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The Physiologist

A Publication for Physiologists and Physiology
Orr E. Reynolds, Editor

Volume 23, No. 2, April 1980

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The Meeting will be held in Toronto at the Sheraton Centre, October 12 through 17, 1980. Joining APS will be the Canadian Physiological Society, the Canadian Zoological Society Section of Comparative Physiology and Biochemistry, and the American Society of Zoologists Section on Comparative Physiology and Biochemistry.

REFRESHER COURSE: PHYSIOLOGY OF CALCIUM AND PHOSPHATE REGULATION

Organizer: F. G. Knox, Mayo Medical School

Physiologic roles of parathyroid hormones and calcitonin.
C. D. Arnaud, University of California (San Francisco)
Physiology of vitamin D.
R. V. Kumar, Mayo Medical School
Control and modulation of intracellular calcium.
A. B. Borle, University of Pittsburgh
*Teaching critique.
J. H. Dirks, University of British Columbia
Role of the kidney in calcium regulation.
W. N. Suki, Baylor College of Medicine
Role of the kidney in phosphate regulation.
V. W. Dennis, Duke University Medical Center
Physiology of calcium and phospate in bone.
L. G. Raisz, University of Connecticut School of Medicine
*Teaching critique.
Roger Sutton, University of British Columbia
*Critique of presentations to define those concepts that should be presented to students.

SYMPOSIA

New perspectives of calcium anatgonists. 1. Intracellular aspects. 2. Excitative-contraction coupling. 3. Stimulus-secretion coupling.
(Sponsored by the APS Publications Committee).
G. B. Weiss;, University of Texas Health Science Center (Dallas)
Man in the cold.
R. F. Goldman, U.S. Army Research Institute of Environmental Medicine
Comparative physiology of diffusion in respiratory gas exchange.
J. Piiper and P. Scheid, Max Planck Institute
Physiology of the splanchnic circulation.
E. D. Jacobson, University of Cincinnati
Neurophysiology of autonomic preganglionic neurons.
(Sponsored by CPS)
F. R. Calaresu, University of Western Ontario
Quantitative dynamic regulation of glucose metabolism in physiology and diabetes.
(Sponsored by CPS)
M. Vranic, University of Toronto
Control of breathing during fetal and early post-natal life.
(Sponsored by CPS)
V. Chernick, University of Manitoba
Hormonal regulation of foregut development.
B. T. Smith, Queen's University
Morphological aspects of renal function.
(Sponsored by CPS)
A. P. Evan, Indiana University
Endocrine regulation of vertebrate seasonal reproductive cycles.
(Sponsored by CSZ SCPB)
R. E. Peter, University of Alberta

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Follicle stimulating hormone.
J. H. Dorrington, University of Toronto
Computer assisted tomography.
E. H. Wood, Mayo Foundation
Protein synthesis.
B. W. O'Malley, Baylor College of Medicine
Review of the history of respiratory gases.
R. H. Kellogg, University of California (San Francisco)
Radioactive iodine metabolism and nuclear accidents.
Lester Van Middlesworth, University of Tennessee
The mechanism and biological value of fever and the significance of endogenous antipyresis.
K. E. Cooper, University of Calgary
Elements of locomotor control.
Serge Rossignol, University of Montreal
Specialization in movement systems: Lesson learned from examination of the physiology of head movement.
V. C. Abrahams, Queen's University
Vestibular physiology: The peripheral response and its central significance.
G. Melville Jones, McGill University
Sympathetic abnormalities in experimental and human hypertension.
Jacques D'Champlain, University of Montreal
Special Adaptations in marine mammals.
Organizer: F. R. Engelhardt, University of Ottawa
Ion and water regulation. J. R. Geraci, University of Guelph.
Biochemical adaptations to diving. P. W. Hochachka, University of British Columbia.
Growth, starvation, and thermoregulation. N. A. Oritsland, University of Oslo.

MINI SEMINAR on Teaching Respiratory Physiology organized by John B. West

ABSTRACTS DUE: JUNE 13, 1980

MINI-SEMINAR ON THE TEACHING OF RESPIRATORY PHYSIOLOGY

At the Fall Meeting of the Society to be held in Toronto in October, there will be a mini-seminar on the teaching of respiratory physiology to medical students. The objective is to describe how this is done in four institutions with a view to helping faculty who have this as one of their responsibilities.

Two hours will be set aside for the mini-seminar which will have an unusual format. Four people from different institutions will be asked to contribute. Each of these will set up posters describing their teaching program in a room which will be set aside for this session. Aspects that might be covered include a list of the lectures and topics covered, laboratories, small discussion groups (if any), texts, additional handouts, teaching aids - in short, anything that is part of the first course in respiratory physiology for medical students. The emphasis will be on what is actually done rather that what ideally might be done.

This initial poster session will last half an hour. It will be followed by brief oral presentations from each participant which will not take more than 15 minutes and therefore will total one hour. The posters will then be manned for an additional half an hour or longer depending upon audience interest.

This format has been chosen because it will allow people with a somewhat peripheral interest to get the gist of the material by attending the oral presentations, but those who want more information can talk to the speakers before and after the oral presentations while they are manning their posters.

The seminar is being organized by the Education Committee of the Society.

John B. West, M.D., Ph.D.

TOPIC CATEGORY ANALYSIS

1980 FASEB MEETING

The 15 topic categories attracting the largest number of abstracts submitted for the 1980 FASEB Meeting in Anaheim were the following, (Total no. of topics-314).

Topic Number	Topic Title	Programming Society	Abstracts Received
131	Hypertension	APS	92
190	Epithelial Tissues	APS	72
271	Regulation of Respiration	APS	69
264	Prostaglandins	ASPET	51
270	Neurol Control of Circulation	APS	51
130	Coronary Physiology and Pharmacology	ASPET	49
081	Neuroendocrines	APS	48
004	Alcohol	ASPET	47
007	Biomedical Pharmacology	ASPET	44
238	Neuropharmacology, General	ASPET	44
258	Nutrition, General	AIN	43
093	Exercise	APS	41
313	Zinc	AIN	41
216	Analgesics and Antagonists	ASPET	40
250	Cyclic AMP	ASPET	40

CONTRIBUTIONS IN SUPPORT OF SYMPOSIA

Through the efforts of the following 1980 Spring Meeting symposia organizers, $5,950 was contributed to the Society to supplement or offset costs for conducting their symposia:

Francois M. Abboud
Donald D. Heistad
Ivor Jackson
Judith R. Walters
Jonathan R. Wolpaw
Paul J. Yarowsky

The Society publicly acknowledges with thanks, the following who contributed to the support of 1980 Spring APS symposia:

Abbott Laboratories
Arnar-Stone Laboratories
Beckman Instruments, Inc.
CIBA-GEIGY Corporation
The Dow Chemical Company
EG&G ORTEC
Hoffmann-La Roche Inc.
Lilly Research Laboratories
Merck Institute for Therapeutic Research
New England Nuclear Corporation
Smith Kline & French Laboratories
The Upjohn Company
Warner-Lambert Company

HONORS AND AWARDS

Dr. **Claude Fortier** of Laval University won $25,000 from the Gairdner Foundation of Toronto in recognition of his contributions to Canadian medicine. Dr. Fortier received the Wightman Award of the Foundation for his "outstanding leadership in medicine and medical science." His scientific career has been devoted to the study of the relationships between the central nervous system and glands such as the thyroid, pituitary, sex and adrenal glands. For more than 20 years he has represented Laval University on provincial, national and international boards.

Dr. **Daniel Kline,** University of Cincinnati College of Medicine was the recipient of the Dr. Harold Lamport Award at the New York Academy of Sciences Annual Meeting in December for his excellence in research and teaching in physiology. Dr. Kline has been on the Editorial Boards of the *American Journal of Physiology* and the *Journal of Applied Physiology.* He is recgonized as an outstanding physiologist, teacher, and investigator.

Professor **John E. Desmedt,** Corresponding Member of APS was given the Dautrebande Prize for 1979. Professor Desmedt, Director of the Brain Research Unit, Faculty of Medicine, University of Brussels, Belgium, was chosen for his original contributions to neuromuscular diseases, to mechanisms of voluntary motor control in man, and to brain mechanisms studies by the evoked potentials methods in relation to maturation, aging and neurological disorders and cognitive performance.

From the Publications Desk

SECRETORY DIARRHEA NEWEST BOOK IN CLINICAL PHYSIOLOGY SERIES

Already the Clinical Physiology Series of the American Physiological Society has been acclaimed as a most important bridge between research and clinical physiology. Samples of recent reviews of *Pulmonary Edema,* edited by Alfred P. Fishman and Eugene M. Renkin, extol the value of these books.

> This book, which is exciting in every way, is witten by a group of physiologists and physicians who are actively engaged in the study of alveolar structure and function.
>
> *The Lancet*

> The text provides an elegantly organized consideration of pulmonary edema. It will enable the clinician to greatly improve his comprehension of the factors that regulate water balance in the lung and the various influences that result in the final common reaction - pulmonary edema.
>
> *JAMA*

Now the Society adds a fourth book to this series, *Secretory Diarrhea.* The content of this book, edited by Michael Field, John S. Fordtran, and Stanley G. Schultz, is described in the preface as follows:

"Diarrhea is one of the major causes of death in the world. In developing countries, it accounts for more fatalities than any other single cause. Even in North America and Europe, it is a leading reason for death and disability among infants and young children. Severe diarrhea is most commonly caused by infection but can also be produced by malabsorption of bile salts or fat and certain hormone-secreting tumors.

"In the past decade we have witnessed major advances in understanding the pathophysiology of diarrhea. Most acute diarrhea appears to result from the stimulation of active electrolyte secretion in the intestines by bacterial enterotoxins and other agents. Cholera is the archetypal secretory diarrhea: the bacterium does not invade the intestinal mucosa but produces a toxin, a subunit of which gains entry into the intestinal epithelial cell and causes a permanent activation of the enzyme adenylate cyclase; the resulting increase in the cellular concentration of cylic adenosine 3', 5'- monophosphate (cAMP) triggers active chloride secretion. Unraveling the mode of action of cholera toxin - its structure, membrane receptor, membrane translocation, and effect on adenylate cyclase - has proven to be a fascinating story, providing insight not only into how enterotoxins cause diarrhea but also into how the adenylate cyclase of eukaryotic cells is normally regulated.

Interest in secretory diarrhea has given rise to basic physiologic and biochemical studies of the mechanism by which cAMP and other intracellular secretory stimuli [calcium, cyclic guanosine 3', 5' -monophosphate (cGMP)] elicit active secretion of salt and water in intestine and other epithelia. A model for active chloride secretion in intestine has been proposed that is consistent with the available facts and also appears applicable to a variety of other electrolyte-secreting epithelia.

"Physiologic studies of intestinal absorption and secretion have also provided the basis for important developments in therapeutics. Thus the addition of glucose to rehydration solutions has made it possible to replace most diarrheal fluid losses orally, a fact of immense importance in those areas of the world where the incidence of severe acute diarrhea far outstrips available hospital facilities. More recently attention has been directed to finding drugs with antisecretory action that can be safely used in patients. The results of the first controlled clinical trial of chlorpromazine in cholera patients are quite promising and should encourage further research into the pharmacotherapy of secretory diarrhea.

"This book chronicles these advances, providing a comprehensive discusion of intestinal absorptive and secretory mechanisms and of their derangement by bacterial enterotoxins, viruses, and other agents. The chapters are divided into four groups:

"Chapters 1 through 5 are concerned with the mechanisms for intestinal salt and water absorption and secretion. Transport models are presented. The possible intracellular mediators for intestinal secretion are discussed, including recent observations on cGMP, the concentration of which in intestinal epithelial cells is elevated by a heat-stable enterotoxin from *Escherichia coli.* The uses of isolated intestinal brush borders and basolateral membranes are also examined, including their use for demonstrating changes in ionic permeabilities and in membrane protein phosphorylation.

"Chapters 6 through 10 are devoted to the specific mechanisms by which infectious agents, including viruses, cause secretory diarrhea. An overview of infectious diarrhea, the clinical and pathophysiologic features of enterotoxin diarrhea, the mode of action of cholera toxin, and the luminal and mucosal factors affecting colonization of the small intestine are all presented.

"Chapters 11, 12, and 13 discuss clinical and pathophysiologic features of secretory diarrhea of noninfectious origin. These include diarrhea associated with hormone-secreting tumors, bile salt- and fatty acid-induced diarrhea and chronic diarrhea of unknown etiology.

"Chapters 14, 15, and 16 deal with therapy. Replacement of fluid losses with oral sugar-electrolyte solutions and possible pharmacologic means for reducing diarrheal volume are discussed.

"This book is intended as a source of basic information about intestinal electrolyte transport and its derangements both for the investigator working in this area and for the clinican who must

deal with secretory diarrhea in patients."

Members may order any of the books in the Clinical Physiology Series at special prices from the American Physiological Society, 9650 Rockville Pike, Bethesda, Maryland 20014.

Secretory Diarrhea (full price $30.00)	$24.00
Pulmonary Edema (full price $30.00)	$24.00
Disturbances in Lipid and Lipoprotein Metabolism (full price $25.00)	$20.00
Disturbances in Body Fluid Osmolality (full price $25.00)	$20.00

VASCULAR SMOOTH MUSCLE — A NEW HANDBOOK OF PHYSIOLOGY

Most serious muscle physiologists eschew the study of vascular smooth muscle because of the difficulties related to its being wrapped up in collagen, elastin, and ground substance, and because of the striking differences among smooth muscles from different vascular beds. Recently, however, the functional importance of this tissue has excited a few of these "professionals," and has caused some cardiovascular physiologists to develop expertise in muscle physiology in order to study this contractile system in the blood vessel wall. Jointly these investigators have amassed information for a new *Handbook of Physiology* entitled *Vascular Smooth Muscle.* The volume was edited by David F. Bohr, Andrew P. Somlyo, and Harvey V. Sparks, Jr.

In twenty-one chapters, this volume deals broadly with the structure, chemistry, and function of vascular smooth muscle. The chapters are organized into six sections and treat vascular smooth muscle from the following aspects: The *structure* is dealt with from the vantage point of the blood vessel wall, the ultrastructure of the individual cell, and the morphogenesis of vascular smooth muscle. The *biochemistry* of vascular smooth muscle reviews the considerable new information that is developing regarding the contractile and regulatory proteins, the chemical functions of the subscellular particles, and the energy metabolism of the cell. Chapters dealing with the *electrolytes and electrophsiology* review the state of our knowledge regarding electrolyte content and fluxes in vascular smooth muscle and the manner in which they influence the membrane and action potentials of the cell. Details of the all-important role of calcium in excitation-contraction coupling are presented. The topic *muscle mechanics* of the system is dealt with from the point of view of the contractile mechanics of the individual cell, of the vessel wall as a whole, and from the point of view of the circulatory correlations of compliance, resistance, and capacitance of the vascular tree. The *regulation* of vascular smooth muscle deals with myogenic activity, physical factors (light and temperature), humoral agents, and neurogenic factors. Finally, in an epilogue that relates smooth muscle to other contractile systems, the *phylogenetic variations* of this muscle are described.

