay now provides a means for investigating how molecular motors impart their motion and/or force to structures such as actin filaments and microtubules. Two motors that have been extensively characterized are myosin and kinesin. Both motors share similarities in structure and function. This symposium will present the latest data and techniques using the motility assay. The symposium will introduce the technique and address its strengths and weaknesses. Special emphasis will be placed on future directions. For example, molecular biological techniques may be used to alter the motor's protein structure and then to observe how these changes are reflected in the motor's mechanical functioning.

### Adaptations to Osmotic Stress in Kidney: From DNA to Organic Osmolytes

Sponsors: APS Renal Physiology Section and Epithelial Transport Group. *Chairs:* J. M. Sands and A. Garcia-Perez. *Participants:* F.-X. Beck, P. H. Yancey, J. M. Sands, M. B. Burg, S. R. Gullans, and A. Garcia-Perez.

Animals need to vary urine concentration results in wide physiological variation in inner medullary tissue osmolality. To survive these changes in osmolality, inner medullary cells must have adaptational mechanisms that allow them to maintain cellular function. This is acheived in part by the accumulating organic osmolytes such as sorbitol, glycerophosphorylcholine, betaine, and inositol. This symposium will explore the evidence supporting a role for organic osmolytes in osmoregulation within the renal inner medulla. The symposium will focus on mechanisms by which marine animals, inner medullary cells in culture, and the renal inner medulla are able to adapt to hypertonic environments. The topics to be discussed include the molecular biology of the aldose reductase gene derived from a continuous rabbit kidney cell line, tissue levels of organic osmolytes and the etiology of the osmotic gap in mammalian inner medullae, and regulation of sorbitol production both in mammalian inner medullae and in cell culture. This symposium will combine studies in cell culture, comparative physiology, and mammalian kidney to examine the regulation of organic osmolytes at several levels: DNA, enzyme activity, and osmolyte production. Thus, this symposium will promote the interaction of participants with different technical skills and backgrounds and focus these skills on the question of renal osmolytes.

# Induction of the Stage of Tumor Progression: Progressor Agents

Sponsor: Society for Experimental Biology and Medicine. Chair: H. C. Pitot. Participants: H. Hennings, T. J. Slaga, Y. Dragan, D. S. R. Sarma, J. C. Barrett, and H. C. Pitot. ate and/or promote carcinogenesis have been identified, only recently has the stage of progression, characterized by the appearance of malignancy and aneuploidy, been clearly distinguished from the reversible stage of promotion. There are clear indications that specific chemical and physical carcinogens may act primarily, if not exclusively, to induce this terminal stage of carcinogenesis in cells that have been initiated and/or promoted. This symposium addresses the characteristics and occurrence of putative progressor agents and their role in and the characteristics of the transition from the reversible stage of promotion to the irreversible stage of progression. The potential role of progressor agents in human carcinogenesis as well as the methods for their identification is also to be considered.

### Mechanical Interactions of the Coronary Vasculature With the Surrounding Myocardium

Sponsor: Biomedical Engineering Society. Chair: F. C. P. Yin. Participants: F. C. P. Yin, Y. Aruyama, D. Van Winkle, R. E. Austin, E. O. Feigl, J. A. E. Spaan, P. Sipkema, and J. Livingston.

Even though it has long been known that coronary flow decreases during cardiac contraction, the mechanisms for this are still not well understood. Even simple questions such as whether coronary resistance is affected by contraction have not been answered. One of the reasons for this lack of knowledge is the complexity of the interaction between the coronary vasculature and its surroundings. Forces from the surroundings can be transmitted to the vessels via the collagenous matrix that connects muscles and vessels as well as via the interstitial fluid filling the nonsolid spaces. The curvature of the wall and presence of cavity pressure introduce regional variations in the forces that further complicates matters. This symposium brings together a multidisciplinary group of cardiologists, physiologists, and engineers to discuss some of the more recent developments in our efforts to understand this complex field. The speakers represent some who have made major contributions to our understanding of coronary physiology as well as those whose expertise lies in other fields but who have an interest in this problem. It is hoped that bringing together people with different backgrounds and approaches to a common problem will not only provide an update as to current techniques and knowledge but also provide guidance as to future avenues of productive investigation.

# Stable Isotope Applications in the Studies of Carbohydrate Metabolism

Sponsor: APS Endocrinology & Metabolism Section. Chair: W. N. P. Lee. Participants: W. N. P. Lee, J. Katz, M. Hellerstein, A. Lapidot, S. M. Cohen, C. Malloy, and G. I. Shulman.

Recent applications of stable isotopes (13C and 2H) and isotopomer analysis have emphasized the utility of isotope distribution within a molecule in the elucidation and quantitation of metabolic pathways. The symposium is designed to convey recent advances in isotopomer study of carbohydrate metabolism from gluconeogenesis to inborn errors of metabolism. Speakers will include Katz and Lapidot, who are pioneers in mass isotopomer analysis; Hellerstein, who has developed many assay methods for the

Through the use of multistage models of carcinogenesis, three distinct stages in this process have been identified: initiation, promotion, and progression. Although the characteristics of the first two stages and agents that act primarily, if not exclusively, to initi-

determination of cytosolic precursor enrichment; and Cohen, Shulman, and Malloy, who are experts in in vitro and in vivo NMR techniques. Presentations will emphasize techniques and concepts of isotopomer study of carbohydrate metabolism using NMR and CGMS. Topics for the symposium have been chosen for an audience with diverse interests from biochemists to clinical investigators. It is hoped that the symposium will generate discussions and interest in the special techniques.

#### Human Physiology in Microgravity: Spacelab SLS-1

Chairs: R. W. Phillips and J. B. West. Participants: R. White, F. D. Gaffney, C. G. Blomqvist, J. B. West, C. Huntoon, C. D. Arnaud, L. W. Young, and R. W. Phillips.

The first spacelab dedicated to life sciences, Spacelab SLS-1, flew on June 5–14, 1991. Spacelab is a cylindrical laboratory about 7 meters long and 4 meters in diameter that is carried in the bay of the shuttle. SLS-1 contained a large amount of sophisticated physiological equipment. The mission included 20 physiological experiments of which 10 were on humans. The human experiments covered the areas of cardiovascular, respiratory, metabolic, muscloskeletal, and vestibular physiology.

The 9-day flight was an outstanding success resulting in large amounts of new data in many areas of the physiology of weightlessness. It was far the most ambitious and comprehensive series of experiments on human physiology in microgravity to be performed to date.

> APS/FASEB Spring Meeting Anaheim, California Wednesday, April 8, 1992, 4:45 p.m.

Physiology in Perspective Walter B. Cannon Memorial Lecture

### "Coupling of Exercise Ventilation to Metabolism: "The Wisdom of the Body" – Revisited"

#### Karlmann Wasserman

Professor of Medicine and Chief Division of Respiratory and Critical Care Physiology and Medicine University of California, Los Angeles

# Comparative Effects of Training and Detraining on Muscle Function

Sponsor: APS Environmental & Exercise Physiology Section. Chairs: S. J. Wickler and D. F. Hoyt. Participants: A. Herrera, G. Tibbits, J. Steffen, D. F. Hoyt, F. Booth, K. Baldwin, R. Edgerton, and S. J. Wickler.

This symposium is designed to I) bring together individuals who study different animal species and model systems exhibiting training and detraining and 2) discuss the diverse methods used to assess training and detraining effects and determine how the results they yield may be compared. Changes in the functional capacity of muscle in response to training and detraining are the concern not only of sports exercise physiologists but also of investigators in the fields of general and comparative muscle physiology. Some recent studies of training and detraining, for example, have reported increases in muscle oxidative capacity (as indicated by enzyme activities), and others have reported decreased or unchanged capacities. Some of these differences are probably due to the use of different animal species or model systems, but some may be due to the use of different methodologies. It would seem timely to assemble some of the authors of these different studies to assess the comparability of the different methodologies and animals systems used in training and detraining. By determining which methodologies are comparable, it will become clearer which species and model systems actually respond in different ways to training and detraining. These may be the promising avenues for future research intended to elucidate the mechanisms of training and detraining at the cellular and molecular levels.

## Excitatory Amino Acid Systems; A New Era in Modification of Central Cardiovascular Neurotransmission

Sponsor: APS Neural Control & Autonomic Regulation Section. Chair: R. W. Rockhold. Participants: R. W. Rockhold, S. F. Heinemann, S. J. Lewis, W. T. Talman, and F. J. Gordon.

This symposium will address the involvement of excitatory amino acid (EAA) receptors in central mediation of cardiovascular and baroreflex function by presenting advances in the area of EAA molecular biology, pharmacology, and physiology. The speakers will detail the role of endogenous EAAs as putative neurotransmitters of cardiovascular information, both within CNS regulatory sites and between the central and peripheral nervous systems, and define the appropriate use of EAA receptor ligands as experimental tools for examination of cardiovascular function. The molecular biology of brain glutamate receptors will be presented to place into perspective the relative importance of interactions between EAA receptors and central cardiovascular control systems. Key questions will provide coherent themes to the presentations and the ensuing discussions. These include 1) Does experimental evidence support a role for 1-glutamate as a neurotransmitter at cardiovascular regulatory sites? 2)) Which EAA receptor types are present in and modify neuronal function at these sites? 3) What are the experimental criteria needed to define EAA receptor mediated events in cardiovascular regulation? 4) What are the appropriate cautions needed in the use of EAA receptor ligands as experimental tools in such studies?

# Strength and Failure of Pulmonary Capillaries

Sponsors: APS Respiratory, Cardiovascular, and Environmental & Exercise Physiology Sections. *Chairs:* J. B. West and O. Mathieu-Costello. *Participants:* J. B. West, E. R. Weibel, E. D. Crouch, L. W. Welling, M. I. Townsley, D. J. Riley, and O. Mathieu-Costello.

Recent work from at least two laboratories shows that when pulmonary capillaries are exposed to large distending pressures, ultrastructural changes develop in their walls. The probable reason for this is stress failure, because calculations show that the wall stresses are extremely high under these conditions. The very high stresses result principally from the extreme thinness of the walls, which is necessary for efficient gas exchange by passive diffusion across the capillary wall. The first speaker (West) will summarize some of the experimental data and set the stage for the later speakers. Weibel will review modern information on the ultrastructure of pulmonary capillaries with particular reference to the capillary wall and its various components. He is the doyen of lung ultrastructure. Because there is evidence that most of the strength of the capillary wall is located in the extracellular matrix, particularly the type IV collagen, the next speaker, Crouch, will describe contemporary views on the structure and function of the various components of the extracellular matrix of the wall of the pulmonary capillary. Crouch works very much at the molecular level and has a particularly strong interest in type IV collagen. An important issue is the strength of type IV collagen, which makes up basement membranes. There are very few studies on this important topic, but they will be reviewed by Welling, who has carried out one of the best studies in this area. Next, Townsley will review what is known about changes in capillary permeability as their transmural pressure is increased and as lung volume is raised. There is evidence that both these factors increase capillary permeability substantially. She will also describe some of her experimental data on capillary wall failure. The final speaker, Riley, is interested in the molecular biology of connective tissue synthesis as a result of increased hydrostatic pressures within the pulmonary vasculature. The most relevant question here is whether an increase in transmural pressure of pulmonary capillaries regulates the composition and thickness of their extracellular matrix. No data are available on this particular point, but Riley's experiments are clearly related to this. This is an interdisciplinary symposium with contributions in the area of morphology, physiology, bioengineering, and molecular biology. The topic itself is very new and it is of great potential importance because stress failure of pulmonary capillaries probably plays a role in the increased capillary permeability seen in lungs during mechanical ventilation. It has also been suggested that stress failure of capillaries may occur in the early stages of pulmonary emphysema.

#### **APS** Membership

Membership applications may be obtained from APS Membership Services, 9650 Rockville Pike, Bethesda, MD 20814-3991. Applications are reviewed and approved by Council on a regular basis throughout the year.

#### FASEB Theme Symposium

### Exercise Modulation of Human Growth

Sponsor: APS Endocrinology & Metabolism Section. Chair: D. M. Cooper. Participants: D. M. Cooper, K. Borer, T. K. Hunt, D. Devol, R. Malina, F. Viteri, and A. D. Rogol.

The goal of this symposium is to examine a number of the mechanisms that may link physical activity to the process of growth. Although growth hormone (GH) released in response to acute exercise seems to function most immediately in glucose "counter" regulation, there is increasing evidence to support the notion that GH stimulated during physical activity may play an important role in the modulation of somatic and cardiorespiratory growth. Episodes of vigorous physical activity occur naturally in healthy, growing children, but whether these spontaneous episodes act to influence growth remains unknown. Although it is now known that GH does possess some of its own growth-enhancing effects, current understanding of growth regulation holds that GH stimulates a variety of mediators (e.g., IGF-1 and IGF-2) that more directly stimulate tissue growth than does GH itself. Moreover, very recent data demonstrate that cellular growth in a variety of tissues is accompanied by substantial increases in IGF even without GH. Finally, there is growing awareness that local tissue phenoma (e.g., stretch of tissues) change in cellular pH may lead to the release of a variety of growth factors. In this symposium a group of physiologists, molecular biologists, anthropologists, and clinicians will present an overview of the ways in which physical activity modulates the process of growth.

### FASEB Theme Symposium

# Gene Regulation of Endothelial Cells as a Response to Injury

Sponsor: APS Cardiovascular Section. Chairs: C. M. Bloor and M. E. Gerritsen. Participants: T. Hla, P. DiCorleto, J. A. Madri, T. A. Lane, D. Loskutoff, M. E. Gerritsen, and C. M. Bloor.

The purpose of this symposium is to describe the gene regulation of endothelial cells as a response to injury. Endothelial cells play a vital role in tissue responses to inflammation, thrombosis, and alterations in the physical and biochemical microenvironment. The active participation of endothelial cells in tissue response to injury depends on rapid alterations in their phenotype. There is an emerging body of information regarding the biochemical mechanisms employed by endothelial cells to modify their phenotypes in response to these events. Emerging evidence indicates that endothelial cell responses to different types of injury likewise depend on a variety of distinct molecular mechanisms. The molecular events that occur in wound healing, inflammation, atherosclerosis, and angiogenesis will be defined. The second objective of this symposium is to provide an integration of the roles of extracellular matrix, growth factor receptors, and cell-cell interactions in the control of endothelial cell growth and differentiation. The scientific value of this symposium to attendees is an update on recent advances in molecular biology related to endothelial-dependent cardiovascular events, e.g., atherosclerosis, thrombosis, angiogenesis, and collateral development.

#### Symposium/Workshop

## An Experience of Various Interactive Teaching Techniques

Sponsor: APS Teaching of Physiology Section. Chair: R. Thies. Participants: J. Engelberg, J. I. Moore, R. Thies, and T. K. Akers.

Medical educators believe that teaching should involve less lectures and more activities involving independent learning and problem solving. Some schools are testing methods to promote such learning, but many teachers are not familiar with these. This workshop will have participants experience four different methods of interactive teaching. First, Engelberg will have attendees become participants in the total group setting. Second, Moore will have them read a one-page scientific article, answer questions individually, and then find common answers in small groups of five to six participants, formed from those sitting near one another. This will involve learning from fellow students. Third, Thies will have the same small groups do a problem-solving exercise that will draw from their varied understanding of physiology. Last, Akers will have the small groups do scenarios that show clinical application of physiological principles. These experiences should make participants want to teach interactively.

#### Debate

# Most of the Pulmonary Vascular Resistance is in the Microvessels

Sponsor: APS Respiratory Section. Moderator: J. Butler. Pro: J. Bhattacharya. Con: T. Hakim.

The subject of this debate has been the focus of controversy at APS Pulmonary Circulation Meetings since efforts to measure the segmental distribution of pulmonary vascualr resistance began in earnest in the 1950s. Recently the matter has been causing even more excitement because of the publications of Dr. Bhattacharava and colleagues reporting considerable resistance in the capillaries by direct pressure measurements (Science 210: 327-328, 1980) and of Dr. Hakim and colleagues showing minimal resistance in the microvessels by the double occlusion and other techniques (J. Appl. Physiol. 67: 1277–1285, 1989). The answer to this dispute is of great importance to our understanding of the way blood flows through the alveolar walls (sheet flow vs. tube flow controversy), the site of the flow limiting segment in relation to gravity in the pulmonary circulation (West's Zones), and the way that lung distension affects the vessels. This debate is a natural sequel to those on the distension versus recruitment and sheet flow versus tube flow controversies.

## APS Conference Cellular and Molecular Biology of Membrane Transport

### November 4-7, 1992 Orlando, Florida

Wednesday, November 4	Thursday, November 5	Friday, November 6	Saturday, November 7	
Registration	Morning Symposium	Morning Symposium	Morning Symposium	
Evening Lecture Molecular characterization of calcium channel proteins William A. Catterall	Structure and function of membrane channels I	Structure and function of membrane carriers	Modulation of membrane transport I	
	Douglas C. Eaton	Douglas M. Fambrough	Lazaro J. Mandel	
	Afternoon Posters	Afternoon Posters	Afternoon Symposium	
	Evening Symposium	Evening Lecture	Modulation of membrane transport II	
	Structure and function of membrane channels II: Molecular approaches to the properties of calcium abannels	The bacterial glucose transporter H. Ronald Kaback	Jack H. Kaplan	
	William F. Agnew			

## Human Anatomy and Physiology Society 5th Annual Meeting

The Human Anatomy and Physiology Society (HAPS) is one of many organizations whose members teach undergraduate physiology. The HAPS members primarily teach in community and junior colleges. Their students are mostly majors in prehealth, allied health, and nursing. HAPS was organized to meet an important need: the professional education of its members. The last meeting was held May 25–30, 1991 in Greenville, SC, under the sponsorship of the Greenville Technical College and Clemson and Furman Universities.

Sessions were of two types. The first two days were designed to update the attenders on various topics. Some subjects were very broad, like ethical conflicts in biology and medicine; AIDS: clinical and epidemiological considerations; and drugs: the altered brain. Some subjects were narrower, for example, what's new about renal anatomy and physiology (by Arthur Vander, who was also the keynote speaker of the meeting) and developing thinking skills.

The latter part of the meeting was taken up with demonstrations and sessions devoted to improving instruction; body composition estimation, MacLab recording and data analysis system, and computer software for neuroanatomy and sensory systems are examples. In addition, there were swap sessions in which small groups shared new techniques that they were trying with their students.

The caliber of the presentations was high and the meeting was very stimulating. The interchange between the speakers and the audience was lively in every session. The meeting certainly achieves its goals of providing useful information to the attenders and it gives them many things to incorporate into their own courses.