This is the second volume in the revision of the *Handbook of Physiology* section on circulation, published between 1962 and 1965. The first of the revised volumes, *The Heart,* Robert M. Berne, Editor and Nick Sperelakis, Associate Editor, was published in 1979. It is the most up-to-date coverage of cardiac structure and function available. Two additional volumes are in preparation: *Microcirculation,* edited by Egene M. Renkin and Charles C. Michel and *Peripheral Circulation and Organ Blood Flow,* edited by John T. Shepherd and Francois M. Abboud.

Members of the Society may purchase the first two volumes of *The Cardiovascular System* at special prices from the American Physiological Society, 9650 Rockville Pike, Bethesda, Maryland 20014.

Volume I. *The Heart,* 1979
978 pages, 612 figures, indexed
$104.00, APS member price
($130.00, nonmember price)

Volume II. *Vascular Smooth Muscle,* 1980
694 pages, 331 figures, indexed
$76, APS Member price
($95, nonmember price)

NOTES FROM CAPITOL HILL

B. A. Curtis, Chairman
Committee on Pulbic Affairs
and Public Information

Budget season is upon us again and this time around, biomedical research did well at the hands of OMB. The President's FY81 budget for NIH is up $138 million (4.4%) with individual research grants up 9%. That's enough to fund 5000 new and competing renewal grants. The administration now joins the House in suggesting stabilization at this number.

The bad news is in the research *training field.* The current budget will allow for no new training grants in FY81. This is bad news, indeed, because the major health lobbies are not terribly concerned about research training. There is also a concern in the Congress that young, well-trained researchers cannot find permanent jobs.

If you think training grants are worth continuing, I suggest you write your members of Congress. It would be well to cite the track record of your program in long-term placement of graduates. An estimate of faculty needs for the next 5-10 years would also help our case. Please send me copies for use in preparing testimony; I will testify before the House Appropriations Subcommittee and Cris Schatte before the Senate.

Renewal of authority for the National Cancer Institute and National Heart, Lung and Blood Institute is needed this year. Senator Kennedy introduced a bill in the last session which has been revised several times. Representative Waxman has just introduced a companion bill. Both bills solidify the NIH structure into law. Until now NIH has been getting along very nicely with very loose authorization. Kennedy's bill would establish a President's Commission to kibitz on the Health budget - for who's benefit is not clear.

Waxman's bill includes some very helpful language on research training.

I will keep you posted on progress although my guess is that a single year extension for NCI and NHLB is all that will pass this session.

XXVIII CONGRESS TRAVEL GRANT AWARDS

In June, and again in August 1979, a travel grant award program for the 28th International Congress in Budapest was announced in *The Physiologist.* Similar announcements were published in the Newsletters of the other Supporting Societies of the U.S. National Committee for IUPS.

As reported in The Physiologist, (Vol. 22, No. 6, pp. 10-11, Dec. 1979) the American Physiological Society submitted proposals to interested Federal agencies for travel grant awards designated for the XXVIII International Congress of Physiological Sciences to be held in Budapest, Hungary, July 13-19, 1980. The APS proposed to handle the funds, with the US National Committee for the IUPS (USNC/IUPS) sponsoring the program and selecting the award recipients.

In substance the APS proposed to administer the travel grant program which would offer a limited number of travel awards to qualified physiologists who are permanent residents of North America (U.S.A., Mexico and Canada) and Hawaii who require such assistance and who plan to participate fully in the Congress. The USNC/IUPS established a screening and selection committee and the APS is acting as fiscal agent and awarding the travel grants. Travel grants have been awarded to individuals in the following participant categories: invited speakers, invited chairmen of Congress and symposia, invited speakers at Congress symposia, and speakers with accepted proffered presentations ("free communications"). A major intention of the Selection Committee was to give particular attention to applications from younger physiologists.

Coordination of proposal review by the Fogarty International Center of NIH resulted in a number of institutes and agencies providing joint funding of $91,000. The following agencies are the sponsors of the NIH contract:

National Heart, Lung, and Blood Institute
National Institute of General Medical Sciences
National Institute of Environmental Health Sciences
National Aeronautics and Space Administration
National Institute of Mental Health
National Institute on Alcohol Abuse and Alcoholism
National Institute of Neurological and Communicative Disorders and Stroke
Science and Education Administration, USDA
Air Force Office of Scientific Research
National Institute of Arthritis, Metabolism, and Digestive Diseases
Fogarty International Center

Further funds from Federal agencies were provided independently by the National Science Foundation, $15,000, the Department of Energy, $15,000 and the Office of Naval Research, $5,000. The APS and USNC (in about equal contributions) added $30,000 more from voluntary assessments of APS members and from interest on the USNC investment fund. These monies add up to $156,000 of which $3,800 was designated for administrative costs and $152,200 directly for the travel awards.

In response to the announcement of the availability of the Awards Program, approximately 800 requests for applications were received (and application forms sent out) by the USNC. Of these, 360 completed applications were returned. A Subcommittee of 5 members of the USNC (Dr. John Cook, Chairperson, and Drs. James Bassingthwaite, David Cohen, Robert Forster and Charlotte Mangum), representing all of the adhering societies as well as different areas of research expertise was selected to appraise and score the applications. In the selection procedure priority in scoring was given to invited speakers and chairpersons and in accord with commitments to the IUPS and the proposals to funding agencies, approximately half of the awardees would be young physiologists (defined as those under 40 years of age).

The Subcommittee scored each applicant by applying various points to an applicant's credentials as follows:

Birthyear received up to 25 Points (those less than 40); attendance days planned for the Congress, less than 2 days - 0 points up to 15 points for 5+ days; invited lecturers and symposium chairpersons 25 points each, symposium speaker 20 points, free communication 10 points; satellite speaker 5 points; publications maximum 15 points (2 per year in good quality journals in past 5 years - 10 points); abstract, maximum of 20 points (average 10 points); scientific purposes and goals of the trip - up to a maximum of 10 points. The results were averaged. Rank-ordered and awardees selected and approved in late November in order to advise applicants of their acceptance before the deadline for submission of registration for the Congress (December 10, 1979). The recipients of the awards were formally notified by the APS by letter on February 1, 1980. The stipend for each awardee was based on the best estimate of APEX High Season Fare Costs (round trip) New York City to Budapest plus an allowance approximating current round trip low cost airfare from an awardee's home city to New York City. The low cost APEX fares were only available for a minimum stay in Europe of 14 days.

There were 211 travel grants awarded. Of these 107 went to young (under 40) physiologists. There were 73 invited speakers and/or chairpersons.

In sponsoring travel grants, the Federal Government regulations restrict the expenditure of the monies to USA residents and stipulate that, when flying from and to the United States, American air carriers must be used. Accordingly, the awardees were divided into two groups. Those eligible for Federal grant funds and those who were not (non-USA residents and USA government employees). There were 8 awardees who were USA government employees, 9 Canadian scientists and one Mexican physiologist (the latter selected at USNC request by Dr. Garcia Ramos of Mexico and his associates in ALAF). These 18 persons plus a few other special cases were funded by the private funds available from APS and USNC sources (as noted above). All together $122,200 of actual award monies came from Federal funds and $30,000 from APS/USNC funds. Awards to persons under 40 amounted to about 54% of the available funding ($82,900).

The award recipients represented persons from 37 states, Washington, D.C., Canada and Mexico as follows:

California	-	31
New York	-	23
Pennsylvania	-	16
Massachusetts	-	13
North Carolina		10
Maryland	-	9
Texas	-	8

Alabama, Florida, Missouri, Oregon and Wisconsin - 6 each

Colorado, Connecticut, Iowa and Louisiana - 5 each
Washington - 4
Illinois, Kentucky, Michigan, Ohio and Virginia - 3 each
Alaska, Arizona, Georgia, Minnesota, New Hamphire and Vermont - 2 each
Washington, D.C., Indiana, Hawaii, Kansas, New Jersey, New Mexico, Oklahoma, Rhode Island, South Carolina, and Utah - 1 each
Canada - 9
Mexico - 1

To minimize administrative expense, since no allowance for indirect costs was included in the government contracts, recipients received their award in the form of a "credit" in their name with the travel agent selected by the U.S. National Committee, Chevy Chevy Chase Travel, Inc. of Bethesda, Maryland.

TAX DEDUCTIONS FOR IUPS CONGRESS ATTENDANCE

To satisfy the Tax Reform Act of 1976 it will be necessary for U.S. travelers to the IUPS Congress in Budapest to document their attendance. For this reason, APS has arranged to have a form "Statement of Professional Activities" available at the meeting for U.S. attendees. When completed, this form will satisfy IRS requirements for preparing personal tax returns.

The form will be available at the Chevy Chase Travel Inc. desk located in Building K at the Congress Center. The form should be completed and returned to the APS representative who will also be located at the same location.

The Executive Secretary of the APS will have these forms authenticated and mailed to the attendees in the U.S. following the Congress.

REPORT OF THE COMMITTEE ON SENIOR PHYSIOLOGISTS

D. B. Dill, Acting Chairman

In this transition period it seems appropriate to review the history of the Committee and to describe the practices that evolved since the origin of the Committee in 1951. With the help of colleagues, an inquiry was mailed biennually to all members age 65 and older. Inquiries about health, interests, activities and needs elicited many replies that often were of historical value.

After some years it was arbitrarily decided to discontinue sending the routine inquiry at age 80 replacing it with an annual personal inquiry on a birthday card. This card picturing Beaumont House at once became popular. Some of the most valuable replies came in response to the birthday greeting. There are 485 Emeritus Physiologists. Of those, 358 are over 70. Of the 358, 106 are 80 or older.

Three years ago I retired as Chairman and Hy Mayerson took over with enthusiasm and success. Then after a year Hy became Emeritus and was left without a secretary. With new members added to the Committee, the APS office assigned names which resulted in confusion in that the routine inquiry was sent to all including the birthday group.

Last Fall Hy was stricken by partial failure of the circulation to one leg. He was unable to take charge of the Committee meeting planned for New Orleans and later he insisted on retiring. I offered to Orr Reynolds to be Acting Chairman until the Anaheim Meeting. I count on the Council to appoint a Chairman at that meeting. In the interim period, I have arranged for reassignment of names of the 80-year-old group in accordance with choices made by Committee members. Each Committee member has been furnished with addresses, birthday dates, and enough birthday cards for this calendar year.

The incoming Chairman will have the task of preparing for the biennual inquiry due to be mailed this Fall and of formulating policies for future guidance of the Committee.

PAST-PRESIDENT EPILOGUE

In response to the request for Past Presidents to amplify or modify published remarks made in their Past-President's Address, the following letter was received:

Dear Dr. Reynolds:

Replying to your kind letter of October 10 about my extending any points made in Past Presidential addresses to APS, I should have answered your first letter with an explanation. The explanation is that I never made a Past Presidential Address. And the explanation for that is that when the XIX International Congress was held in the autumn (or late summer?) of 1953 in Montreal, the Council of APS decided that the Autumn meeting of APS should be omitted that year. It was partly a feeling that the two meetings were too close together, and partly also a courtesy to the Canadians to avoid any semblance of competing or interfering with the attendance success of their Congress.

Since I had been President of APS in 1952, I am in the position of having no Past Presidential Address to have after-thoughts or extensions about.

I do have one small after-thought, namely that this is perhaps fortunate for all concerned. After all in 25 years conditions have changed so much that I am saved the task of recantation to the extent of perhaps as much as 90 to 95% of anything I might have said in 1953. And the budget of *The Physiologist* is saved the cost of print and paper needed for such recantation.

Sincerely,
Eugene M. Landis

AMERICAN MEDICAL RESEARCH EXPEDITION TO EVEREST, 1981 A CALL FOR ASSISTANCE

Next year a physiological expedition will be going to Mt. Everest with plans to make measurements of human cardiopulmonary function at altitudes far higher than have been attempted before. Historically, physiological expeditions to high altitude have contributed much to our knowledge of the effects of hypoxia on man. Expeditions such as the Anglo-American Expedition to Pike's Peak in 1911, the International High Altitude Expedition to Cerro de Pasco, Peru in 1921-22, and the International High Altitude Expedition to Chile in 1935 made major contributions to our understanding of the physiological effects of extreme hypoxia.

The chief objective of the American Medical Research Expedition to Everest is to obtain information on cardiopulmonary physiology at altitudes above 26,000 feet (7900 m). Such measurements have not been attempted before. However, they are of considerable physiologic interest because there is abundant evidence that the hypoxia of these altitudes is very near the limit of man's tolerance. The first successful ascent of Mt. Everest by two climbers without supplementary oxygen in May, 1978 was an event of great physiologic signficance.

Naturally, only relatively simple measurements can be made at these extreme altitudes. However, even these will throw considerable light on how the cardiopulmonary system adapts to this extraordinary environment. We expect to make the first measurements of alveolar gas composition, maximal ventilation, maximal oxygen consumption, heart rate, rhythm, and ECG wave form above 26,000 feet (7900 m).

A small laboratory will be erected on the South Col of Everest (26,200 feet; 8000 m). Maximal work will be studied with a bicycle ergometer and venous blood samples will be taken for analysis at the main laboratory lower on the mountain. In addition, scientists in this South Col laboratory will equip climbers with miniature tape recorders and other equipment so that further measurements can be made up to the summit, at an altitude of 29,028 feet (8848 m). Another laboratory will be set up at 20,000 feet (6100 m). This will be thermally insulated and equipped with electrical power so that more sophisticated measurements can be made there.

The personnel of the expedition will include six experienced Himalayan climbers, six South Col scientists, and six other scientists. The expedition will leave the U.S.A. in July and return in November 1981.

The Scientific Advisory Committee of the Expedition includes D.B. Dill (leader of the 1935 International High Altitude Expedition), Robert F. Grover, Thomas H. Hornbein (Everest summitter in 1963), Nello Pace, and John W. Severinghaus, all of whom are members of the American Physiological Society.

Grants of approximately $200,000 from the National Heart, Lung and Blood Institute will cover the cost of developing and buying scientific equipment. Another $200,000 is needed to cover the costs of climbing equipment, food, porters, oxygen, and transportation. We need your help.

Contributions are tax deductible.

Contributors of $25 or more will receive a postcard from the expedition. Contributors of $100 or more will also receive a poster of Mt. Everest. Contributors of $500 or more will be sent regular newsletters.