> Allen Rovick Rush Medical College

## **US/USSR Exchange Program**

Under the sponsorship of the US/USSR Bilateral Exchange Program in Physiology, Yuri V. Natochin and Rimma G. Parnova of the Sechenov Institute of Evolutionary Physiology and Biochemistry of the USSR Academy of Sciences visited Richard M. Hays of the Department of Medicine, Albert Einstein College of Medicine in June and July 1991. Natochin has published widely in the areas of comparative physiology and osmoregulation and has contributed to the problem of water and electrolyte balance under conditions of space flight. Parnova's interests are primarily in ADH-induced signaling mechanisms. Their visit followed a visit by Hays to the Sechenov Institute in October 1990.

Natochin, Parnova, and Hays began their studies on the relationship of volume regulation to the actin cytoskeleton, and the ADH-induced signaling system, at Albert Einstein during the month of June and transferred their activities to the Mount Desert Island Biological Laboratory, Salsbury Cove, Maine during July, where they were joined by Arnost Kleinzeller of the University of Pennsylvania in studies of the actin cytoskeleton in the dogfish rectal gland. In the course of their visit, they were able to present their past work to a large number of American colleagues and to attend the APS conference "From Channels to Cross Bridges", which was held on Mount Desert Island in July.

In addition to support from the APS, the Soviet investigators received support from the Mount Desert Island Biological Laboratory. Parnova also received a grant from the Soros Foundation.

In the fall of 1991, Yan Komissarchik of the Institute of Cytology in Leningrad will visit Hays at Albert Einstein, as a continuation of the exchange program.

> Richard M. Hays Albert Einstein College of Medicine



Yuri Natochin (l) and Rimma Parnova (r) with Richard M. Hays during their visit to the Albert Einstein College of Medicine in June 1991.

### **APS Conference Goes to School**

Attendees at the first APS Conference, "From Channels to Cross Bridges," had to go to school to participate in the meeting. Boarding yellow school buses, the attendees were transported back in time from the hotel to the Mount Desert Island High School, which served as the conference center with the symposia presented in the auditorium, posters in the library, and box lunches in the cafeteria.

While the meeting site might have been a high school, the science presented was nowhere near the secondary school level. The 289 scientists from throughout the world discussed the latest work in the fields of membrane channels, receptor-effector coupling, and cell motility.

The APS Conference was organized by a committee chaired by Martin Morad of the University of Pennsylvania. Assisting in coordinating the meeting was the staff of the Mount Desert Island Biological Laboratory (MDIBL), which sits nestled in the rocky Maine coastline at Salisbury Cove.

The meeting opened on Sunday, July 14, with greetings from Stanley G. Schultz, APS President-Elect, Frank Epstein, MDIBL President, and Morad. The scientific sessions started with a plenary lecture by Shosaku Numa, Kyoto University, who recently cloned the calcium and sodium channels that regulate heart and brain function. During the course of the 3-day conference, 40 internationally recognized speakers presented the results of their studies on membrane channel structure and function and on cell motility. In addition, attendees contributed 104 abstracts for presentation in poster format.

The culmination of the meeting was a presentation by Sir Andrew Huxley. The grandson of English biologist Sir Thomas Huxley and a brother of novelist Aldous Huxley, Andrew Huxley won the Nobel Prize with Alan Hodgkin in 1964 for their work describing how channels in membranes transmit electric signals. Huxley provided the attendees with a summary of the work presented at the APS Conference and provided the attendees with some insights into his career and the outstanding scientists he has had the pleasure to know and to work with.

Mount Desert Island and the Acadia National Park proved to be an outstanding venue for the first APS Conference. The high school, which sits in the shadow of Cadillac Mountain, provided the attendees with secluded areas for the discussion of their work and the work of their colleagues. MDIBL opened its research laboratories for a welcome reception, and attendees also had the opportunity to sample local cuisine during a clam and lobster bake.

The contributions of students to the meeting also were recognized by the presentation of two APS Student Awards supported by the generosity of AXON Instruments and







Lobster and Clam Bake

Adams and List. The awards, for the best student firstauthored abstracts, were presented to Daniel H. Cox, Tufts Medical School, for an abstract entitled "Calcium Channel Modulation by Norepinephrine and GABA," and Beth B. Hogans, University of Maryland School of Medicine, for an abstract entitled "Calcium Permeation of Voltage-Dependent Sodium Channels at Large Driving Forces."

#### 1991 APS Conference Registration "From Channels to Cross Bridges"

Registration Category	Total	
APS Members	56	
<b>APS</b> Retired Members	5	
Nonmembers	132	
Invited Speakers	51	
Students	33	
Guests	12	
TOTAL	289	



(l-r) D. H. Cox, Sir Andrew Huxley, S. G. Schultz, B. B. Hogans



Poster Sessions

## **Know Your Sustaining Associates**

#### **Fisons Pharmaceuticals**

The Pharmaceutical Division of Fisons is an international researchbased pharmaceutical company committed to provide excellent health care products for prescription and consumer use. Fisons develops and manufactures a wide variety of pharmaceutical products, with markets in more than 100 countries. Fisons is recognized as a world leader in the treatment of respiratory problems and allergies and also markets products for cardiovascular disorders, neurological diseases, and dermatological problems. Fisons has a major commitment to research and development to generate superior future medicines for these and other therapeutic areas including immunological and metabolic diseases.

#### R. W. Johnson Pharmaceutical Research Institute

Established in 1988, the R. W. Johnson Pharmaceutical Research Institute (PRI) pools the research and development resources of five successful Johnson & Johnson companies into a single worldwide, world-class R & D organization.

PRI integrates the considerable research achievements and potential of groups that were previously associated with McNeil Pharmaceutical, Ortho Pharmaceutical Corporation, Ortho Biotech, Johnson & Johnson Biotechnology Center, and Cilag International Research Center. Already one of the strongest pharmaceutical R & D companies in the world, PRI has forged alliances with other research organizations worldwide to accelerate drug discovery efforts.

Research and development at PRI focuses on reproductive medicine, dermatology, hematology/oncology, immunological disorders, central nervous system disorders, and infectious diseases, among other therapeutic areas. The world's best and brightest in science and medicine are working at PRI to discover and develop pharmaceutical and biotechnological products that will enhance health and life.

### A Look Back

David G. Greene Department of Physiology State University of New York Buffalo, New York

Between my first and second years at the Harvard Medical School, I took a summer in neuroanatomy with Dr. David Rioch. The course alternated days between the anatomical laboratory and the physiological laboratory where we did dog experiments under the supervision of Drs. Arturo Rosenblueth and Robert Morrison. This experience added to what I learned of mammalian preparations in the first year physiology course and gave me an enduring interest in what can be learned in the physiology laboratory.

In the first months after graduation, I was kept out of a formal program because of health problems and I lived at home with my father, who was professor of medicine and responsible for teaching rounds at Buffalo General Hospital. I was well enough to go on rounds, however, and my father involved me in the preparations for the discussion of the cases the following day.

Although his library was extensive, we both noted that the best material came not from textbooks of internal medicine but from Best and Taylor's *The Physiological Basis of Medical Practice.* I then had a brief stint in pathology before beginning my internship. These experiences led me to an appreciation of the importance of organ physiology as the basis for sound thinking about clinical medicine.

Upon leaving the Army after World War II to resume my postdoctoral education, I wanted to gain a better grounding in physiology, working in a field of physiology that had relevance to clinical internal medicine. Fortunately I was steered to Dr. Eleanor Baldwin, who was part of the Coumand and Richards team studying heart and lung function. When I went to Dr. W. W. Palmer, chairman of medicine at Columbia University, to complete the arrangements, he told me, "A year spent in a physiology laboratory one of the best things you can do to further your education." A year later, when I went to continue the arrangement, I reminded Palmer of his comment, to which he replied, "A second year is twice as good."

Upon my return to Buffalo General Hospital, I set up a cardiopulmonary laboratory in the Coumand-Richards-Baldwin pattern.

My experiences in teaching medicine or clinical physiology in Third World countries (Mexico and Paraguay) and in teaching house staff and fellows who have graduated from Third World medical schools have impressed me with the positive benefits of hands-on experiences in the mammalian laboratory. In the mammalian laboratory one can practice handling tissues, controlling bleeding, etc.

Twenty of 30 years ago this experience was lacking in graduates of Third World medical schools and showed in comparison with US medical school graduates. Now, unfortunately, with the reduction of handson laboratories in North American medical schools, the difference is not apparent.

The foregoing autobiographical account of the way I developed an interest in physiology is offered as an example of what the discipline can contribute to a career in clinical medicine. I strongly believe that the investigative approach to organ physiology is an essential part of science, one that can interact with clinical disciplines with mutual benefit.

These interactions can, perhaps, best be carried out in smaller units centered

on a system or an organ with joint contributions from the laboratory basically oriented, the laboratory clinically oriented, the clinic, and the operating room.

Since knowledge doubles every 15 years, one of the necessary adaptations for the scientist is to narrow progressively his or her field of expertise. In clinical cardiology the progression of this subdivision is clear. At the time of World War I, Paul D. White was advised that the was foolish concentrating on diseases of the heart because he would starve. Now we have subdivision of cardiology that few cardiologists claim to encompass completely.

They are electrocardiography, including arrhythmias; pacemakers; implantable defibrillators; electrophysiological studies; nuclear cardiology with exercise stress observations as well as MUGA scans; echocardiography and doppler examinations; and invasive cardiology with measurements of pressures, flows, shunts, with contrast the sizes of vessels and organs, the correction of abnormal shunts, valve defects, and artereial narrowing with balloons, stents, and lasers.

In my first year on the faculty of the medical school in Buffalo, I audited the first-year physiology course for medical and dental students and acted as an instructor in the medical section laboratory exercises. Two year later I took and passed the board certification examination in internal medicine. Many of the questions I answered on the basis of my everyday clinical practice. But the second most frequent identifiable source for the correct answers to the questions was my experience in auditing and teaching the first-year physiology course.

Some of the most enjoyable experiences have been physiological activities in the field. These have included an Antarctic trip on the *Alpha Helix*, trekking in the Himalayas before the International Congress of Physiology in New Dehli in 1974, and egging expeditions with (or for) Hermann Rahn in the Faeroe Islands, Alaska, and Spitzbergen

One of the greatest truths which I rediscovered as many other have is that

the field is where the work gets done most efficiently. Without mail, telephone, lectures, seminars, grant requests, students, family, site visits, and shopping, one really can get a lot of work done.

### **News From Senior Physiologists**

#### Letter to Horace Davenport

"I just celebrated my 72nd birthday and currently I am working approximately 30 hour a week as an emeritus professor of medicine and pharmacology and cell biology at the University of Cincinnati," **Noble O. Fowler** reports.

"My research interests center on pericardial physiology and I am still publishing in that area. I am seeing some patients, working in the cardiology clinics, and writing book chapters. I have just had published the book *Diagnosis of Heart Disease*. I also serve on several editorial boards and review a number of papers for journals."

#### Letters to David G. Greene

"It is now over 15 years since I retired at the age of 70," writes **Lyle Beck** from Bloomington, IN. "For 13 of those years I worked in the laboratory and library with two faculty members in the branch department of pharmacology, which I started in 1961 at the Indiana University School of Medicine, Bloomington campus. The last two years I have been playing around with a Macintosh SE computer and, occasionally, going to an IU library. Somewhat over a year ago I was "promoted" to the rank of Distinguished Service Professor Emeritus of Pharmacology."

**Carl F. Essig** writes, "I am fully retired and 'actively' enjoying life in Lexington, Kentucky. Most of my career was spent near Lexington at the Addiction Research Center which was part of the US Public Health Service Hospital. Physiology has enriched my life, stimulated my investigative drives, made me a better teacher, and made me a better physician. I hope the future will hold chances for others to have opportunities similar to mine.

In my opinion the freedom of full retirement is in itself a form of enjoyment. It also allows time for extensive travel. I doubt that it is possible to persuade those who do not believe in retirement, but to me it can be the best period of ones life."

#### Letters to Helen M. Tepperman

"I am enjoying a nice Indian summer of my career at the age of 72," pens John C. Vanatta from Houston. "The Texas law was changed in 1989, just in time to allow me to continue teaching beyond the age of 70. I have had the following landmark events: I am coauthor for three of the last four editions of the monograph, "Moyer's Fluid Balance-A Clinical Manual." The fourth edition has been translated and published by a doctor at the University of Indonesia in Jarkarta. I am noted to be an "adalah guru besar fisilogi dan" on the cover of the translation. It is also to be translated and published in Spanish in 1992."

Vanatta also writes that he and Loy W. Frazier, a former student and now chairman of physiology at Baylor University, have published a review and presented a poster at the FASEB meeting in Atlanta.

"One of my chief functions is to help students having academic difficulty. One of my prize successes was a student who had flunked two freshman medical school courses before entering our physiology course. With a change in study habits she made a B in our course, a B + in neurobiology. The student went on to make up the deficiencies and sailed through the next three years with two As, three B+s, four Bs, and only one C. She graduated in June and got first choice of the residences she applied for.

"I no longer have a laboratory at the school, but I have space in a private laboratory off campus where I can continue some of my chemical studies. I perform the animal work in Frazier's laboratory when necessary."

"I am sure anyone looking over my curriculum vitae would have a hard time deciding whether I was a physiologist, a pharmacologist, or a physician," said **Ashley Thomson** from Winnipeg. "My choice would be a "people doctor" with special interests in teaching and what now is called nephrology. In teaching I have been particularly blessed with a number of excellent students who have continued investigative careers in cardiovascular pharmacology, electrolyte metabolism, and clinical medicine.

"I still do 'Ethics' and I am attempting to write some historical aspects of dialysis and transplantation in that area. Mark Nickerson and I are trying to put together some earlier studies on adrenergic blockade in clinical shock and intrarenal blood flow in acute renal failure. I have done two "People to People" trips to the Orient and was a visiting professor in Taiwan since my retirement.

**Majorie Zucker** writes, "I haven't retired since I have another year and a half on my grant, but I am getting ready to do so. Fifty years is enough, even of blood platelets!"

She said that her membership on the board of directors of the Right to Die Society is most interesting. "This organization helps to develop, legalize, implement, and distribute living wills or advance directives. Largely through the efforts of the Society 45 states now have such laws and the federal Patients' Self-Determination Act will go into effect next winter. This law mandates all health care organizations that receive federal aid to develop policies regarding advance directives, provide information to patients about the state's laws, and provide education for health care workers and the public."



## NIH, Texas To Cosponsor Animal Welfare Program On Rodent Research

The National Institutes of Health's Office for Protection From Research Risks, Division of Animal Welfare, and the University of Texas Health Science Center at Houston are cosponsoring an animal welfare workshop program on "Dilemmas in Rodent Research: Scientific, Regulatory, Ethical Perspectives."

The one-and-a-half days workshop, set for December 5–6 at the Wyndham Warwick in Houston, is designed for those responsible for the management of laboratory animal programs, including institutional animal care and use committee members, administrators, laboratory animal veterinarians, and investigators and their staffs.

The program theme will be the scientific and ethical perspectives of rodent use. The program will focus on rodents in research with emphasis on transgenics and the Public Health Service, Food and Drug Administration, and Department of Agriculture regulations.

There also will be a moderated protocol review workshop with participants acting as members of an institutional animal care and use committee.

For information concerning program content and logistics, contact Paula Knudson, 713-792-5048; FAX, 713-794-4264; for information concerning future programs contact Roberta Sonneborn, 301-496-7163; FAX, 301-402-0527.

## A Newspaper Speaks Out About Animal Activists

(In Maryland an animal rights organization, In Defense of Animals, has been picketing since spring the Chevy Chase home of Dr. Sharon Juliano, protesting her use of cats in her neurological research project at the Uniformed Services University of the Health Sciences in Bethesda. The Potomac Almanac newspaper spoke out against the activists, publishing the following editorial and editorial cartoon, which are reprinted with the permission of the newspaper and the cartoonist.)

### **Cruel Vigil**

Since April, animal rights protesters have been camping in front of a local researcher's home, visibly opposing her use of kittens for neurological research. Week after week, the protesters hold night vigils at Dr. Sharon Juliano's house, hoisting signs with pictures of cats and others that say Have a Heart, Sharon.

Animal rights activists accuse Juliano of being cruel and unkind to kittens because she removes their toes to study the brain's reaction. We see a distinct irony in activists calling for kindness and fair treatment for animals, but denying it to other human beings. In their concern for animals, they would tolerate the long-term suffering of people, who eagerly await the results of Juliano's research.

The protesters intend their photographs of cuddly kittens and big-eyed monkeys to stir emotion. Far more emotional pictures come to mind of humans who are neurologically impaired. Picture someone who shakes so much from Parkinsons disease that he cannot feed himself, or imagine a victim of paralysis struggling to get out of bed. Science does not have cures for them yet. But researchers are trying—and they say they won't get very far if they can't use animals.

Our fundamental disagreement with the animal rights activists is this—they believe an animal's life is worth as much as a human's. We do not. They argue that animals should not be used for testing under any circumstances. Yet without animal research, the medical community never would have found a vaccine for



GRANDMA. HER DIALYSIS TREATMENTS ARE GONNA MAKE IT PRETTY TOUGH TO GET THAT ATV YOU'VE HAD YOUR EYE ON. AND, HEY, SHES GOT A RIGHT TO DIE, ANYWAY.



THE GREAT ETHICAL QUESTIONS OF OUR DAY--WHICH OF THE FOLLOWING HAS MORE RIGHT TO LIVE?



A LAB RABBIT. SOME FASCIST SCIENTIST WANTS TO KILL HIM JUST TO DEVELOP A VACCINE TO SAVE A FEW MILLION GREEPY, POLLUTING HUMANS. WHO'S CUTER, REALLY--GRANDMA, OR THIS LITTLE GUY? BESIDES, YOU WOULDN'T BE CAUGHT DEAD WEARING HIS FUR, NOW, WOULD YOU? CAN'T SAY THAT ABOUT GRANDMA'S JEWELRY.\_



polio, mastered the surgery for heart transplants or developed AZT, the groundbreaking drug that helps those who suffer from AIDS. No one likes it that animals must die so that doctors can improve human life. But researchers cannot test a potentially lifesaving drug or practice a new technology on a computer.

We do not dispute that the animal rights movement serves a valuable purpose. As a result of its scrutiny, animals are treated more humanely. Nor do we oppose activists speaking their piece. Our Constitution rightfully permits all groups to have their say. But we believe an individual's right to privacy should take percedent. Juliano has a right to live in her home without being publicly berated for her work. Protests have a place – the work place, where the perceived offense is happening. The demonstrations at Juliano's home fall within the First Amendment, but they land outside society's standard for acceptable behavior.