Checks should be made out to AMREE, 1981 and sent to Box 9038, Bakersfield, CA 93389 in the reply paid envelope.

John B. West, M.D., Ph.D.
Section of Physiology, M-023
University of California, San Diego
La Jolla, California 92093

1981-82 ADVANCED RESEARCH FELLOWSHIPS IN INDIA

Twelve long-term (six to ten months) and nine short-term (two to three months) research awards, without restriction as to field, are offered for 1981-82 by the Indo-U.S. Subcommission on Education and Culture. Applicants must be U.S. citizens at the post-doctoral or equivalent professional level. The fellowship program seeks to open new channels of communication between academic and professional groups in the United States and India and to encourage a wider range of research activity between the two countries than has previously existed. Therefore, scholars and professionals who have limited or no experience in India are especially encouraged to apply.

Fellowship terms include: $1,000 - $1,500 per month, depending on academic/professional achievement and seniority, $350 per month payable in dollars and the balance in rupees; an allowance for books and study/travel in India: and international travel for the grantee. In addition, long-term fellows receive international travel for dependents; a dependent allowance of $100 -$250 per month in rupees; and a supplementary research allowance up to 34,000 rupees.

The application deadline is July 1, 1980. Application forms and further information are available from the Council for International Exchange of Scholars, Attention: Indo-American Fellowship Program, Eleven Dupont Circle, Washington, D.C. 20036, telephone (202) 833-4978.

FREDERICK SARGENT, II

1920-1980

Frederick Sargent, II, M.D., died March 3, 1980, at Houston, Texas, of congestive heart failure. He was 60 years old. He is survived by his wife, Anne, two daughters, Fredericka and Laura, a stepson, Peter, and two adopted children, Ann and Drick. The home address is Mrs. Anne Sargent, 10722 Cranbrook, Houston, Texas 77042, telephone (713) 783-2284.

Dr. Sargent was born January 11, 1920, in Chicago, Illinois. After high school in Chicago and Massachusetts, he attended the Massachusetts Institute of Technology, and received the B.S. in meteorology. He qualified in medicine at Boston University School of Medicine, and interned at Presbyterian Hospital in Chicago. He did his military service in the U.S. Air Force. He never practiced medicine, but chose an academic career in human biology and human ecology. His early work was at the Harvard Fatigue Laboratory and at the U.S. Army Medical Nutrition Laboratory in Chicago. His academic career included a professorship in physiology at the University of Illinois (Urbana), a deanship at the University of Wisconsin (Green Bay), a provostship at Western Washington University (Bellingham), and finally a professorship in human ecology at the University of Texas School of Public Health (Houston).

Dr. Sargent was a vigorous researcher and a prolific writer. His areas of interest were broad: human nutrition, human responses to heat and cold, human ecology, the history and philosophy of medicine. He was an early and important member of the International Society for Biometeorology. His other societies included the American Physiological Society and the American Institute of Nutrition. Perhaps his most influential book was *Human Ecology,* which he edited. His last book is in the press (1980) and will be published posthumously: a biography of the Illinois pathologist and Hippocratean environmentalist, Dr. William Peterson.

Dr. Sargent's early death is a grievous blow. We have lost a fine man, a true friend, a splendid colleague.

Robert E. Johnson, M.D., Ph.D.
Professor of Biology Emeritus
Knox College
Galesburg, Illinois

THOMAS BRUCE CALHOON

1926-1980

Dr. Thomas Bruce Calhoon, Chairman of the Department of Physiology, University of Louisville School of Medicine died on February 2, 1980. Dr. Calhoom was a distinguished scientist and a respected and effective teacher in the medical community. He is survived by his wife, Carmen, and two children, Kenneth and Kay.

A lectureship is being established in his name and any contributions would be greatly appreciated.

William B. Wead, Ph.D.

ZOYA BARBASHOVA

D. B. Dill

In the Spring of 1979 I received a birthday message from Zoya Barbashova who wrote one of the introductory chapters for "Adaptation." It came from her home address and was poetic and affectionate, and I guessed something was wrong. I received word from her colleagues in the Institute of Evolutionary Physiology of her death from a "serious illness" on January 8, 1980. Following is my letter to her colleagues and her birthday greeting to me:

"Dear Dr. Griger'eva: I am distressed to learn of the death of my good friend Professor Zoya Barbashova. Before I met her at the Institute in 1961 I had admired her achievements and had invited her to write a chapter for the handbook I was to edit. During the meeting that arrangement was confirmed. She and her husband and the Doctors Zimkin entertained me at dinner one evening and then took me on a walking tour of some of the historic sites of your beautiful city. Sunday morning I was honored when she came to see me off on the train for Helsinki. Ever since then we have kept in touch. The chapter she wrote was an outstanding feature of the Handbook. My last word from her was in April 1979, a poetic and affectionate greeting in addition to her picture dating back to the time of our meeting. It became part of the record of the symposium honoring my 88th birthday. I express my deepest sympathy to you and her other colleagues and to members of her family."

David Bruce Dill

Professor Barbashova to Dr. Dill: Leningrad, March 29, 1979.

"Dear Professor Dill: With all my heart and with the best wishes I congratulate you on your birthday. I would like to present you on your birthday the sun and the moonlight, the breezy air from high altitude, many flowers, and all the things you want. But it is only my dream. In fact I send you my photo made in time of our personal acquaintance in Leningrad. Then I was happy to receive your invitation to write the chapter in your excellent Handbook. I and my colleagues admire your high efficiency, your youthful mobility. Be healthy, be happy! We give you a solemn vow to follow your example. Remember me to your wife and to other members of your family."

Cordially yours, Zoya I. Barbashova

COUNCIL OF ACADEMIC SOCIETIES BRIEF

ASSOCIATION OF AMERICAN MEDICAL COLLEGES • 1 DUPONT CIRCLE NW • WASHINGTON DC
(202) 828-0400 WINTER, 1980 VOL. 5., NO. 2

The CAS Brief is prepared by the staff of the AAMC Council of Academic Societies and is distributed through the auspices of your member society.

REPEAL OF SECTION 277 AND CLINICAL LABORATORY LEGISLATION PROPOSED IN HOUSE. On January 31, the House Subcommittee on Health and Environment reported out H.R. 4000--a series of Medicare and Medicaid Amendments. Two of the amendments, offered by Congressman David Satterfield (D-Va.) and accepted by the Subcommittee, are of particular interest to CAS societies.

Section 227. The first Satterfield amendment would have the effect of repealing the teaching physician payment provisions of Section 227 of the 1972 Social Security Act. During the past eight years, HEW has attempted to implement Section 227 by using a threshold approach to determining whether teaching physicians could be reimbursed on a reasonable charge rather than a reasonable cost basis. Past drafts of Section 227 regulations have stated, for example, that unless a given percentage of all patients in the teaching hospital have a private-patient relationship with a teaching physician, no fees could be billed for professional services in that hospital. These regulations were widely criticized as discriminating against physicians in teaching hospitals and encouraging a return of two standards of patient care among teaching hospitals. The Satterfield amendment to H.R. 4000 would preclude HEW from adopting the threshold approach by overturning the provision of Section 227 which placed physician services on a cost basis unless HEW-specified conditions were met. Thus the Satterfield amendment would essentially repeal Section 227 and would partially resolve academic medicine's long battle over this issue.

Clinical Laboratory Regulation. The second Satterfield amendment would modify and curtail HEW's current approach to clinical laboratory regulation. The impetus for this amendment was two-fold: (1) the widespread concern about the recently proposed "Personnel Standards for Clinical Laboratories" and (2) a section in the Ways and Means Committee version of H.R. 4000 which mandated the application of a uniform quality assurance program, which would include personnel standards, to all classes of laboratories. The Satterfield amendment, while not changing HEW's authority to assure quality in clinical laboratories, directs HEW to use discretion in clinical laboratory regulation. For example, it instructs HEW to (1) only impose such requirements as are found necessary to correct identifiable deficiencies; (2) issue requirements that will be cost-effective and not unduly restrictive of personnel; and (3) take into consideration the different classes of laboratories (e.g., research laboratories).

H.R. 4000 will be considered by the House Interstate and Foreign Commerce Committee in the near future. It is hoped that the Commerce Committee and, subsequently, the full House will act favorably on both the repeal of Section 227 and the limitation of clinical laboratory regulation.

FY 1981 BUDGET REVEALED. In late January, President Carter sent his $615.8 billion FY 1981 budget request to the Congress. Again this year, the budget request for biomedical research is not adequate to keep pace with inflation. The total NIH

budget request is $3.58 billion which provides only a 4.4% increase over the current year. The ADAMHA budget was set at $1.26 billion or 6% above the FY 1980 level. With inflation estimated at 10-13%, both NIH and ADAMHA will experience cuts in constant-dollar terms if Congress approves the President's request. One area of major concern in the FY 1981 NIH budget is research training. Proposed expenditures for all types of training will drop from $176.4 million to $163.5 million. No new or competing awards are proposed for any of the programs supporting research training including competing training grant renewals but individual awards and training grants already awarded will be funded. This hiatus in research training support is apparently due to the Administration's desire to commit a greater portion of limited funds to its higher priorities--providing stability and adequate funding for investigator-initiated (R01 and P01) grants and increasing stipend levels for current research trainees.

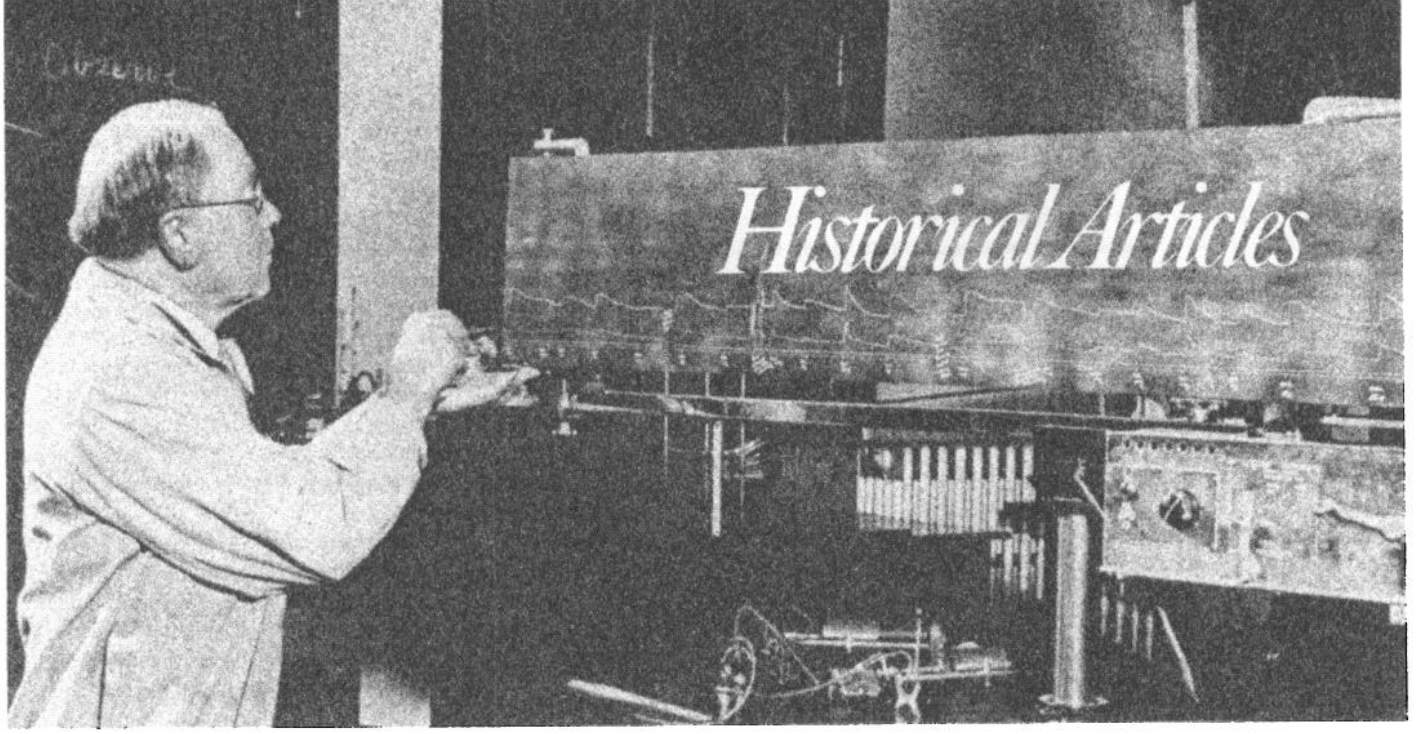
Another aspect of the President's budget which is of concern to the medical schools is capitation grants. Not only are no funds requested for medical school capitation for FY 1981, but the President has also requested a rescission of capitation funds for the current year.

GRADUATE MEDICAL EDUCATION: PROPOSALS FOR THE EIGHTIES. This report prepared by the AAMC's Task Force on Graduate Medical Education has been endorsed by the Executive Council and is to be widely distributed for discussion. The report has chapters on The Quality of Graduate Medical Education, The Transition Between Undergraduate and Graduate Medical Education, National Standards Formulation and Accreditation, Graduate Medical Education and Specialty Distribution, and Financing. An invitational conference to consider the report has been scheduled for September 28-29 in Washington, D.C. Specialty boards, specialty societies, other national organizations involved in graduate medical education, health insurance groups, and governmental agencies will be invited to participate. The Task Force, which was chaired by Dr. Jack D. Myers of the University of Pittsburgh, used five different working groups involving over 70 individuals in preparing this major report. Copies will be available in March and will be sent to CAS officers and representatives free of charge. For additional copies send $3.50 for book rate or $5.25 for priority mail. There are discounts for orders of six or more.

REPORT OF THE AD HOC COMMITTEE ON CLINICAL RESEARCH TRAINING AVAILABLE. Spurred by the concerns of medical students and academic societies about the decreasing interest and participation of physicians in research and academic careers, AAMC formed an ad hoc Committee on Clinical Research Training in June, 1979. The Committee recommended 32 actions which can be taken by AAMC, medical schools, professional societies and the Federal government to address this problem. For copies of the Report contact Tom Morgan or Diane Plumb at AAMC.

MEDICAL SCHOOL FACULTY SALARIES. The 1979-80 Report on Medical School Faculty Salaries is now available from the AAMC. The Report provides salary percentiles for 29,857 full-time medical school faculty by rank, department and region. Copies may be ordered by sending a remittance or purchase order for $6.00 to AAMC, Attention: Membership and Subscriptions.