## **APHIS Responds to Questions From IACUCs About New Animal Welfare Regulations**

The National Academy of Sciences' Institute of Laboratory Animal Resources (ILAR) submitted a series of questions to the Regulatory Enforcement and Animal Care division of the Animal and Plant Health Inspection Service (APHIS), US Department of Agriculture, to learn how the agency interprets some portions of the recently promulgated regulations of the Animal Welfare Act. The questions were derived from a survey of institutional animal care and use committees (IACUC) at five small and five large universities. The questions and responses are reprinted here with the permission of ILAR.

1. During its review of animal protocols, is the IACUC obliged to evaluate the methods and sources used by the principal investigator (PI) in his/her consideration of alternatives to procedures that may cause more than momentary pain, if that pain will be abrogated entirely by the use of analgesics or anesthetics?

To answer this question one must first clarify "procedures that may cause more than momentary or slight pain or distress." As the IACUC evaluates protocols, the following questions should be asked: Does the animal feel pain? Can the animal be expected to feel pain? Certainly during the recovery period following a surgical procedure, even when analgesics are used, the animal may be expected to experience pain. Conversely, when surgical procedures are performed and the animal is not allowed to recover from anesthesia, the only discomfort that the animal may experience is during the induction of anesthesia. Therefore, in general, most survival surgical procedures may cause more than momentary or slight pain or discomfort.

The "written narrative description of the methods and sources used to determine that alternatives were not available" is indeed not easy for the IACUC to evaluate. It is not the intent of this regulation that the IACUC evaluate the databases or sources cited. The intent is that the PI consider alternatives to procedures that may cause pain. Questions that should be asked are: Is there a nonsurgical or noninvasive model? Is there a model that does not require surgery? Is there an in vitro model? Suggested items that the investigator may wish to include in the narrative are the databases(s) searched, the key words used in the search, selected references on animal models or alternatives, etc.

2. The PI has provided written assurance that "the activities do not unnecessarily duplicate previous experiments." Will that statement, signed by the PI, satisfy the requirements or is it necessary for him/her to provide evidence of a literature review?

It is stated in section 2.31 (d)(1)(iii) of the animal welfare regulations that it is the *IACUC's* responsibility to determine that the investigator has provided "written assurance that the activities do not unnecessarily duplicate previous experiments." A written assurance consisting of a statment signed by the PI will satisfy this regulation. It is up to the IACUC, however, to determine what type of information should be included in the investigator's assurance. This may vary based on the needs and experience of the Committee.

## Ten Years Later: The Silver Spring Monkey Case

It was 10 years ago on September 11 that police raided a Silver Spring, MD, research facility, confiscating 17 monkeys and charging the principal investigator with 119 counts of animal cruelty.

Although the researcher, Edward Taub, was to be exonerated on all counts, the name Taub and the Silver Spring monkeys were linked forever in the animals of research.

The most recent chronicle of this episode has been prepared by the Coalition For Animals & Animal Research (CFAAR) and is entitled, "The Silver Spring Monkey Incident: The Untold Story." Written by Taub, the article gives insight to the still ongoing battle of PETA (People for the Ethical Treatment of Animals) to win custody of the two monkeys still being held by the National Institutes of Health as well as detailing the police investigations, the law and the lawyers, manipulations of and by the media, and what the research involving the Silver Spring monkeys has accomplished in the decade past.

For reprints contact CFAAR, P.O. Box 8060, Berkeley, CA 94707-8060.

## Three More States Enact Break-in Laws

Three more states—Iowa, North Carolina, and Wisconsin—have enacted laws specifically protecting research facilities from break-ins, destruction of property, and theft of animals.

The action brings to 21 the number of states enacting such laws since 1988. Other states enacting such law this year are Arkansas, Montana, North Dakota, Oklahoma, Texas, and Washington. Seven states considering enactment of such laws are Nebraska, Nevada, New Jersey, New York, Pennsylvania, Rhode Island, and Tennessee.

States passing break-in bills before this year are Arizona, Georgia, Idaho, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maryland, Massachusetts, Minnesota, and Utah.

## PETA's Annual Report: Another Case of Half-Truths

The annual report for the People for the Ethical Treatment of Animals (PETA) tells of its efforts to rescue 82 rabbits from a Gaithersburg, MD, school but fails to tell the membership that it later killed 18 of the rescued rabbits.

According to the report "... 82 rabbits were being held in a public school basement in filthy, dark, rusting cages in a Future Farmers of America program to provide students with instruction in 'responsible pet ownership.' "Following "repeated" negotiations with the school, PETA gained custody of the animals, taking them to PETA's three-acre animal sanctuary and cemetary where the rabbits "had a safe place to stay while they received veterinary care and awaited adoption."

What was not said in the report was that PETA had killed 18 of the rabbits because, as PETA's sanctuary veterinarian Wendy Thacher told the press when the killings were learned by the media last April, "There was no place else for them to go. We did not want them crammed in here because that would be against our philosophy."

As the Montgomery (MD) Journal said editorially in commenting on the annual report, "A curious omission, considering that PETA officials vociferously defended the action as nothing to be ashamed of, including executive director Ingrid Newkirk writing that 'cuthanasia beats the socks off' being stuck in a hutch and bred.

"Oh well, it must have just slipped their minds."

"Or maybe members should just read between the lines at the part of the report that said after PETA got custody, the rabbits were 'given appropriate medical treatment'.

"Hmmmmmmm."

#### APHIS

(continued from p. 295)

3. "The Secretary intends that such person (nonaffiliated member of the IACUC) will provide representation for general community interests in the proper care and treatments of animals." Can the nonaffiliated member receive compensation by the institution for the time involved in protocol review or is that a conflict of interest?

It is generally accepted that reimbursement for expenses does not constitute conflict of interest. Compensation for the member's professional time, however, may create potential for a conflict of interest. Nominal compensation that is not considered to be pay for service or to infer affiliation with the institution might not be regarded as a conflict of interest.

4. If the details of a test drug or proprietary procedure are required for a complete review of animal care and use, what obligation do members of the IACUC have to protect the privileged nature of these drugs or procedures?

It is stated in the Animal Welfare Act [AWA; U.S. Code, Title 7, Section 2143(6)(B)] that "no . . . part of this Act shall be construed to require a research facility to disclose publicly or to the Institutional Animal Committee during its inspection, trade secrets or commercial or financial information which is privileged or confidential." Furthermore, the AWA states [U.S. Code, Title 7, Section 2157(a)] that it is unlawful for any member of an IACUC to release any confidential information of the research facility, including trade secrets.

In most instances, it will be possible for the IACUC to review an animal study proposal of an experiment or project involving proprietary information without the risk of disclosure. This may be accomplished by the PI using generic descriptions if appropriate or blanking out the proprietary information from the proposal.

An example of this might involve an animal study proposal needed to test a new drug. It should be possible for the committee to review such a proposal without having knowledge of proprietary information such as the chemical formula, molecular structure, etc. It may be important, however, for the committee to know information such as the pH (if administered parenterally), target cell or site of action, and expected or potential side effects or outcome (based on similar compounds) in order to properly evaluate the proposal.

#### 5. The standards indicate that animal health certificates should be signed by a licensed veterinarian. Previously we were under the impression that for interstate or intercontinental shipments of animals the signer must be accredited by the USDA. Have these regulations changed?

The regulations pertaining to interstate and international movements of animals have not changed. Many states and foreign countries have animal health regulations requiring certification that the animals are free of or are protected against specific diseases. These regulations protect against the introduction or spread of animal diseases. All states and countries have these regulations for domestic farm animals; however, not all have similar regulations for nonagricultural animals. Health certification for compliance with these regulations requires the signature of an accredited veterinarian. Information regarding state or international animal health regulations can be obtained from the state veterinarian or other animal health officer in your state.

The animal welfare regulations require health certification to ensure the well-being and safety of dogs, cats, and nonhuman primates that are being transported. If the state or country receiving the animals does not require additional health certification for imported dogs, cats, or nonhuman primates, the health certificate may be signed by a licensed veterinarian who is not accredited.

## 6. May paralytics be used alone in mammals for immobilization if no pain is anticipated in the study?

Section 2.31(2)(1)(iv) of the animal welfare regulations states that painful procedures will be performed with appropriate analgesics unless justified and will not include the use of paralytics without anesthesia. The intent of this regulation is that when necessary, animals that might experience pain will be provided appropriate pain relief and any withholding of such medication should occur only when scientifically justified. The further intent of this regulation is that paralytics not be used in place of anesthetics for restraint.

It is well recognized that a paralytic agent can obscure or prevent an animal from demonstrating a pain response. Such agents, however, do nothing to change the animal's pain perception or distress. Consequently, when paralytic agents are used, appropriate anesthesia, analgesia, or tranquilizers must be administered if the procedure performed on the animal causes or can be expected to cause pain or distress. Paralytics may be used alone if the IACUC determines that the procedure does not cause pain or distress.

## 7. What is the appropriate unit to be registered? Can a large institution located in several different geographical areas be covered by a single registration?

It is stated in Section 2.30(a)(e) of the regulations that "A subsidiary of a business corporation, rather than the parent corporation, will be registered as a research facility . . . ." We interpret this to mean that registration must be at the level of the lowest legal entity of the parent corporation. It will be up to the legal counsel of the facility to determine what that lowest legal entity is.