CAS INTERIM MEETING. The 1980 CAS Interim Meeting will be held in Washington on March 18-19. The first segment of the meeting will consist of three small discussion groups on the topics of (1) Health Manpower, (2) Essentials of Research Training Programs, and (3) Development of Policies to Assure an Adequate National Research Effort. The second day of the meeting will include a Plenary Session for reports from each discussion group leader and a Business Meeting.



CARBONIC ANHYDRASE, OR, THE STRANGE CASE OF THE DISAPPEARING SCIENTIST

Horace W. Davenport
William Beaumont Professor of Physiology
The University of Michigan

Awhile back Joseph Hawkins, the organ of Corti man whom I have known for more than forty years, asked me to give a talk to the Kresge Hearing Research Institute on "What's New in Carbonic Anhydrase." I didn't talk on what's new, because I don't know what's new. I do know something about what's old, and that is the story I am going to tell you.

One of the things that impresses me more and more as I grow older is how quickly scientists disappear. I have expressed this once before, in my Past-President's Address to the American Physiological Society (1). I might say that address is chock full of wisdom, and it contains Davenport's Dictum, the one about condoms in the stomach. But the point now is that I said: "It is the sense of having made some lasting contribution which is the real reward of science. One's contribution may be very small indeed. A life's work may end as half a sentence in a textbook, and there is no name mentioned. A better man may leave a small paragraph, and the work of only the best may inform a whole chapter."

Scientists do disappear, and that is what has happened to me in respect to carbonic anhydrase. The last five papers I have seen on the function of carbonic anhydrase in the stomach do not have my name in the bibliography. A massive physiological review on urinary acidification (2) contains a great deal about carbonic anhydrase, but the bibliography goes Data, Davis, Delrue, but no Davenport. There is no reason why my name should be preserved, for so far as carbonic anhydrase is concerned, I'm dead, and I have been dead for a long time. Now I will call up the ghost.

I stopped work on carbonic anhydrase in 1945, and that was long before the two modern themes developed. One is the structure of carbonic anhydrase, a single polypeptide chain with a zinc molecule in it. That gives a lot of pleasure to physical chemists who work on structure and function. The other theme is the multiple forms of the enzyme, and geneticists have a lot of fun with that.

Even the method of measuring carbonic anhydrase has changed. The old and simple method was devised by my Oxford tutor, John Philpot and his wife (3). One blew carbon dioxide through a bicarbonate solution and measured the time it took for bromphenol blue to change color. The other was Meldrum and Roughton's (4). Two solutions were suddenly mixed in a glass boat which was violently shaken, and the rate of evolution of carbon dioxide was measured manometrically. Nowadays, one uses carbonic anhydrase to catalyse an esterification reaction. So the methods I used are dead too.

One of the really great American contributions to science has been the demonstration that blood obeys the laws of physical chemistry. That was largely the work of L. J. Henderson, and it is summarized in his book. *Blood* (5), which you ought to know. The culmination of that work is the paper by Van Slyke, Wu and McLean (6) who asked whether blood obeys the law of electrical neutrality of solutions, the law of osmotic equilibrium and the law of the Donnan equlibrium. They used the blood of a Manchurian pony for interesting reasons I won't go into, and they found that the answer was Yes, more or less. Van Slyke, who got his Ph.D.

at Michigan in 1907, was one of the major contributors to biochemistry, particularly biochemical methods. McLean had several important careers I would like to tell you about some time. He had a great influence on my life, again for reasons I won't detail. He died just shortly after his twentieth birthday, being a February 29 man. All these studies were equilibrium ones; blood was equilibrated with oxygen and carbon dioxide and then analysed. Velocity of reaction was not measured.

The pioneer study of equilibrium was essentially finished in 1923 (6, 7), but in the 1920's someone was thinking about the velocity of reactions in blood. Hartridge and Roughton (8) were measuring the rate of reaction between oxygen and hemoglobin. Hydrostatic pressure drove two solutions into a mixing chamber and then down a long, narrow tube. If mixing is nearly instantaneous and if you know the rate of flow through the tube, the distance from the mixing chamber is proportional to the elapsed time. Many versions of the method are still being used.

The man doing most of the thinking about reaction rates was F. J. W. Roughton, Francis John Worlsley Roughton, pronounced to rhyme with plough, to use the confusing English spelling. Roughton was a true English eccentric. Physically, he was far from svelt. Among his habits was to push a pencil up his nose. Like many Englishmen, he wore his handkerchief in his sleeve. He would pull it from his sleeve, swallow it and then slowly draw it from his mouth. He had paroxysmal tachycardia, and in Franklin's *Life of Barcroft* (9) there is a picture of Barcroft lecturing with data on Roughton's tachycardia and stroke volume on the blackboard behind him. Having tachycardia was great good luck, for he didn't go into the army during the First World War and be killed as most of his contemporaries were.

In those days Cambridge was one of the major centers for the study of blood, and Joseph Barcroft was in the middle of it. Roughton was to give a talk to one of the innumerable undergraduate clubs at Cambridge. Roughton read the work on blood coming out of Copenhagen, and comparing it with Barcroft's work he realized that Barcroft really didn't understand what was going on in Denmark. Barcroft was a simple person. Another great Cambridge physiologist once said to me: "Barcroft was a very stupid man. He got all hot and bothered if you suggested he use a logarithm." The only trouble with this judgment is that Barcroft, from the day he started until the day he died, made a tremendous number of important discoveries and opened up new fields. Roughton, characteristically, went up to Barcroft and said, in effect: "Mr. Barcroft, you really don't know what you are talking about." Now, here's the point of being a great man. Barcroft replied. "Great. Come and work with me, and show me how to do it right." Consequently, Roughton had a tremendous devotion to Barcroft.

One day when Barcroft was 75 he met Roughton on the steps of the Physiological Laboratory. He talked with Roughton about a number of things and then ran to the bus. On the bus he died, so the last person Barcroft talked to, aside from the bus driver, was Roughton, which was appropriate.

My first contact with Roughton occurred when I took the Final Honour School examinations at Oxford. That was one of the traumatic experiences of my life. I still have anxiety dreams about it, and at the Centenary Meeting of the British Physiological Society in Cambridge in 1976 I heard Alan Hodgkin confess that he too has nightmares about his corresponding examination at Cambridge (10). There was Roughton with his messy hair hanging out beneath his mortar board, examining me in Physiology and Biochemistry. I was in a white tie and gown trying to measure sugar in blood. One question on a Practical was to determine the energy cost of walking four miles an hour, so I had to put on a nose clip and a Douglas bag and walk around the Parks with a stop watch in my hand. Then I analysed the gases with Roughton looking over my shoulder.

The questions in the Final Honour School were good; only the answers have changed. "Write an essay on pain." That would require one to know about Sir Henry Head. "What is the evidence that the impulse in nerve fibres is transmitted by local electrical currents?" I well remember Jack Eccles rushing in to tell us about Hodgkin's cold-block experiment (11). "What is known about the properties and functions of the cortical hormone of the suprarenal gland?" Remember, this is 1937. "Explain how carbonic anhydrase came to be discovered, and give an account of its properties and function." I didn't answer that question, because I didn't know the answer. Part of the answer is what I will try to tell you now.

As you know, the Henderson-Van Slyke work showed that bicarbonate is the major form in which carbon dioxide is carried in blood. There are two reactions: ionization of carbonic acid and hydration of carbon dioxide. Van Slyke and his collaborators thought about the problem, but they rejected the idea there was any other major form of carbon dioxide in blood.

The rate of hydration was known to be slow. Thiel, from Marburg, published papers in the Berichte in 1913 (12) on the subject. He added base quickly to a solution of carbon dioxide, changing the color of an indicator. The longer the base was in the solution, the more base he had to add to reach the same end point. This was a crude method, but it worked.

In the middle of the 1920's the chief scientists working on blood in Copenhagen were August Krogh and Cristian Bohr, Niels Bohr's father, but the person who concerns us here is a man named Faurholt. Faurholt was Bjerrum's student, and do you know who Bjerrum was? Zwitter ions. Faurholt published two papers (in French) on the rate of reaction of carbon dioxide with water (13). To separate the several forms of carbon dioxide in solution, Faurholt put dimethylamine into the mixture. Dimethylamine formed a carbamino compound with dissolved carbon dioxide at once. Then he put barium chloride into the solution to precipitate the bicarbonate as barium carbonate which could be centrifuged out. By this means he showed that the hydration of carbon dioxide was very slow indeed.

The next Dane to work on the subject was O. M. Henriques who was employed in the State Serum Institute. I ask you, why should there be a State Serum Institute? The answer is that this is 1928, and there are no sulfa drugs and no antibiotics. When a patient was dying of pneumonia, someone typed his bacillus and administered the right antiserum. So there had to be a Serum Institute.

Henriques exposed a sample of blood to a vacuum, and he measured the rate at which carbon dioxide came off as a gas. He published five papers in a row in what used to be called the Gearshift and Crankshaft when graduate students were expected to read German (14). I don't know why there should be five papers instead of only one. When I referee a similar set of papers, I always recommend they be consolidated, but no one ever pays any attention.

In the first paper, Henriques, using Faurholt's data, calculated what we always tell students: that blood goes through the lungs too fast for the uncatalysed reaction to be the major one. Next, he showed that carbon dioxide is bound to hemoglobin. What he actually showed was that it comes off very rapidly at first, within five seconds which was the shortest interval he could measure, and then slowly. It also comes off a solution of hemoglobin rapidly. Then he dialysed hemoglobin against carbon dioxide and bicarbonate, and he calculated from the Donnan relation that

much of the carbon dioxide must have been bound to the hemoglobin. In the fourth paper he showed that reduced blood binds more carbon dioxide than oxygenated blood, which is again what we tell students. Finally, he summed up the physiological implications.

Henriques published essentially the same papers in a long review in Ergebnisse der Physiologie (15), and he concluded that the rapid evolution of carbon dioxide was the result of the breakdown of carbamino compounds of hemoglobin and the slow evolution was the result of dehydration of carbon dioxide.

Van Slyke was supposed to be the major authority on carbon dioxide in blood, and he quickly took up Henriques' observations (16). He found that Henriques was right, that carbon dioxide does come off blood rapidly. But it comes off just as rapidly from a solution containing a little bit of hemoglobin as from a soultion containing a lot, and this indicates catalysis. Van Slyke repeated that he had been right in the first place; there is no carbamino compound. He got quite huffy about it, just as Hopkins got quite huffy (17) when a couple of Canadians (18) said that glutathione was not a dipeptide. Van Slyke at the end of his paper said that there must be catalysis of the ionization of carbonic acid. He gave absolutely no justification for that nutty idea.

Henriques replied (19), argument and no evidence. There can't be catalysis on account of the shape of the carbon dioxide output curve.

Dirken and Mook, who had a rapid reaction method for measuring changes in pH, showed that if hemoglobin is present in a solution, hydration and dehydration of carbon dioxide are very fast (20). Likewise, Brinkman and Margaria, who were postdoctoral students at Cambridge, demonstrated that there actually is catalysis of the reaction of carbon dioxide with water (21). The catalyst is hemoglobin.

Here we find a problem. The Cambridge group showed that addition of hemoglobin to a solution catalyses the reaction, and to guarantee that they were using pure hemoglobin they said it was prepared by Adair's method. Gilbert Adair was the first man to know that hemoglobin is a molecule, that it does not absorb oxygen like activated charcoal. He spent much of his life trying to measure the molecular weight of hemoglobin by osmotic pressure methods. He obtained a molecular weight of "near 66, 800 (22)," which isn't bad considering the problem of salt effects. This was 1910 to 1930 or thereabouts, and there were't any ultracentrifuges or Tiselius apparatuses or immunoelectrophoresis. Anyone who said that the hemoglobin he used was prepared by Adair's method assumed the hemoglobin was pure. But it wasn't.

Roughton, with his student Meldrum, showed that the catalyst was not hemoglobin (23). They shook a solution of laked red blood cells with chloroform, which coagulated the hemoglobin, and the supernatant contained the catalyst. That was the limit of purification of carbonic anhydrase for a long time. Meldrum and Roughton called the catalyst *carbonic anhydrase* at the suggestion of Philip Eggleton.

Do you know another reason why Philip Eggleton should be remembered? The answer is that with Grace Eggleton he demonstrated that creatine in muscle is actually phosphorylated (24). He called the compound "phosphagen." Fiske and Subbarow (25), at Harvard, discovered it independently and called it "phosphocreatine."

Another example of multiple discovery is that William C. Stadie, who had been a junior colleague of Van Slyke, discovered carbonic anhydrase independently, apparently not having read the English literature (26). Stadie soon afterwards gave up blood chemistry and did important work on diabetes. I have a memory of him. He was a very senior man at Penn when I was very junior. I accepted a job at Harvard, and Stadie said to me: "Davenport, we are sorry to lose you, but you are going to the Athens of medical America." I have often wondered what is the Corinth of medical America. New York? What's the Sparta? What's the Boeotia. Wasn't Boeotia the place renowned for its stupidity?

We finally come to my participation in all this. My tutor at Oxford was John Philpot, who was an authentic genius. I remember one day at my tutorial he showed me the schlieren method for measuring boundaries in the ultracentrifuge which he had invested that morning. He assigned me essay topics, and one of them was the digestive tract. I read all the current theories of the mechanism of acid secretion, all of them ridiculous. When I read him my essay, Philpot suggested that lactic acid formation might be responsible.

I became a graduate of Oxford and remained there another year working in Biochemistry with R. B. Fisher. Fisher was known to everyone as David Fisher, his wife having refused to marry a man named Reginald. Toward the end of his career he was Dean of the Medical School in the University of Edinburgh. That he was an Englishman and not medically qualified yet was the Dean of a great Scottish medical school means that he must have had some very good administrative ability. If you have known English scientists, you will recognize the type: great brilliance. He turned out five new ideas a day. I talked with Fisher about acid secretion, and he said there must be carbonic anhydrase in the stomach. I knew that Meldrum and Roughton (4) had attempted to study the distribution of carbonic anhydrase and that they had not found any in the stomach. I think I know the reason they missed it, but not having the exact facts, I won't tell you about it.

Nevertheless, Fisher persuaded me early in June 1938 to look for carbonic anhydrase. On Monday I set up the Philpot method, and on Tuesday I found it (28).

Fisher arranged for me to spend a week in Cambridge, learning the proper carbonic anhydrase method from Roughton's assistant, Vernon Booth. I then went back to Caltech to be a graduate student under Henry Borsook. I persuaded Borsook to allow me to do my Ph.D. thesis on carbonic anhydrase. He let me have $100 of Caltech's money to have the apparatus built. I borrowed a freezing microtome and a microscope and applied Linderstrom-Lang's method (29) to determine the cellular locus of carbonic anhydrase. Linderstrom-Lang was an important man in his day, but like others, he too has disappeared. He froze a piece of tissue and cut slices for enzyme analysis, using ultramicromethods he had developed. A slice of an annulus around the tissue was used for cell counting, or the other way around, for I forget which. I did a similar job, doing the actual work for my thesis in a month. I demonstrated that there is a very strong correlation between the number of parietal cells and the carbonic anhydrase concentration (30). The correlation was too good to be true, but it was true.

One of the sermons I give is about cooking data. I had an emotional investment in the results. I knew that acid was probably secreted by the parietal cells. I wanted carbonic anhydrase to be in the parietal cells and nowhere else. My data showed that there was probably some carbonic anhydrase in the surface epithelial cells as well, and I couldn't find any way of cooking my data that would eliminate carbonic anhydrase from the surface cells. I have often had a similar experience: the results turn out the way I don't want them to, and in the long run I find it is better that way.

After that I went on to other work. Fisher and I had an idea, not a very good idea but an idea, that if we could show that acid secretion is independent of the particular anion secreted, I could then focus on the secretion of the hydrogen ion. I did the experiments, first on rats at Caltech and then on dogs when Whip-

ple gave me a fellowship at Rochester. The stomach secretes hydrobromic acid if it is given a chance (31). In fact, it rather prefers to secrete that instead of hydrochloric acid. Going on to the next anion, I showed that the gastric mucosa thinks it's a thyroid gland in the way it handles iodide (32). In those days, the next anion on such a list was thiocyanate which was being used to measure extracellular space. I had a terrible time, for when I loaded my dogs with thiocyanate, I couldn't get their Heidenhain pouches to secrete acid. It finally dawned on me that thiocyanate was inhibiting acid secretion. My colleague, Joseph Ross, suggested that carbonic anhydrase might be inhibited by thiocyanate and that was the reason acid secretion was inhibited.

Following the suggestion, I showed that thiocyanate does inhibit carbonic anhydrase. Then I stated a whole series of assumptions. If the assumptions are correct, a series of equations must apply, and inhibition is explained. The assumptions turned out to be wrong, as we will see, but at least I stated them explicitly (33). I thought I really had accomplished something.

I went back to Caltech for a visit the next summer, in 1940, and I met a classmate of mine named Norman Horowitz. Do you know what he did? When Beadle and Tatum started to study the genetics of biochemistry, rather than the biochemistry of genetics, Norm Horowitz was one of the two men they hired to help with the biochemistry. He had a scientific gold mine in neurospora. Horowitz asked me if I had read the paper in Nature showing that sulfanilamide inhibits carbonic anhydrase (34).

This was 1940, and sulfonamide drugs were hot stuff. When a drug is first discovered, it has no side effects, and for a while it cures everything. Then side effects begin to show up. With sulfanilamide, there was metabolic acidosis and some odd effects on the kidney.

The person who discovered the inhibition of carbonic anhydrase was Thaddeus Mann, and I will flunk any endocrinologist who can't identify him. Later he became the king of sperm, and his wife was Cecilia Lutwak-Mann who showed that progesterone controls synthesis of carbonic anhydrase in the placenta. Mann knew about carbonic anhydrase, because he was working with Keilin (pronounced Kayleen and not Kylin). Keilin was the major authority on metal-containing proteins (35). After their iron-containing hemoglobin was removed from the red blood cells, there was a copper-containing protein. After that, there was a lot of zinc left over, and that must be in carbonic anhydrase, which it was (36). Mann also knew about the effects of sulfanilamide in promoting the secretion of an alkaline urine. Carbonic anhydrase was in the kidney, for Alfred Wilhelmi had kicked me in to finding it there (37). Mann decided that the effects of sulfanilamide on the kidney could be explained if sulfanilamide inhibits carbonic anhydrase. So one Sunday morning he showed that it does.

I spent a very unhappy year trying to find whether sulfanilamide inhibits acid secretion, and I couldn't show that it did. Soon the issue was settled by a short paper in Nature by Feldberg, Keilin and Mann (38). Feldberg, like Mann, was a German-Jewish refugee who had been taken in by the English. In 1933-36 he earned a major place in the history of physiology by doing the experiments demonstrating that acetylcholine is the parasympathetic trasmitter (39). Keilin and Mann wanted to test my idea about thiocynate, carbonic anhydrase and acid secretion, but they were a pair of biochemists. Feldberg was the physiologist who knew how to anesthetize a cat. Together they showed that carbonic anhydrase in the stomach is inhibited by sulfanilamide but acid secretion is not. So my idea was all wrong.

I have analysed this in some detail (40). There is simply too much carbonic anhdrase there, and the same thing applies to the red blood cells. Persons taking sulfanilamide survive, because more than 99.9% of the carbonic anhydrase must be inhibited before carbon dioxide exchange is affected (41). The carbonic anhydrase theory of acid secretion was dead, and I announced the fact by writing an editorial for Gastroenterology called: "In Memoriam, The Carbonic Anhydrase Theory of Gastric Acid Secretion (42)." I tell you about this to point another moral. One disease of scientists is sticking to a theory, right or wrong. But when I was a young man, I said "Pooh, pooh. What I said previously really isn't right after all." If I had deliberately tried to get a reputation for being "a scientist of inflexible integrity (43)" I could not have done better for myself. Don't be afraid to admit you're wrong, for you will get credit for it.

About this time a man named Richard Roblin introduced himself to me. He worked for American Cyanamid, and he synthesized sulfonamide durgs. He knew about the inhibition of carbonic anhydrase, and he knew about carbonic anhydrase in the kidney. He took me to lunch at the Statler in Boston and asked me whether it would be worth while to synthesize a drug which would inhibit carbonic anhydrase in the kidney. I said he was wasting his time. He didn't pay any attention to me, and a couple of years later American Cyanamid through Lederle marketed Diamox.

Here's another moral. When you write a grant application, you say that if you really understand the basic principles, you can cure cancer or sodium retention or whatever. The point is that even though you are the expert on the subject, you may not know what you are talking about.

That is the history of carbonic anhydrase as seen by one disappearing scientist. It's too bad scientists disappear, but we will all disappear anyway. Some time as the night closes in, there will be one man left who knows that pi is an irrational number. Then the roof of the cave will fall on him, and no one ever after will know that pi is an irrational number.

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ARTOIS-BAILLET LATOUR HEALTH PRIZE

This second Prize will be given in recognition of an outstanding contribution to the diagnosis, prevention or treatment of hereditary diseases. Nominations for the Prize must reach the Secretary General of the National Fund for Scientific Research, Egmontstreet 5, 1050 Brussels, Belgium, before July 1, 1980. Each nomination must be accompanied by a report, written in English, of no less than 3 pages detailing the scientific qualities of the nominee. The 1980-1981 Prize will be in the amount of four million Belgian Francs and will be awarded in the Spring of 1981.

STUDY OF REPRODUCTION

The Society for the Study of Reproduction will conduct a free placement service, August 11-14, 1980, during its 13th Annual Meeting held at the University of Michigan, Ann Arbor, Michigan. This service will be available to Society members and non-members alike. Both prospective employers and employees are encouraged to register. Individuals who will not be able to attend the meeting but wish to utilize the service, as well as those who wish to preregister for the service, should request the necessary materials from Mr. Claude Cruse, Business Manager, Society for the Study of Reproduction, 309 W. Clark Street, Champaign, Il 61820.

EMERITUS MEMBER CONTRIBUTIONS

Contributions to the Society may be made to the General Operating Fund or other designated purpose. The donor may commemorate an event or memorialize an individual.

We gratefully acknowledge the contributions recently received from the following Emeritus Members.

David I. Abramson
David E. Bass - in memory of Dr. Albert H. Hegnauer ("Hank")
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ANNUAL ABSTRACT SERIES OF EDUCATIONAL MATERIAL

Presented by Members of Educational Materials Review Board of APS

This is the fifth annual collection of abstracts of educational materials presented by the Educational Materials Review Board of the American Physiological Society under the direction of the Education Committee. Board members have submitted abstracts of review articles, papers, textbooks, books, manuals, handbooks and symposia which they have found valuable in teaching physiology. Selection of items is wholly at the discretion of members and where more than one member chooses to abstract the same material, each abstract is presented. We hope you continue to find this collection useful in teaching physiology.

The original three collections constituted the entire issue of The Physiology Teacher. The abstracts are supplementing a regular issue of The Physiology Teacher Section of The Physiologist, a practice initiated in the 1979 issue.

M. C. Shelesnyak
Executive Editor
The Physiology Teacher

CELL PHYSIOLOGY

1 BIOMEMBRANES: FUNDAMENTALS IN RELATION TO HUMAN BIOLOGY. James S. Beck. McGraw-Hill Book Company, New York, 1980.

Biomembranes are a fundamental topic in modern physiology and remarkable progress has been made in research laboratories dedicated to the study of membrane phenomena. This 172 page monograph provides an introduction to current concepts on the structure, function and biogenesis of membranes. The chapter on structure and composition of membranes is excellent apart from a weak section on integral membrane proteins. Likewise the chapters on membrane biogenesis, fission and fusion are concise, well thought out introductions to these topics. The weakest sections in the whole book are those on membrane transport, e.g., there is no mention of the progress made over the last decade on mechanisms of ion permeation across artificial phospholipid membranes and nerve cell membranes. This weakness is compounded by a poor bibliography: references to the works edited by Eisenman and Andreoli should have at least been included. Nevertheless, this monograph gives a good unified introduction to the fundamentals of biomembranes. It is strongly recommended as background reading for undergraduate courses in cell biology and physiology.

Ernest M. Wright

2 MEDICAL CELL BIOLOGY. Charles J. Flickinger, Jay C. Brown, Howard C. Kutchai and James W. Ogilvie. Saunders, Philadelphia, 1979.

This text is designed as an introductory text for first year medical students and a source for review for residents and practicing physicians. It is based on an integrated approach to cell biology that has been practiced at the University of Virginia School of Medicine. Topics covered include biochemistry, genetics and the general physiology of cells. At least in the area of the reviewer's competence, the material is up to date and references provided at the end of each chapter provide an adequate starting point for more advanced study. The book is well illustrated both in terms of line drawings and reproductions of electronmicrographs. Despite the fact that this book is a collaborative effort, the style is uniform throughout largely due to the efforts of the senior author. It is highly recommended as a text for undergraduate cell biology courses and for integrated cell biology courses in graduate programs. In more traditional physiology courses it is useful as a supplementary text.

Ernest M. Wright.

3 PESTICIDE DEGRADING PLASMIDS: A BIOLOGICAL ANSWER TO ENVIRONMENTAL POLLUTION BY PHENOXYHERBICIDES. Pemberton, J. M. In: Ambio., Vol. 8, No. 5, pp. 202-205. 1979

Microorganisms have a key role in the degradation of naturally produced organic chemicals. Synthetic molecules essential for agricultural productivity are appearing in soil in ever greater amounts. Most have no natural counterparts. Examples such as 2,4-D and 2,4,5-T challenge the natural mechanisms of microbial degradation. Many bacteria carry extrachromosomal genetic elements in plasmids which are modified by environmental chemicals. Plasmids for degradation of 2,4-D are known to exist; they have evolved and spread as a response to usage of 2,4-D. This fact insures that no conceivable pollution of the environment can result from use of 2, 4-D or structurally similar chemicals such as PCPA. There is every reason to anticipate that plasmids for degrading 2,4,5-T and TCDD can be produced. May it not be desirable to increase the flow of phenoxyherbicides into the soil to stimulate the evolution and dissemination of pesticide degrading microbial plasmids?

Charles G. Wilber

CIRCULATION

4 CIRCULATORY SYSTEM DYNAMICS Abraham Noordergraaf Academic Press New York, 1978, P.351.

This is an excellent textbook for graduate level studies on mechanics of the circulatory system and its components. A brief introduction to the entire cardiovascular system operation is followed by two chapters on pressure and flow measurement methods. The description is extensive, up-to-date, and rigorous in explaining principles. The next three chapters are devoted to detailed analyses of pressure and flow phenomena in the arteries, veins and microvessels. Although the analyses are involved and require an in-depth background in hydraulics, the author attempts with success to show the principal paths that various investigators took to explore basic mechanics in various sectors of the circulation. The chapter on the heart begins at the muscle cell level but quickly moves to the discussion of how to estimate the contractile state of the muscle or of the heart as a contractile chamber. Again the coverage is unbiased and the explanation is lucid. In the remaining three chapters, problems inherent in the closed circulatory loop, clinical circumstances including the assist devices and neurohumoral controls are discussed. Throughout the book emphasis is on quantitative understanding and the reader can check his understanding by attempting problems and answers provided at the end of each chapter. This textbook is recommendable for those students, whether medical or bioengineering, who want to learn analytical approach to circulatory mechanics.

Kiichi Sagawa

5 THE PERICARDIUM AND CARDIAC FUNCTION. Shabetai, R., L. Mangiardi, V. Bhargava, J. Ross, Jr., and C.B. Higgins. In: Progress in Cardiovascular Diseases 22:107-134, 1979.

Recent studies have shown that acute changes in the diastolic pressure-volume relation of the left ventricle can be produced by a variety of interventions. These include increases in arterial pressure, use of vasodilator therapy, and ischemia. Data suggests that these acute shifts in the diastolic pressure-volume relation may be mediated by the interaction of the right and left ventricle inside a stiff pericardium. This review carefully details the physiologic effects of the pericardium on both systolic and diastolic function. It will be extremely useful to clinicians and physiologists in better understanding how the presence or absence of the pericardium can affect hemodynamic descriptors of cardiac performance. Although some data suggests that acute shifts in the diastolic pressure-volume relation may be due to ischemia with associated contracture, most studies are compatible with the hypothesis that acute shifts are produced by alterations of the intrapericardial pressure, whose stiffness enhances the interaction of the right and left ventricles. This review covers three general areas: 1) normal physiologic role of the pericardium, 2) the contribution of the pericardium to abnormalities of cardiac function, and 3) the effects of diseases of the pericardium on cardiac function. Since much of this kind of information has not yet found its way into standard text books on physiology or cardiology, this article will be particularly valuable.

W.W. Parmley

COMPARATIVE PHYSIOLOGY

6 ENERGETICS OF GROWTH IN HOUSE MARTIN'S (DELICHON URBICA). Bryant, D.M. and A. Gardiner. In: Journal of Zoology, Volume 189, pp. 275-304. London, 1979.

Growth and maintenance in any warm blooded species involves critical problems of energetics. This paper tells how the house martin faces the challenge of growth. Quantitative information is presented on respiration, nestling growth, assimilation, feeding, waste output. Nestling respiration is interesting. It is divided into 3 phases of development: 1, a poikilothermal stage; 2, a transition phase; 3, a fully, effective homeothermal phase. The shift of energy allocation, from over 70% of the available going to growth during the first few days of nestling life, to the situation at 21 days, when virtually all the energy available goes to maintenance, is clearly presented. Comparative physiologists will find this clear presentation valuable as another example of how a different species handles a common problem for homeotherms.