Animal	ILAR, FY 1978 <sup>a</sup>	APHIS, FY 1982 <sup>b</sup>	Health Designs (est.), 1983 <sup>c</sup>	APHIS, Fy 1984 <sup>6</sup>	APHIS, Fy 1986 <sup>b</sup>	APHIS, Fy 1989 <sup>b</sup>
Mice	13,413,813		8,500,000			
Rats	4,358,766		3,700,000			
Hamsters	368,934	337,790	454,479	437,123	370,655	389,042
Guinea pigs	426,665	459,246	521,237	561,184	462,699	481,712
Other rodents	79,993					
Rabbits	439,986	453,506	509,052	529,101	521,773	471,037
Cats	54,908	49,923	55,346	56,910	54,125	50,812
Dogs	183,063	161,396	182,245	201,936	176,141	156,443
Other carnivores	4,990					
Ungulates	144,595					
Nonhuman primates	30,323	46,388	59,336	55,338	48,540	51,688
Birds	450,352		$100,000^{d}$			
Amphibians			500,000 <sup>d</sup>			
Fish			$4,000,000^d$			
Wild animals		69,043		232,541	144,470	153,722
Total	19,956,388	1,576,556 <sup>e</sup>	18,581,875	2,074,133 <sup>e</sup>	1,778,403 <sup>e</sup>	1,754,456 <sup>e</sup>

APHIS, Animal and Plant Health Inspection Service; ILAR, Institute of Laboratory Animal Resources.

<sup>*a*</sup>From National Research Council. 1980. P. 32 in National Survey of Laboratory Animal Facilities and Resources: Fiscal Year 1978. A report of the Institute of Laboratory Animal Resources Committee on Laboratory Animal Facilities and Resources. NIH Pub. No. 80-2091. Washington, D.C.: U.S. Department of Health and Human Services.

<sup>b</sup>From Animal and Plant Health Inspection Service. 1983-1990. Animal Welfare Enforcement. Fiscal Years 1982, 1984, 1986, 1989. Reports made by the Secretary of Agriculture to the President of the Senate and the Speaker of the House of Representatives. Washington, D.C.: U.S. Department of Agriculture. Reporting of mice and rats is voluntary, and data on these animals are not included in the annual reports.

<sup>c</sup>From Office of Technology Assessment (OTA). 1986. P. 60 in Alternatives to Animal Use in Research, Testing, and Education. Pub. No. OTA-BA-273. Washington, D.C.: U.S. Congress. Data are estimates from a 1984 report entitled Survey and Estimates of Laboratory Animal Use in the United States, which was prepared by Health Designs, Inc., Rochester, New York, for OTA.

<sup>d</sup>Estimates are the highest of a rough range.

<sup>e</sup>Total does not include numbers for mice and rats.

#### **APS Conferences**

Integrative Biology of Exercise Colorado Springs, Colorado September 23-26, 1992

Cellular and Molecular Biology of Membrane Transport Orlando, Florida November 4-7, 1992

### APS Member Appointed To DHHS Committee On Scientific Integrity

The US Department of Health and Human Services has established a Public Health Service Advisory Committee on Scientific Integrity to review and evaluate the policies and procedures for detecting, deterring, and investigating scientific misconduct.

The 11-member committee includes Stuart Bondurant, dean of the School of Medicine at the University of North Carolina and a member of APS. The committee chairman is Nicholas H. Staneck, who is of the Historical Center for the Health Sciences at the University of Michigan.

The advisory committee will provide advise to both the Secretary for Health and Human Service and the Assistant Secretary for Health on matters relating to scientific misconduct. The committee will review on an ongoing basis the policies and procedures of the Public Health Service as they relate to misconduct in science.

### Robert S. Hutton Scholarship Fund

The Robert S. Hutton Scholarship Fund has been established. Checks for this purpose should be made payable to Regents of the University of California. This scholarship fund will be graduate student support.

Reggie Edgerton, a professor at UCLA and a long-time friend and associate of Hutton's, will be working on this project. Contributions to this fund may be mailed directly to Regents of the University of California, UCLA Chairman's Office, Department of Kinesiology, Slichter Hall, 405 Hilgard Avenue, Los Angeles, CA 90024-1527.

### APS Members on the Move

Humberto Fernandez-Moran, A. N. Pritzker professor emeritus of biophysics, leaves for Portugal in October to assume the post of special science counselor at the Embassy of Venezuela in Lisbon, Portugal.

Formerly at the Eastern Virginia Medical School, Norfolk, Edward G. Smith, has moved to the University of Pennsylvania Hospital, Center for Sleep and Respiratory Neurobiology, Philadelphia.

Chun S. Park, Department of Physiology, University of Massachusetts Medical School, is now professor of physiology at the University of Ulsan College of Medicine, Seoul, Korea.

Stephen L. Dodd of the Louisiana State University has joined the Department of Florida at the University of Florida, Gainesville.

**Bruce K. Rubin** has accepted a position as associate professor of pediatrics at St. Louis University. Rubin was at the University of Alberta, Edmonton.

Formerly at the Alliance Pharmaceutical Corporation, San Diego, **Sidney J. Stolzenberg** is now in the Division of Cardio-Renal Drug Products, Food and Drug Administration, Rockville, Maryland.

**Richard M. Raymond** has moved from Loyola University Medical Center to Carolinas Medical Center, Department of Emergency Medicine, Charlottee, North Carolina.

Leon G. Fine, who has been in the Division of Nephrology, University of California at Los Angeles, has joined the Department of Medicine, University College of Middlesex School of Medicine, London, England.

Formerly at the Veterans Administration Medical Center in Albuquerque, **Oscar U. Scremin** has moved to the West Los Angeles Veterans Administration Medical Center, California.

## **Rokitka Receives International Award**



Mary Anne Rokitka, assistant professor of physiology at the State University of New York at Buffalo, has been awarded the 1991 Charles W. Shilling Award by the Underseas and Hyperbaric Medical Society.

The award was presented in recognition of Rokitka's "tireless efforts on behalf of the society and its Great Lakes Chapter," which she helped found in 1980 and headed as its first president. Rokitka was honored last year with the establishment by the Great Lakes Chapter of the Undersea and Hyperbaric Medical Society of an annual award named in her honor (*The Physiologist* 33: 186, 1990).

A member since 1977, Rokitka has been affiliated with the SUNY and is assistant professor of physiology and director of the hospital nursing program and assistant to the vice president for health sciences.

### APS Member Elected to NAS



Susan E. Leeman is professor of physiology and director, interdepartmental neuroscience program at the University

of Massachusetts Medical Center, Worcester. During the course of work directed toward purification of a corticotropin-releasing factor, Leeman discovered two other biologically active substances in bovine hypothalamic extracts: one, a sialogogic peptide that was subsequently isolated and characterized as the peptide, substance P; the other, another vasoactive peptide, distinct from substance P, was also isolated in her laboratory and named neurotensin. Both peptides were sequenced and synthesized, opening up two new fields for investigation. Substance P and neurotensin are widely but selectively distributed throughout the central and peripheral nervous systems, the gastrointestinal tract, many endocrine cells, and subserve multiple physiological functions.

Members are invited to submit nominations for honorary membership. Send nominations and documentation of the candidate's contributions to physiology to the APS Honorary Membership Committee, 9650 Rockville Pike, Bethesda, MD 20814, by December 1, 1991.

#### Laser-Doppler Blood Flowmetry

A. P. Shepherd and P. A. Öberg (editors) Hingham, MA: Kluwer Academic Publishers, 1990, 416 pp., illus., index, \$110.00

This book is an excellent introduction to the history, theoretical principles, and applications of laser Doppler flowmetry. Sheperd and Öberg have done an admirable job of compiling an excellent and much needed text incorporating important original bsic data on laser Doppler flowmetry. Laser doppler flowmetry has suffered from overly ambitious expectations without proper familiarization with its advantages and disadvantages. Therefore, many of us would benefit from making the first six chapters of this book required reading for anyone contemplating using this technology.

Chapter 1 contains a very clear and thorough qualitative and quantitative description of the basic discoveries of Johann Doppler 150 years ago. It further recounts a brief summary of the key steps in the discovery of the laser and its application to Doppler velocimetry. The narrative of Michael Stern's initial studies at NIH on laser Doppler velocimetry in tissues is particularly fascinating. The subsequent steps leading to development of the current commercial instruments are described. This first chapter provides a superb yet concise background for those individuals who want a understanding of the basic principles and history behind laser Doppler velocimetry (and flowmetry).

The next five chapters are more detailed. Bonner clearly describes the mathematical principles behind the laser Doppler technique. Holloway, Öberg, and Borgos give interesting descriptions of the development and unique features some of the first three laser Doppler flowmeters to be commercialized. In chapter 6, Öberg presents innovations and precautions, that is, potential artifacts and unique features of this technique. This is a particularly important section that should aid in the interpretation of data acquired from any of the commercially available laser Doppler flowmeters.

The remainder of the book, chapters 7-19, focuses on particular applications of laser Doppler flowmetry to specific tissues. Included are chapters on intravascular catheter velocimeters, cutaneous (three chapters: one on the pharmacologic and dermatologic applications; one on the plastic and reconstructive surgical applications; and one on the perpheral vascular disease applications), skeletal muscle, gastrointestinal, respiratory tract, central and peripheral nervous systems, renal, bone, cochlear, and retinal applications. Most of these chapters are clearly written and quite enlightening. While I am a "believer" in laser Doppler flowmetry, the book would have benefitted from a more critical evaluation of the problems and pitfalls of laser Doppler flowmetry. Many clinicians and physiologists have had at least a brief exposure to the technique.

Laser Doppler flowmetry may have suffered from individuals expecting to see a single stable blood flow value. However, temporaland spatial heterogeneity of blood flow are real physiological phenomena contributing to the variability of flow measurements in small (1-mm<sup>2</sup>) tissue regions. Even an ideal technique would demonstrate variations in measured flow. Superimposed on these physiological variations are the technical artifactual variations of laser Doppler flowmetry. This book begins to unravel some of these "mysteries" of laser Doppler flowmetry.