Charles G. Wilber

DEVELOPMENT AND AGING

7 CELLS AND SENESCENCE. Rosen, R. Intl. Rev. Cytol. 54, 161-191, 1978.

This article is an overview of the literature concerning the senescence of cells and cell populations. It considers this literature in light of the question whether or not the senescence of multicellular organisms is the result of events occurring at the cellular level. Three specific questions are addressed: (1) Do individual cells in culture or in the multicellular organism senesce? (2) If so, does the senescence of individual cells in multicellular organisms explain the senescence of these organisms? and (3) If not, what cellular properties can explain the senescence of multicellular organisms? The author concludes that postulated cellular "models" of aging, e.g., the senescence of individual cells, clonal aging, and the spanning of cells in culture, all represent phenomena distinct from the senescence of multicellular organisms. The author further concludes that the causes of the latter senescence originate not only in changes in the functional state of individual cells in an organism's cell populations but also, importantly, in breakdowns in interactions between its cells. This article will be of interest to those seeking some insight into the complex phenomenon of senescence.

D.E. Buetow

ENDOCRINOLOGY AND METABOLISM

8 THE PHYSIOLOGY OF THIRST. J. T. Fitzsimons. Monograph of the Physiological Society No. 35, Cambridge University Press, New York, 1979. 572 pages, 156 Figures, 40 Tables, $69.50.

This is a scholarly and comprehensive monograph which could serve both as a textbook on the subject for indepth coverage, and as a handbook to provide a gateway to the research literature. The subject matter includes historical perspectives in the physiology of thirst, thirst and the causes of drinking, comparative physiology, cellular dehydration, extracellular dehydration, hormones in drinking, the renin-angiotensin system in drinking, pharmacology of drinking, sodium appetite, and clinical aspects of thirst. This book is a comprehensive and critical review of many different aspects of thirst and drinking behavior. It is emphasized that thirst is an emergency mechanism to replace an actual deficit of fluid. When fluid and water are freely available, thirst is probably experienced rather infrequently, thus drinking is largely anticipatory of future needs of water governed by cues from the diet and habit. The monograph deserves an important place in any physiology library and would be particularly useful to students interested in the broad areas of salt and water metablism and clinicians interested in abnormalities of salt and water metabolism including, among others, hypertension.

F. G. Knox

ENVIRONMENTAL AND EXERCISE PHYSIOLOGY

9 INCREASED GROWTH IN MINNOWS EXPOSED TO PCBs. Bengtsson, B-E. In: Ambio., Vol. 8, No. 4, pp. 169-170. 1979

Phoxinus phoxinus (L), a minnow, was fed food having respectively, in micrograms of PCB mixture per gram dry weight of feed, PCBs in several concentrations: 0.88, 3.9, 8.3, 32. and 78. The treatment period was 29 days. Eight minnows were in each feeding group and in a control group. The PCBs showed a growth promoting effect. All PCB fed groups showed statistically greater increases in weight than the controls. The PCB fed groups did not vary among themselves; i.e. the lowest PCB level gave the same growth stimulation as the highest. It is postulated that the PCBs disturb the hormonal system in Phoxinus and "that the occurrence of stimulated growth is related to seasonal variations in the metabolic activity of the fish." The results also serve as a caution for those using weight loss as a sign of toxicity, at least in fish.

Charles G. Wilber

10 THE REPRODUCTIVE ECOLOGY OF THE HOUSE MOUSE. Bronson, F.H. In: Quarterly Review of Biology, Volume 54, pp. 265-299. Stony Brook, New York, 1979.

This review paper is useful in demonstrating the widespread impact that physiological factors have on the biological success of animal species. House mice are commensal with man. As a species the house mouse, Mus musculus, is highly successful. It has established itself nearly everywhere on planet Earth. The author develops the thesis that the unique plysiological pattern of reproduction in the house mouse results in great ecological flexibility of the species and the capacity to colonize a remarkably broad spectrum of habitats and climates. The role of pheromes and pheromal cueing are especially interesting to the physiological success of this species. Students of physiology will find this review helpful in the appreciation of key role that functional processes play in animals in their natural surroundings.

Charles G. Wilber

11 ENVIRONMENTAL STRESS: INDIVIDUAL HUMAN ADAPTATIONS. Folinsbee, L.J., J.A. Wagner, J.F. Borgia, B.L. Drinkwater, J.A. Gliner, and J.F. Bedi (Eds.). Academic Press, New York, 1978.

This volume represents a symposium held in honor of S.M. Horvath, bringing together scientists interested in identifying the role of factors which explain individual differences in the response to environmental stresses. The contributors dealt with heat, cold, altitude, air pollution, and exercise as a stressor. Each section begins with a review of the effects of that particular hostile environment. Some of the highlights include: (1) a careful study of the effect of alcohol on individuals exposed to cold; (2) a study of cutaneous vasodilatation not only in human subjects but also under the heavily furred skins of baboons (Rowell); (3) and most importantly, adequate attention is given to a comparison of males and females when challenged by extreme environments. Except for the early work of Dubois, for many years there was very little physiological literature which compared male and female subjects. Lately it has been recognized that female subjects do have physiological mechanisms to be studied: in this volume comparisons between male and female subjects in the heat are included in three papers (Nadel, Hori, Kuhlemeier), during work (Lind, Bruce), in cold exposure (Buskirk, LeBlanc, Keatinge), and at altitude (Grover, Hannon, and Powles). This excellent book will be used by exercise physiologists, environmental physiologists, adaptational physiologists, and physiological ecologists.

G.E. Folk, Jr.

12 MAN IN EXTREME ENVIRONMENTS. Sloan, A.W. In: American Lecture Series in Environmental Studies. Charles C. Thomas, Sprinfield. pp. 132. 1979.

This monograph is designed to give a state of the art introduction to the mechanisms by which human beings adapt and fail to adapt to extreme environmental insults. Chapters are devoted to adaption and such various processes as temperature regulation, respiration, heat, cold, deep water, mountains, the stresses of aviation, and space flight. The author is an accomplished investigator and serves as Professor and Head of the Department of Physiology, University of Capetown, South Africa. The book should serve as a quick route to becoming acquainted with this field of physiology. It might also serve effectively as an "enrichment" document for students in medical physiology or for graduate students in physiology. Its use as an outline for a seminar on physiological adaptation in man is obvious. The book is well written, easy to read, and reliable.

Charles G. Wilber

GASTROINTESTINAL PHYSIOLOGY

13 SMOOTH MUSCLE. Bülbring, E. and T.B. Bolton. Br Med Bull 35: 209-312, 1979.

This volume contains 14 reports, reviews and discussions contributed in another attempt to achieve a more complete understanding of smooth muscle and how it may be controlled. The general excellence of the presentations make it difficult to select particular papers for mention. Topics (plus opening remarks by the editors) include cell junctions and structural aspects of contraction (G. Gabella); mechanisms of contraction (S.V. Perry and R.J.A. Grand); maintenance of ionic composition (A.F. Brading); membrane properties (M.E. Holman and T.O. Neild); functional diversity of smooth muscle (K.E. Creed); blood-vessels (W.R. Keatinge); autonomic innervation and transmission (G. Burnstock); mechanism of peristalsis (G.D.S. Hirst); drug receptors (A.S.V. Burgen); cholinergic mechanisms in smooth muscle (T.B. Bolton); postjunctional adrenergic mechanisms (E. Bülbring); prostaglandins and smooth muscle (E.W. Horton); clinical studies on gastrointestinal smooth muscle (H.L. Duthie); and human vascular muscle (B.F. Robinson and J.G. Collier). In this volume there is very little of the uneveness and variability that is frequently found in works compiled by a panel of authors. The articles in general are well written. A noteworthy feature of the volume is the large number of references on and pertaining to smooth muscle. The editors of this important volume are to be congratulated for bringing this wealth of information into a critical comprehensive review. This volume should be on the shelves of all college and university libraries, available to graduate students and undergraduates alike.

M. F. Tansy

14 TRENDS IN AUTONOMIC PHARMACOLOGY. Kalsner, Stanley. Urban and Schwarzenberg, Baltimore-Munich, 1979.

This collection of reviews, written by 15 internationally-known leaders in their respective fields of specialization summarizes the current status of selected topics in autonomic pharmacology. The general excellence of the presentations make it difficult to select particular papers for mention. However, that of G. Campbell on non-adrenergic, noncholinergic transmission in the autonomic nervous system: purinergic nerves and J. Fozard on cholinergic mechanisms in adrenergic function are particularly noteworthy. M.D. Gershon's section on the mammalian enteric nervous system: a third autonomic division presents an interesting point of view. Finally, the chapter on intracellular sources of calcium for activation of smooth muscle by E.E. Daniel is worth singling out. There is a more than adequate bibliography at the end of each section, and a subject index closes the book. This book would be a worthwhile addition to a specialized library collection, institutional or private, on the autonomic nervous system. Its primary utility, however, would be as a reference source.

M.F. Tansy

15 APPLIED PHYSIOLOGY OF THE MOUTH. Lavelle, C.L.B. John Wright and Sons Limited, Bristol, 1975.

Editor Christopher L.B. Lavelle, who is Senior Lecturer, at the University of Birmingham and 12 contributors have produced a book which is intended as a text for students of dentistry and medicine. Most of the contributors are British, but the scope of the chapters is eclectic and gives a representative sampling of developments in the physiology of the oral cavity. The book updates and expands materials written by some of the present authors and covers literature up to 1973. The bibliographies are adequate for the periods covered. Some of the chapters are nicely illustrated, others hardly at all. A surprising diversity of topics is covered, including the metabolism and functions of the soft connective tissues of the mouth, the metabolism of the oral mucosa, calcium and phosphorus metabolism and calcification, bone growth and remodelling, mechanisms of tooth eruption, dental plaque and associated deposits on the teeth, salivary glands and saliva, defence mechanisms of the mouth, basic immunology, mastication, deglutition, the effect upon the oral tissues of dietary deficiencies and hormonal imbalance, the blood-supply of the oral tissues, pain, physiological responses to dental treatment, age changes in the oral structures, the healing of wounds, and taste and olfaction. In summary, in spite of some weak spots (i.e. deglutition) and a few absences, the book provides an important, almost necessary review for the new researcher in the area and a valuable breadth of material for the actively engaged worker. As a supplement to traditional texts in medical physiology, the book will be a useful teaching tool.

M. F. Tansy

NEUROBIOLOGY

16 SEROTONIN AND FEEDING. John E. Blundell. In: Serotonin and Health and Disease, Vol. 5 Clinical Applications. W.B. Essman (Ed.) Spectrum Press, New York, 1979.

An excellent review of a diverse physiological, pharmacological and anatomical literature which suggests that changes in brain serotonin metabolism may significantly affect food intake, food preference and body weight. The article includes a valuable discussion of methodological problems in this field and concludes with a brief treatment of clinical implications. Except for an earlier article by Blundell (Intern. J. Obesity, 1:15, 1977) which is not available in many libraries, this article represents the only systematic treatment of the subject currently available.

S.P. Grossman

17 THE HIPPOCAMPUS AS A COGNITIVE MAP. John O'Keefe and Lynn Nadel. Clarendon Press, Oxford, 1978.

A most interesting attempt to present the facts of hippocampal anatomy and electrophysiology, together with results of hundreds of behavioral studies of the effects of hippocampal lesions in the context of a theory of spatial orientation that ascribes to the hippocampus a function of 'cognitive mapping' which is fundamental to the appreciation of absolute, unitary space. The authors elaborate this notion to account for the experimental and human clinical data which suggest that the hippocampus may play a significant role in learning, memory consolidation and/or retrieval. The book presents an excellent review of the literature for the serious student of hippocampal functions, but is too detailed and technical to serve as a text in all but the most advanced seminars.

S.P. Grossman

18 A STEREOTAXIC ATLAS OF THE RAT BRAIN. SECOND EDITION. Louis J. Pellegrino, Ann S. Pellegrino, and Anna J. Cushman. Plenum Press, New York, 1979.

This revision of Pellegrino and Cushman's 1967 atlas has been expanded significantly to include (a) coronal sections through all of the cerebellum and most of the caudal brainstem; and (b) 23 parasagittal sections. The end-result is the most comprehensive stereotaxic atlas currently available, including 122 photomicrographs and extensively labelled corresponding line drawings, covering the brain from the olfactory bulbs to the caudal brainstem. A comprehensive index of structures and a separate index of abbreviations greatly simplify the use of this atlas. A 'must' for the laboratory and an excellent aid for the student of rat neuroanatomy.

S.P. Grossman

RENAL AND ELECTROLYTE PHYSIOLOGY

19 THE RENAL CIRCULATIONS. Brenner, B. M., and R. Beeuwkes III. Hospital Practice 13, No. 7: 35-46, 1978.

This review discusses the functions and closely correlated anatomies of the renal circulations. The plural is used advisedly, since there are several specialized microcirculations in the kidney. These include the glomerular, cortical peritubular capillary, and medullary circulations. The glomerulus is discussed first. Topics covered include microscopic anatomy, dynamics of glomerular filtration, and importance of negatively charged structural elements in the glomerular capillary wall. The second microcirculation, the cortical peritubular capillary, is specialized for reabsorption of fluid and solutes. Topics covered include its anatomy, pressure relationships which favor the uptake of reabsorbed fluid, and vascular-tubular relationships. Finally, the medullary circulation and its specialized role in the urinary concentrating mechanism is considered. Countercurrent diffusion exchange and its implications for medullary functions are described. The review describes many of the recent advances in our understanding of the renal circulations which we owe to the authors and their colleagues. The article is written in a readable, uncomplicated style, is nicely illustrated, and is recommended to teachers, students, and physicians.

G. A. Tanner

20 METABOLIC REQUIREMENTS FOR RENAL FUNCTION. Epstein, F. H. Hospital Practice 14, No. 6: 93-102, 1979.

This review surveys renal metabolism. Most of the energy consumed by the kidneys is used in tubular transport (chiefly reabsorption of filtered sodium), so this subject is emphasized. The relationships among oxygen consumption, ATP utilization, and sodium transport are presented. The role of the basolateral cell membrane Na-K ATPase in sodium transport is considered. The important role of sodium transport in energizing the transport of other solutes (e.g. glucose, amino acids, chloride) is discussed. Regional differences in metabolism in the cortex, outer medulla, and inner medulla are summarized. Also, examples of differences in enzyme activities and transport functions in individual nephron segments are presented. Much work remains to be done on the relations between metabolism and transport. Basal metabolism of the kidney, i.e. metabolism of nontransport functions, is also discussed. The kidneys catabolize several polypeptide hormones (e.g. insulin, glucagon, PTH) and are an important site of gluconeogenesis. This review provides a readable introduction for the nonexpert.

G. A. Tanner

21 BRADYKININ-INDUCED RENAL HEMODYNAMIC ALTERATIONS: RENIN AND PROSTAGLANDIN RELATIONSHIPS. Flamenbaum, W.J., J. Gagnon and P. Ramwell. Am. J. Physiol. 237: F433 - F440, 1979.

This article focuses on the mechanism by which bradykinin induces renal hyperemia and the role of the renin-angiotensin system as a modulator of the vasomotor action of bradykinin in the dog kidney. The investigators studied the effects of bradykinin infusion alone, bradykinin infusion after inhibition of prostaglandin synthetase, and bradykinin infusion after inhibition of angiotensin II, on renal hemodynamics and the secretory rates of prostaglandin and renin. The authors demonstrate that the increase in RBF brought on by the infusion of bradykinin is primarily independent of the effect bradykinin has on prostaglandin synthesis and release. The hyperemia is not sustained with a constant infusion of bradykinin and increases in renin secretion are associated with return of RBF toward control levels. These data are consistent with the hypothesis that regulation of renal blood flow is the result of a balance between controlling factors which induce vasodilation such as bradykinin and certain prostaglandins and controlling factors which induce vasoconstruction such as the renin-angiotensin system. This article should be of interest to those who are interested in understanding the controlling factors which regulate renal hemodynamics.

H.M. Randall

22 QUESTIONS AND REPLIES: ROLE OF THE COLLECTING TUBULE IN FLUID, SODIUM, AND POTASSIUM BALANCE. Jamison, R. L., H. Sonnenberg, and J. H. Stein. Am. J. Physiol. 237 (Renal Fluid Electrolyte Physiol. 6): F247-F261, 1979.

This editorial review considers how the collecting tubule system handles sodium, water, and potassium. It is now generally accepted that this portion of the kidneys plays a major role in the day-to-day regulation of fluid and electrolyte balance. Dr. Jamison briefly reviews the subject and then poses seven questions which are answered by Drs. Sonnenberg and Stein. The topics covered include: 1) factors that affect sodium transport by the collecting tubules, 2) factors that affect potassium transport, 3) pitfalls of the microcatheterization and micropuncture techniques which have been used to study collecting tubule function, 4) possible reasons for discrepant results obtained with the two techniques, 5) comparisons between results obtained by in vivo and in vitro micropuncture, and 6) major unresolved questions concerning function of the collecting tubule system. The format of the review is especially enlightening, since it presents side-by-side two expert answers to the same questions. The review points out numerous areas that need further study, and for this reason is valuable for graduate students and researchers.

G. A. Tanner

23 GLOMERULAR PERMEABILITY AND DYNAMICS. Knox, F. G. Physiologist 22, No. 6: 34 - 38, 1979.

This brief review discusses 1) glomerular dynamics in the rat and dog, and 2) the permeability of the glomerular capillary to macromolecules. The author summarizes evidence that glomerular filtration pressure equilibrium does not exist in the normal dog, in contrast to the rat. This difference may explain why glomerular filtration rate increases strikingly with renal blood flow in the rat, but does not do so in the dog (and man). Recent evidence that the glomerular filtration membrane acts as a negatively charged electrostatic barrier impeding the transglomerular passage of negatively charged macromolecules is summarized. The author suggests that glomerular pores are 20 - 30 angstroms in radius. This is probably too small; the data presented suggest pores closer to 40 angstroms in radius. Due to steric hindrance and viscous drag effects a 40 angstrom radius pore would reduce the filterability of neutral macromolecules in the 20 - 30 angstrom radius range. The article is graphically illustrated, and provides a good introduction to exciting new developments in this area for students and teachers.

G. A. Tanner

24 THE RENAL KALLIKREIN-KININ SYSTEM. Levinsky, N. G. Circ. Res. 44: 441-451, 1979.

This article reviews the literature on the renal kallikrein-kinin system until July, 1978. The components of the plasma and renal kallikrein systems are described first. Then some of the problems in assaying the renal kallikrein system are presented. The interactions among the three renal hormonal systems (kallikrein-kinin, prostaglandin, and renin-angiotensin-aldosterone) are clearly presented. The physiological role of the renal kallikrein system is considered in detail, but, according to the author, is still not certain. Kinins are potent renal vasodilators and increase salt and water excretion. A possible role for the renal kallikrein system in the pathogenesis or pathophysiology of some forms of hypertension, kidney disease, and fluid and electrolyte disturbances is considered last. Each section of the article is accompanied by a brief summary. The subject of this review is receiving a great deal of attention these days, and is a fertile area for investigation. This clearly written review is recommended for researchers and graduate students.

G. A. Tanner

25 NONPRESSOR MECHANISMS IN CNS-INDUCED NATRIURESES. Mouw, D.R., A.J. Vander, J.J. Bourgoignie, S.S. Kutchinski and N.P. Mathias. Am. J. Physiol. 237: F157 - F166, 1979.

The subject of this article is the role of the central nervous system in regulating extracellular fluid [Na^+]. In a series of anesthesized dogs, CSF [Na^+] was raised by ventriculocisternal perfusion of an artificial CSF perfusate. Control, experimental and recovery clearance periods were studied in which rates of Na^+ excretion were compared with RPF, GFR, mean arterial blood pressure and arterial renin activity. Results of this study were compared with a time control series in which CSF [Na^+] was maintained constant. As CSF [Na^+] increased above control, renal hemodynamics and blood pressure remained stable while the rate of Na^+ excretion increased significantly above control. Plasma renin activity decreased during high Na^+ perfusion and then increased during recovery. No increase in urinary natriuretic factor was noted during natriuresis but their studies were inconclusive. Thus, the authors conclude that the natriuresis that follows an increase in CSF [Na^+] is not caused by hypertension or by changes in renal hemodynamics. These data may be interpreted such that the periventricular neurons are significant regulators of Na^+ balance; on the one hand they effect an increase in Na^+ excretion, possibly by causing the release of some natriuretic factor and on the other hand, effect a decrease in Na^+ excretion by signaling an increase in plasma renin activity. This article should be of significance to those who wish to develop a better understanding of the means by which the CNS regulates Na^+ balance.

H.M. Randall

26 RESPONSE OF THE COLLECTING DUCT TO THE DEMANDS OF HOMEOSTASIS. Schafer, J. A. Physiologist 22, No. 5: 44-53, 1979.

This review discusses recent investigations on collecting duct function and structure. The methods of study- in vivo micropuncture or microcatheterization and in vitro perfusion of isolated collected ducts- are presented briefly. Then the quantitative importance of the collecting ducts in regulating water, sodium, and potassium excretion is considered. Next, selected experimental studies on collecting duct sodium and potassium transport, with representative data, are presented. The role of aldosterone and unidentified hormonal factors in controlling sodium and potassium transport is considered. The final section deals with the effect of antidiuretic hormone (ADH) on water permeability in the collecting duct. Studies with isolated collecting duct, toad urinary bladder, and artificial membranes have contributed importantly to newer knowledge in this area. The past decade has seen a revolution in ideas about the nature of the pore changes in the luminal cell membrane induced by ADH. This review serves as a fine introduction to this area for physiologists in general.

G. A. Tanner

27 HORMONES AND THE KIDNEY. Stein, J. H. Hospital Practice 14, No. 7: 91-105, 1979.

This article considers three types of relationships between the kidney and hormones: 1) hormones or special substances which are produced by the kidneys (renin, prostaglandins, kallikrein, and 1,25-$(OH)_2$-vitamin D_3), 2) hormones which affect renal function (renin-angiotensin-aldosterone sequence, ADH, prostaglandins, adrenocortical hormones, kallikrein-kinin system, parathyroid hormone, and thyroid hormone), and 3) hormones which are metabolized by the kidneys (insulin and parathyroid hormone). Major topics covered are: 1) the renin-angiotensin-aldosterone system (factors controlling renin release, actions on the kidneys, role in hypertension, effects of mineralocorticoid deficiency or excess), 2) pathophysiology of Bartter's syndrome, 3) production and actions of renal prostaglandins, 4) renal kallikrein-kinin system 5) effects of PTH on the kidney, and 6) renal synthesis of 1,25-$(OH)_2$-vitamin D_3. A minor correction: angiotensin converting enzyme (=kininase II) degrades the active kinin, and does not produce it. Interrelationships among the various hormonal systems are discussed. The article presents numerous examples of clinical disorders associated with hormone imbalances and relates these disorders to basic physiology. This review is recommended for medical students and physicians.

G. A. Tanner

28 FEEDBACK CONTROL OF GLOMERULAR BLOOD FLOW, PRESSURE AND FILTRATION RATE. Wright, F.S. and J.P. Briggs. Physiol. Rev. 59: 958-1006, 1979.

The subject of this review is the regulation of glomerular function by feedback control involving composition and volume flow of filtrate passing through the loop of Henle and distal tubule. The anatomical features of the juxtaglomerular apparatus and its components are discussed, in terms of a possible role in regulating GFR by sensing changes in filtrate in the early distal tubule. Several hypotheses and lines of evidence which favor negative feedback control of GFR, involving the juxtaglomerular apparatus were discussed. As the rate of flow increases through the loop of Henle, both filtration rate and glomerular capillary pressure decrease, presumably because of a change in vascular resistance in the afferent arteriole. An increase in chloride transport to the macula densa appears to be the required signal necessary for activating the feedback mechanism. Doubt remains as to whether the vasoconstrictor agent that causes constriction of the afferent arteriole is angiotensin, exclusively. The sensitivity of the feedback system can be altered as conditions change; increases in interstitial fluid volume or pressure reduce the magnitude of the response while decreases have the opposite effect. This change in sensitivity may be important in understanding the physiological role of this mechanism, in that the variable gain helps the kidney regulate systemic fluid volume balance by regulating GFR. This review should be useful for those who wish to understand more fully the mechanisms responsible for controlling extracellular fluid volume.

H.M. Randall

29 FEEDBACK CONTROL OF GLOMERULAR BLOOD FLOW, PRESSURE, AND FILTRATION RATE. Wright, F. S., and J. P. Briggs. Physiol. Rev. 59: 958-1006, 1979.

This review considers evidence for feedback control of glomerular function. The first part discusses anatomical studies on the juxtaglomerular apparatus, the probable site of transfer of information from distal tubule to glomerular blood vessels. Next, the results of micropuncture experiments are presented. The basic observation is that an increased rate of perfusion of Henle's loop elicits a fall in glomerular pressure, blood flow, and filtration rate in the perfused nephron. The authors present evidence that 1) the signal initiating feedback is a change in chloride transport by macula densa cells, 2) the feedback response can be modified by changes in renal interstitial pressure or volume, and 3) the effector site is the afferent arteriole. The involvement of renin and angiotensin in feedback is not certain. Finally, the article considers the possible role of feedback in 1) autoregulation of renal blood flow, 2) acute renal failure, and 3) regulation of salt and water excretion. Many aspects of the feedback mechanism remain controversial. This scholarly review is recommended for graduate students and researchers.

G. A. Tanner

RESPIRATION

30 SLEEP APNEA, HYPOPNEA AND OXYGEN DESATURATION IN NORMAL SUBJECTS. Block, A. J., P.G. Boysen, J.W. Wynne and L.A. Hunt. In: N Engl J Med 300:513-517, 1979.

This study will be of interest to those who have special interest in the breathing abnormalities during sleep. The subject topics studied in this paper include the following: (a) incidence of breathing abnormalities and oxygen desaturation during sleep in normal subjects, (b) difference in sex distribution of periodic breathing and desaturation during sleep, and (c) relationship of increasing age and obesity to abnormal breathing and desaturation during sleep in males. This study involved continuous measurements of oxygen saturation, electroencephalogram, electroocculogram, airflow and chest movements during sleep. Abnormal breathing and desaturation during sleep does appear to be predominantly a male phenomenon. This article will be particularly valuable to the physiologists interested in sleep physiology, respiratory physiology and clinical investigators interested in periodic breathing and severe hypoxemia in chronic obstructive lung disease.

C.M. Banerjee

AUTHOR INDEX

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THE PHYSIOLOGY TEACHER

CONTROL OF PLASMA ALDOSTERONE IN MAMMALS

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Introductory courses in Human or Mammalian Physiology often leave the student with the impression that aldosterone secretion is mediated exclusively by pituitary ACTH and the renin-angiotensin system. A great number of studies indicate, however, that other factors such as direct adrenal stimulation by plasma potassium or the rate of aldosterone inactivation by the liver are important regulation points. I have summarized many of these potential controls of plasma aldosterone levels in a diagram for teaching purposes (Fig. 1). Hopefully, this diagram is instructive for beginning students and will stimulate thought and questions from advanced or graduate students in higher level courses. The following short review documents the controls which appear in this figure. At the end of this paper are topics for discussion that are prompted by Figure 1.

The Renin-Angiotensin-Aldosterone System

In mammals, the major control of aldosterone is probably via the reninangiotensin system (see reviews 17, 58, 59). Renin, a proteolytic enzyme is released from the juxtaglomerular complex of the kidney and converts angiotensinogen (a plasma $_{a2}$-globulin) to angiotensin I. Angiotensin I undergoes further enzymatic cleavage to angiotensin II. Angiotensin II, an octapeptide, exerts a powerful arteriole pressor effect, directly stimulates adrenal zona glomerulosa aldosterone secretion and participates in feedback inhibition of renin release. Angiotensinase then converts angiotensin II to a decreased or inactive form. Recent information suggests that the ability of the adrenal gland to respond to angiotensin II is not constant but changes with an animal's sodium status (15, 27).