> Bruce Klitzman Director Plastic Surgery Research Laboratories Duke University

#### The Lung: Scientific Foundations (Volume 1 & 2)

R. G. Crystal and J. B. West (editors in chief); P. J. Barnes, N. S. Cherniack, and E. R. Weibel (associate editors) New York: Raven, 1991, 2,462 pp., \$225

In the wake of a number of books published in the areas of the lung biology and pulmonary physiology, yet another volume of the lung might seem redundant, but this book offers something special. **The Lung** in two volumes is a compendium of fundamental science and yet advanced with minimal dead space. The material is divided into eight sections and consists of 193 chapters contributed by 311 authors and edited by 5 editors. All these participants are the leaders in their own fields.

The coverage is extensive. The scope of each chapter is enormous but is limited to about 10 pages so that the content is condensed. Each chapter is well referenced. Accordingly, it is an important source book. It is practically everything for everybody in the lung business. It spans from cell and molecular biology to integrative systemic morphology and physiology. There is an overarching concept, relating structure and function.

A major part of the book is devoted to just the lung, its architecture and components from organ to organelle and its biological processes. It goes over the lung tissue and its unique supporting structure and its two types of circulation. The gas exchanger, endocrine, defense, and other functions of the lung are extensively covered. The other part consists of the processes that ventilate and manage the lung. The design of the thoracic cage, respiratory muscles, innervation of the lungs, and respiratory muscles and their functions as a whole are all integrated. The strategy of lung ventilation and gas exchange with respect to the metabolism and gas exchange in the peripheral tissues is well focused. Because of its central role in the organism, the organ is well connected not only by circulation and blood-borne material but also by strategic location of sensors and their neural connection with the nervous system for feedback control of ventilation. The quantitative physiology is clearly documented.

The function of the lung during exercise and sleep is well incorporated in the context. Because of the diversity, functions of several other systems have to be incorporated for unification. The result is a comprehensive lung volume with a broad scientific foundation.

Apart from the traditional coverage of adult organism, the book deals with the fetal, postnatal, and aging aspects of the lung. Also, areas of adaptation to special environment, comparative physiology, lung injury, defense, and repair have been featured.

In a large and diverse work like this, cross-reference between the chapters would have increased usefulness of the book. However, that task would have delayed its publication and defeated the purpose of presenting the advances in the field up-to-date. The fact that the book is well-indexed (80 pages) takes care of the problem of cross-referencing.

The book should be useful to teachers and advanced students and to basic science and clinical researchers. It is important to note that the contents of the chapters are expected to have bias of the authors.

The volumes weigh 5 kg each and look durable, as if they will be of good use for some time to come.

> Sukhamay Lahiri Professor University of Pennsylvania

## Comparative Physiology, Vol. 7: Comparative Aspects of Sodium Cotransport Systems

R. K. H. Kinne (editor) Basel: Karger, 1990, 277 pp., illus., \$195

This book is a collection of seven articles loosely organized around the central theme of sodium's role in the secondary active transport of organic and inorganic solutes. The ubiquity of sodiumsolute cotransport as a cellular strategy for movement of solutes against their electrochemical gradients was recognized 20 years ago by Schultz and Curran in their classic review on the subject. The present work provides an eclectic overview of the diversity of this common mechanism. The articles range from a very broad examination of the Na cotransport of amino acids in marine animals to a subject as specific as the role of Cl<sup>-</sup> in the activation of (some) Na cotransport processes. Most of the articles are written for a reader familiar with membrane transport.

The first chapter, by Robert Preston, provides the most thorough overview of its subject, Na cotransport of amino acids in marine invertebrates. With 17 tables providing summaries of the results contained in approximately 350 references, this review provides an encyclopaedic update of the author's 1982 article written for the American Zoologist. In the present work, Preston emphasizes the value of marine invertebrates as systems to study the kinetics and energetics of secondary active cotransport. Although there is coverage of transport processes in so-called "internal tissues" (i.e., gut, hepatopancreas, coelomocytes, and neural tissue), the thrust of the discussion is on the extremes of transport kinetics and energetics displayed by processes found in the integumental epithelium of softbodied marine invertebrates, i.e., those tissues that are directly exposed to sea water. The concentration of amino acids in marine invertebrate tissues is large, typically in excess of 100 mmol/kg cell water, which is maintained in the face of external concentrations in sea water than are often < 100 nM. Therefore, transport of amino acids into the integument must occur against chemical gradients that can exceed 10<sup>6</sup> to 1. There is an extended discussion on the possible role of D-amino acids, recently found to exist in large concentrations in the tissues of some marine invertebrates, in the energetics of these transport process. However, the bulk of the presentation is a systematic discussion of the adequacy of the Na-cotransport paradigm to account for the extreme solute gradients characteristic of the invertebrate integument. Of particular interest to this reviewer were Preston's discussions of the "pumpleak" model as it is expressed in mammalian systems compared to the situation in marine invertebrates, where the low passive permeability to amino acids allows secondary active transport to approach a thermodynamic equilibrium between the electrochemical gradients for Na and solute, and of the metabolic cost of maintaining large amino acid concentration gradients. This review will serve as the standard source for this field for several years.

Of the five articles, the second, by Berteloot and Maenz, is the most narrowly focused in that it is restricted in its review of Nadependent acidic amino acid transport, via system  $X_{AG}$ , to observations made in mammalian cells and tissues. This narrow focus eliminated any discussion on the interesting literature on transport of anionic amino acids in, for example, fish and insect intestine. However, the authors' "comparative view" is evident by their effort to develop a common model for transport of these compounds derived from their analysis of the large literature on acidic amino acid transport in liver, intestine, kidney, and the nervous system. The discussion of the effects of K<sup>+</sup>, H<sup>+</sup>, and Cl<sup>-</sup> on the Nacotransport of aspartate and glutamate is comprehensive and readily understandable. The reader will find more challenging the discussion of a kinetic model that incorporates the available data into a single model that, with a minimum number of assumptions, attempts to describe transport as observed in a diverse set of tissues.

Although the requirement for Na<sup>+</sup> is often absolute for cotransport systems in animal cells, increasing evidence points to the need, in many cases, of multiple ions to achieve maximum activation of transport. The article by Bogé and Pérès examines the requirement for chloride in the activation of Na-cotransport systems. Again, the focus is on processes found in vertebrates, thereby eliminating discussion of recent interesting results on transport in, for example, crustaceans. Instead, the focus is on chloride's effect on organic solute transport in mammalian, avian, and teleost tissues, in which chloride has been found to play a role in the uptake of several structural classes of  $\alpha$ - and  $\beta$ -amino acids (notably glycine and taurine, respectively) and several biologically important amines. The authors suggest that the current literature supports the existence in the plasma membrane of epithelial, nerve, and blood cells of "a new multi-ion-dependent transport system sensitive to both sodium and chloride ions," displaying a "certain substrate specificity" for amino acids and amines. The role of chloride in this process is suggested to be that of a catalytic, rather than energetic, activator because gradients of Cl-, in the absence of an electrochemical gradient for Na<sup>+</sup>, typically do not support active solute accumulation in whole cells and tissues. The latter issue is clearly controversial in light of the evidence, reviewed by the authors, for the cotransport of Cl- with at least some solutes (e.g., taurine). The authors' suggestion of a single system in these diverse systems seems a bit contrived in light of many differences in, for example, specificity for organic solute demonstrated by chloride-sensitive processes in different tissues.

The fourth article is a brief, but satisfyingly complete, summary of the current understanding of renal phosphate transport in three groups of animals: mammals, birds, and fish. The latter two groups differ markedly from the former because of the presence of a potent secretory pathway for phosphate. Issues of regulation of transport were absent in the other articles in this volume. In contrast, the regulation of Na-phosphate cotransport was the central theme of Renfro and Gupta's work. The authors provide an understandable account of the roles of the three factors known to influence renal phosphate transport: PTH and glutacorticoids, calcium and phosphate availability, and acid-base status. A Na-phosphate cotransporter is present in the luminal membrane of all three animal classes; its downregulation by PTH is clear in mammals and birds and suspected in fish. The authors offer some speculation on the probable presence of other regulated processes in birds and fish that are responsible for the secretion of phosphate. The authors' discussion of their work using primary cultures of flounder proximal tubular cells provides the basis for speculations on the existence of dual regulatory pathways for phosphate transport, including evidence for a stimulatory effect of diacylglycerol on a luminal step involved in phosphate secretion.

The final article is the shortest, a brief overview of sodium transport systems in fish and crustacean gills by David Towle. Development of models of cellular mechanisms of sodium transport in aquatic animals has been complicated by the fact that, until recently, so much of the primary data has been generated using whole animal or perfused gill preparations. While there is general agreement on a model for sodium (salt) excretion in saltwater-adapted animals (involving a basolateral Na,K,Cl cotransporter and an apical Clchannel), there is more controversy concerning the cellular mechanisms associated with sodium accumulation from freshwater. Towle incorporates into that data base recent work using isolated membrane vesicles to provide support for a model involving parallel Na/H and Cl/HCO<sub>3</sub> exchangers (including evidence for an electrogenic, 2 Na:1 H antiport in crustacean gill). Although this is a widely accepted model, this reviewer was disappointed that there was no discussion of the possible role of electrogenic an H-ATPase and apical Na-channels, as described in recent years for frog skin.

> Stephen H. Wright, Associate Professor University of Arizona Health Sciences Center

Assistant Professor in Physiology, Department of Physiology and Biophysics, University of Illinois at Urbana-Champaign. Applications are invited for a full time, tenure-track position in molecular or cellular physiology at the assistant professor level starting August 1992. The successful candidate must hold a doctoral degree and is expected to develop a vigorous, independently funded research program and to participate in undergraduate and graduate teaching. She/he will join a strong department with broad expertise in cellular, molecular, and systems physiology. While a candidate with research interests in cellular and molecular aspects of cardiovascular physiology is preferred, candidates with interests outside this area will be considered. Salary will be commensurate with experience and qualifications. Deadline for receipt of applications is December 1, 1991. Interviews may take place before December 1, but all applications received by this date will be fully considered. Applicants should submit a curriculum vitae, list of publications, statement of future research plans, and names and phone numbers of at least three references to Dr. Philip M. Best, University of Illinois, Department of Physiology and Biophysics, 524 Burrill Hall, 407 S. Goodwin Ave., Urbana, IL 61801 (217-333-8176). Women and minority applicants are encouraged to apply. [EOAAE]

Research Scientist. Responsible for developing a nonradioactive technique for labeling and in situ hybridization in neuroglial cell cultures; preparing and maintaining glial cell culture; performing immunocytochemical and cell transfection studies; performing routine physiological and molecular biological experiments; analyzing data; preparing scientific reports and manuscripts. Candidate must have PhD in animal science physiology; documentation of at least 2 years post-doctoral research experience including biochemistry, molecular biology, and morphology; documented experience of at least 2 years in biochemistry (all types protein and enzyme assays, electrophoresis, receptor-binding analysis including equilibrium, kinetic, and competitivedisplacement analysis); molecular biology (radioactive and nonradioactive in situ hybridization on tissue culture and fixed sections, RNA and DNA isolation and purification, Northern blot analysis); and morphology (14C and 3H-autoradiography, histochemistry and immunocytochemistry, Nissl, silver stain). Candidate also must have documented evidence of brain research and statistical and computer experience with

#### **Positions Available**

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 will not be 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 February 15 for the April issue). Mail copy to APS, 9650 Rockville Pike, Bethesda, MD 20814.

microcomputers. Salary \$26,000 per year for 40-hour week. Send resumes to 7310 Wood-ward Avenue, Room 415, Detroit, MI 48202. Reference #70191.

Assistant Professor of Physiology. The Department of Animal Biology, School of Veterinary Medicine at the University of Pennsylvania has a full-time tenure track opening for a physiologist to join an interactive, multidisciplinary department, within the biomedical community at the University of Pennsylvania. Individuals working at any level of analysis are encouraged to

Biology of Aging: Observations and Principles. Robert Arking. Englewood Cliffs, NJ: Prentice Hall, 1991, 420 pp., illus., index, \$48.00.

Multiple Muscle Systems: Biomechanics and Movement Organization. Jack M. Winters and Savio L-Y. Woo (Editors). New York: Springer-Verlag, 1990, 801 pp., illus., index, \$69.00.

The Beta-Adrenergic Receptors. John P. Perkins (Editor). Clifton, NJ: Humana, 1991, 416 pp., illus., index, \$89.50.

Myocardial Hypertrophy: A Symposium. Eleanor L. Ison-Franklin and Harold Sandler (Editors). Washington, DC: Howard University Press, 1991, 219 pp., illus., index, \$60.00.

Associated Human Reproductive Technology. E. S. E. Hafez (Editor). Bristol, PA: Taylor & Francis Group, 1991, 266 pp., illus., index, \$99.50.

New Developments in Fundamental and Applied Radiobiology. Colin B. Symour & Carmel Mothersill (Editors). Bristol, PA: Taylor & Francis Group, 1991, 448 pp., illus., index, \$88.00. (Proc. of the 23rd Anapply, although the department's strength is at the cell/molecular level. Applicants should have a PhD or equivalent degree in physiology or related field and postdoctoral training, be prepared to maintain an independent, extramurally funded research program, and participate in departmental tcaching. Send CV, names and addresses of three referees and a statement of research program to Dr. Michael Kotlikoff, Department of Animal Biology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104-6046. [EOAAE]

Chairman, Department of Physiology, Georgetown University School of Medicine is seeking a new Chairman of the Department of Physiology. Candidates are expected to demonstrate the capacity for leadership of an active research program in molecular or cellular physiology and direct the teaching programs of the Department of Physiology which lead to MS, MD and PhD degrees. The Georgetown University Medical Center provides a strong environment in basic and clinical research and its expanding programs provide an environment conducive to growth in physiology. Individuals interested in this opportunity should apply to Dr. Jeffrey Cossman, Chairman, Physiology Search Committee, Georgetown University School of Medicine, 3900 Reservoir Road, N.W., Washington, DC 20007. [EOAAE]

#### **BOOKS RECEIVED**

nual Meeting of the European Society for Radiation Biology, Dublin, 1990).

Diagnostic Pathology of the Liver and Biliary Tract. Boris H. Ruebner, Carolyn K. Montgomery, and Samuel W. French (2nd ed.) Bristol, PA: Taylor & Francis Group, 1991, 492 pp., illus., index, \$125.00.

Stress and Emotion: Anxiety, Anger, and Curiosity, Vol. 14. Charles D. Spielberger, Irwin G. Sarason, Zsuzsanna Kulcsar, and Guus L. Van Heck (Editors). Bristol, PA: Taylor & Francis Group, 1991, 340 pp., illus., index, \$64.50.

Imaging, Measurements, and Analysis of the Heart. Samuel Sideman and Rafael Beyar (Editors). Bristol, PA: Taylor & Francis Group, 1991, 445 pp., illus., index, \$85.00.

*Free Radicals and Food Additives.* Okezie I. Aruoma and Barry Halliwell (Editors). Bristol, PA: Taylor & Francis Group, 1991, 201 pp., illus., index, \$77.00.

*Tinnitus: Diagnosis/Treatment.* Abraham Shulman, et al. Philadelphia, PA: Lea & Febiger, 1991, 571 pp., illus., index, \$95.00.

## **APS Sustaining Associate Members**

The Society gratefully acknowledges the contributions received from Sustaining Associate Members in support of the Society's goals and objectives

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#### **IUPS Fellowship Available**

The International Union of Physiological Sciences is offering a fellowship to promote teaching of physiology in the Third World. The recipient must be on the physiology faculty of a medical school in the Third World, and he or she must return to that faculty for a minimum of 3 years following completion of the fellowship. The recipient's home institution must certify that a position will be available for the fellow after the training. The fellowship should run for 6–12 months, and the stipend will be \$US 25,000/year, prorated for periods less than 12 months. Preference will be given to younger applicants.

The chief purpose of the fellowship is to promote the teaching of physiology. Hence the recipient will be expected to attend (and if feasible, participate in) an entire course of physiology in a well-established university, including all lectures, conferences, demonstrations, laboratories, and other exercises. Minimal participation in research is permitted, provided that it never interferes with the chief purpose as outlined. Candidates should make arrangements with the physiology department of the prospective host institution prior to submitting an application; the fellow's visit must coincide with the period during which the host institution gives its main course in physiology.

Applications must be in English and should include I) curriculum vitae, 2) a statement by the applicant of how she/he will utilize the award (not to exceed 2

pages), 3) a statement from the host institution that they will accept the applicant, and 4) a statement from the applicant's home institution that the applicant has a full faculty position in physiology and will return to that position at the completion of the fellowship. Regrettably, only 1 award for 12 months (or possibly 2 awards for 6 months each) can be made. Selection will be made by an international committee.

Deadline for receipt of applications is March 1, 1992. Send applications to Professor Heinz Valtin, Department of Physiology, Dartmouth Medical School, Hanover, NH 03756.

#### Plan for Managing Cost of Biomedical Research

In response to Congressional concerns expressed in the FY 1991 House and Senate Appropriations Reports, the National Institutes of Health (NIH) has prepared a financial management plan entitled, "A Plan for Managing the Cost of Biomedical Research." This document, developed by NIH in consultation with the biomedical research community and the various National Advisory Councils and Boards, outlines the principles on which the plan is based, identifies the specific goals of the plan, and discusses the cost management measures to be taken. Copies are available from Office of Grants Inquiries, Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20892. 301-496-7441.

#### **Call for Workshops: ABLE**

Each year at its annual meeting, The Association for Biology Laboratory Education (ABLE) presents 12–15 tested, innovative, hand-on workshops suitable for undergraduate biology laboratory courses. Workshops cover diverse disciplines and levels within biology, ranging from exercises aimed at nonmajors to ones appropriate for advanced, specialized upperdivision courses. Workshops that successfully apply new ideas, materials, or approaches, or that use nontraditional organisms in a classroom setting are especially sought.

The 1992 meeting will be at the University of Nevada, Las Vegas, June 3-5. If interested in presenting a workshop, please contact the workshop chairperson by November 15, 1991: Roberta Williams, University of Nevada, Las Vegas, Dept. of Biological Sciences, Las Vegas, NV 89154-4004. Tel: 702-739-3203.

#### Scientific Meeting

Third International Conference on Sound and Vibration in Pregnancy: Pregnant Women at Work, Gainesville, FL, February 7, 1992. *Information:* Robert M. Abrams, University of Florida, Department of Obstetrics and Gynecology, Box J-294, JHMHC, Gainesville, FL 32610. Tel: 904-392-3179.