The release of renin in the mammalian kidney is governed by at least four factors; rate of renal perfusion, tubular sodium levels, neural input and angiotensin feedback. Concepts about renal vascular reception are based upon non-filtering kidney studies in adrenalectomized, renal denervated dogs (e.g., 4). A decrease of renal perfusion in these studies resulted in the release of renin through a mechanism independent of sodium delivery to the macula densa, renal nerves or catecholamines. This effect probably is mediated by the stretch of the afferent arteriole at the level of the juxtaglomerular cells. Experimental conditions which alter intratubular sodium content such as diuretics (3, 69) and retrograde tubular injection (67) suggest that sodium relations within the macula densa also affect renin release. Stimulation of the renal nerves caused renin secretion in dogs (32) and renal denervation decreased plasma renin activity (62) while stimulation

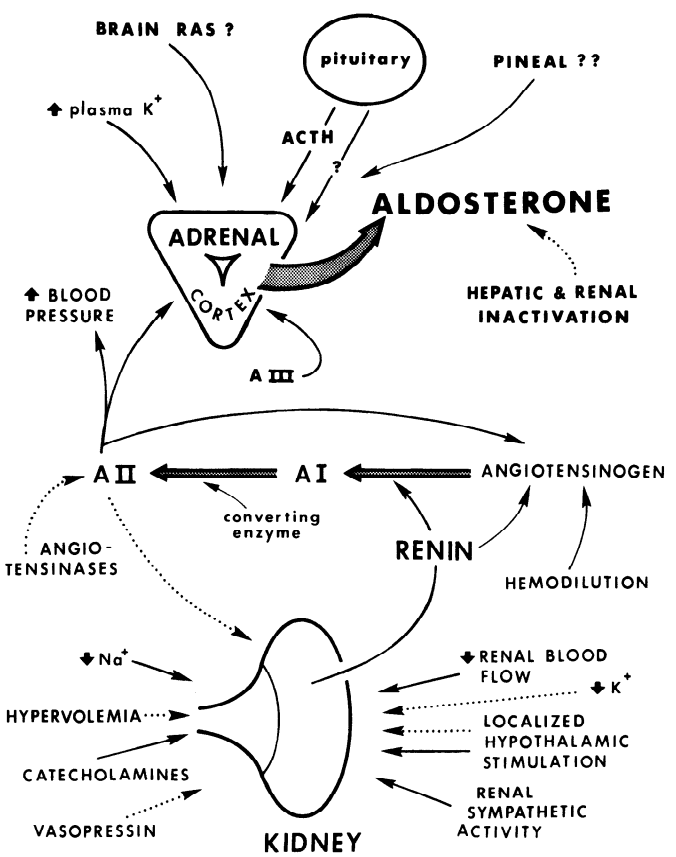

Fig. 1. Control of Plasma Aldosterone in Mammals. Solid arrows (——►) represent stimulatory effects, broken arrows (·····►) indicate inhibition, and double arrows (⟹) identify secretion or chemical conversion. Upward (↑) or downward (↓) arrows respectively signify increasing or decreasing levels. A number of other factors affecting aldosterone are not pictured. Also not depicted are aldosterone's effects on Na^+, K^+ and extracellular volume. (RAS = renin-angiotensin system; ACTH = adrenocorticotropin; AI = angiotensin I; AII = angiotensin II; AIII = [Des-Asp^1] angiotensin II.)

in various parts of the brain either increased or decreased renin (71, 72). At least part of this renal input seems to be mediated by cardiopulmonary receptors (66). Angiotensin II given to dogs (63) and sheep (7) prevented renin release during sodium depletion and suggests a short-loop negative feedback mechanism. In addition, physiological levels of vasopressin (65) and alterations in plasma potassium levels (1, 12) have been reported to prevent renin release.

Control points in this scheme also appear to affect renin-angiotensin system precursors. James and Hall (31) have postulated that sodium ions in the macula densa may activate "inactive renin" (also called "prorenin" or "big renin"). In dogs isovolemic, isoncotic hemodilution increases plasma angiotensinogen (57). A number of reports indicate angiotensinogen levels decreased after hypophysectomy or adrenalectomy (see 58) and others suggest a positive feedback control on angiotensinogen may exist, for when angiotensin II was administered to dogs (8) and rats (48, plasma levels of angiotensinogen increased.

In the past few years it has been recognized that the heptapeptide, (Dep-Asp^1) angiotensin II (angiotensin III) may play an important role in the control of aldosterone secretion (see 11). This compound has equal biological activity with angiotensin II and is present in the plasma of man and dog. In rats, it exceeds plasma levels of angiotensin II. It has not been resolved if (Dep-Asp^1) angiotensin II is locally generated in the adrenal cortex from angiotensin II or is formed directly from angiotensin I.

Also, within the last few years, evidence has accumulated suggesting the presence of a brain renin-angiotensin system (see 56). Proteins and polypeptides similar to all the components of the kidney renin-angiotensin system have been identified in brain tissue and cerebral spinal fluid with activities that exceed plasma titers. Ultrastructural studies such as those of Kobayashi (35, 36) on the mouse hypophysial pars intermedia have shown parallel changes in granulation of certain brain parts and the adrenal zona glomerulosa during sodium deficiency. A rigorous verification of any function for the presumptive brain renin-angiotensin system has not appeared in the literature to date.

Other Controls

Several observations question the primacy of the renin-angiotensin system. In man during the early stage of fasting (14) and in a number of clinical conditions (47) renin activity changes while aldosterone levels are either constant or are inversely related to plasma renin. In anephric men, aldosterone levels were normal (46) and angiotensin II (4ng/kg/min) had no effect on aldosterone levels (41). Increased plasma aldosterone levels have been observed in nephrectomized patients in response to sodium depletion during hemodialysis (38, 39). In nephrectomized rats aldosterone levels also rose after sodium depletion (54) while in salt-loaded, hypophysectomized dogs, there was only a transient increase in aldosterone after angiotenin II infusion (18). Aldosterone levels were still regulated in dogs in response to hemorrhage despite the absence of the kidneys and head (40). All of these observations suggest that there are other controls in addition to the renin-angiotensin system.

Adrenocorticotropin (ACTH) appears to have a permissive role over aldosterone release. Hypophysectomy and certain hypothalamic lesions caused a drop in plasma aldosterone in dogs (18) and sodium deficient rats (51, 52). ACTH, when infused into sheep (5), American oppossum (33) and yellow-bellied marmot (34), for example, caused increased aldosterone levels.

Other cranial factors, in addition to ACTH, seem to be involved in aldosterone regulation. The aldosterone response to sodium deficiency in hypophysectomized dogs and rats was not restored by ACTH (42, 53) nor did patients with panhypopituitarism respond to this compound (44). Growth hormone plus ACTH restores the aldosterone response in hypophysectomized rats (51) and ACTH plus human growth hormone augmented aldosterone production in diced human adrenal glands (30); however, growth hormone replacement does not make panhypopituitarism patients responsive to ACTH (44). Likewise, conflicting information exists for prolactin as a cranial controlling factor (see 29). Also, vasopressin alone restored aldosterone levels following specific hypothalamic lesions in rats (52) thus creating another candidate for status as a cranial factor. Vasopressin, like angiotenin II (13), has centrally mediated effects upon aldosterone levels that are opposite the effects mediated by the kidney. Thus, the central actions of angiotensin II and vasopressin may represent feedback mechanisms which attenuate the systematic changes caused by the circulating hormones.

For a brief period of time, the pineal was considered to be a major controller of aldosterone. Farrell (23) reported that a compound ("adrenoglomerulotropin") extracted from beef pineal glands stimulated aldosterone secretion in dogs. In as subsequent study (24), adrenoglomerulotropin was identified as a specific carbolamine derivative which, at even 100 times the aldosterone stimulating dose, had no effects on cortisol. Other researchers have failed to repeat these results. In sheep, for example, this carbolamine had no effect on aldosterone secretion (6) while in dogs, pinealectomy showed similar negative results (16). The recent discovery of renin-like activity in the pineals of rats (28) may reopen interest in the relationship between the pineal and the adrenal zona glomerulosa.

Plasma potassuium is also an important factor governing aldosterone levels. Dietary potassium loading increased aldosterone biosynthesis *in vitro* (9) and *in vivo* (10), in the rat. This ion likely acts directly on the adrenal, for potassium salts increased aldosterone secretion when infused into nephrectomized decaptitated dogs (43) or into hypophysectomized, nephrectomized dogs as well as into the arterial supply of the isolated dog adrenal (19). *In vitro* effects of angiotensin II and ACTH upon the zona glomerulosa have been shown to be highly dependent on the incubation medium [K^+](25). In fact, potassium levels may represent a common step in the mechanism of aldosterone release since several factors known to evoke aldosterone biosynthesis (angiotensin II, sodium depletion, ACTH and hyperkalemia) all result in the increase in adrenocortical potassium (2).

The rate of aldosterone metabolism is an additional potential factor determining plasma concentrations. Clearance studies in dogs (20) indicate that the liver is the primary point of destruction. In many cases of essential hypertension in man, hepatic clearance of aldosterone decreases (50, 61), possibly as a consequence of increased binding to an aldosterone carrier protein. Nowaczynski's group (50) has shown an effect upon the proportions of renal versus hepatic metabolites of aldosterone by ACTH and postural changes. This aspect of aldosterone regulation has been given very little attention.

Other potential controls and exogenous factors further complicate the understanding of the mammalian control system. In man NH_4Cl specifically increases aldosterone levels, possibly through an effect on acid-base balance (55) and potassium concentration. Prolonged weightlessness (37), sleep (60) and pregnancy (70) also increase aldosterone levels in humans while hypoxic decompression (64) and immersion (22) have the opposite effect. Anesthesia, posture, ambulation, and disease can also profoundly influence circulating aldosterone. In addition to

all these factors a complex interrelationship exists between the levels and effects of aldosterone and the renal prostaglandins and kallikrein-kinin system (see 26, 45, 49, 68).

Topics for Discusssion

1. It is notable that in mammals, aldosterone itself does not participate in short-loop feedback upon the production site (see also 21). Possibly this lack of direct modulation between aldosterone levels and synthesis is a factor in the pathologies associated with aldosteronism.

2. It is difficult to view the involved scheme depicted in the figure as part of a typical servo-mechanism for homeostatic control of sodium and extracellular volume, for a much simpler system could attain these ends. Instead, perhaps this system is an anticipatory device (i.e., feed forward control) which compensates for the long lag time between aldosterone secretion and effect.

3. Does this complex regulatory web mean that aldosterone's primary role in mammals is to effect some factor such as potassium which requires highly precise modulation?

4. Aldosterone is an extremely potent hormone having physiological effects at concentrations of 10^{-12}g/ml and hence may require a highly refined control system.

5. Does the apparent complexity of this system exist in reality? Are many of the potential controls really artifacts, unimportant evolutionary vestiges or significant only in pathogenesis? How applicable is a composite diagram such as this to any given species?

6. Several factors affecting aldosterone are not depicted in this scheme. It might be instructive for discussion groups to speculate upon the point of action of the prostaglandins, kinins and a variety of exogenous influences such as postural changes, immersion, anesthesia and pregnancy.

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TEACHING MODELLING CONCEPTS: ENTER THE POCKET-SIZE PROGRAMMABLE CALCULATOR

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Last year, a series of articles on the state-of-the-art in physiological simulation appeared in the Physiology Teacher (1-4). Physiological simulations were described which could be performed on several different types of computers, and it was pointed out that complete computer systems usually cost several thousand dollars or more.

In addition, an article by D. Ingram (5) appeared later concerning the role of computer models in the teaching of Physiology. Although arguments for and against using computer models were presented, it was pointed out that modelling could help to overcome a major teaching problem. This problem results from"the fact that students fail to see a system in an integrated way."

This concept is so important in the understanding of how many physiological systems work that it has become an essential part of the education of the student of Physiology. For this reason, I would like to proffer one solution to two main arguments against using computer models in teaching. These two arguments, which were given by Dr. Ingram, are:

a)"That the computers available for use in teaching are often unreliable and difficult to access."
b)"That computers are an expensive extra cost which cannot be afforded."

Not long ago, a leading scientific newsstand magazine (6) carried an article entitled "Programmable calculators - computer power in pocket-size packages." In this article it was pointed out that the programmable calculator armed with a printer approaches the utility of a microcomputer. Like a microcomputer, it can be programmed to solve problems automatically. It does this simply by remembering the keystroke sequence needed to solve a particular problem. The keystroke sequences are the same as those you would use ordinarily if you were using the calculator to make a particular computation, except that in the *program mode* the keystroke sequence is placed in the calculator's memory. This has the benefit that no specialized programming "language" such as FORTRAN or BASIC has to be learned.

The programmable calculator which I use is the Hewlett-Packard model HP-97. It lets you write programs simply by pressing the keys on the keyboard much as you would ordinarily do if you were using the calculator manually to solve some particular equation. These "programs" are stored in the calculator's memory and can even be recorded on a small magnetic card for later use. An invaluable feature of the HP-97 is its built-in thermal printer. For some applications, such as program editing or systems modelling, the printing capability is indispensable.

To illustrate how the HP-97 can be used in the modelling of physiological systems consider the block diagram shown in Figure 1. This familiar model characterizes the basic features of the renal and fluid volume system for arterial pressure regulation. The physiological concepts pertaining to the model have been explained elsewhere, and for a complete discussion the reader is referred to the original source (7).

The systems equations used for the model are given in Table 1. For simplicity, only linear equations were used. Programming the model was further simplified by the fact that Blocks 1-8 form an uninterrupted feedback loop which comprises the main body of the model. Once these blocks were programmed and made to function satisfactorily, then Blocks 9-11 were added. It should be stated that the program presented here is by no means the only one which could be used for the simulation, but it serves the purpose of maintaining simplicty.

TABLE 1

Program Description and Equations for the Model of Figure 1

Block 1 (steps 64 - 85)

$UO = A\,P/5 - 19$
$UO = A\,P/100 - 0.38$

Block 2 (steps 86 - 88)

$\Delta E/\Delta t = NI - UO$

Block 3 (steps 89 - 93)

$\Delta E = K_1 \cdot \Delta E/\Delta t$

$E = E_1 + \Delta E$

Block 4 (steps 20 - 23)

$BV = E/3$

Block 5 (steps 24 - 30)

$SFP = BV/K_2 - 28.7$

Block 6 (steps 31 - 32)

$PGVR = SFP - RAP$

Block 7 (steps 41 - 43)

$CO = PGVR/RVR$

Block 8 (steps 60 - 63)

$AP = CO \cdot TPR$

Block 9 (steps 37 - 40)

$RVR = 0.07\ TPR$

Block 10 (steps 44 - 56)

see note below

Block 11 (steps 33 - 36; steps 57 - 59)

$$TPR = \frac{\text{Normal TPR}}{\text{Met. Dil.}}$$

Programming notes:

E_1 is the value of E in storage register #1.

K_1 is a proportionality constant (0.06 L·min/ml) that converts $\Delta E/\Delta t$ from ml/min to L accumulated during 60 minutes; thus, each iteration is the equivalent of one hour of physiological change.

K_2 is the circulatory compliance (0.14 L/mmHg).

Block 10. In programming this model Block 10 was not set up to function explictly as indicated in Figure 1. Instead, a special algorithm was devised which would increment (+) or decrement (-) the TPR by 0.1 mmHg/L/min during each iteration. This + or - only occurs if CO is greater or less than its normal value (5 L/min), respectively. This causes the Normal TPR to change at the rate of 2.4 mmHg/L/min per day. Physiologically, the Normal TPR changes only about one-third this rate, but by using the value of 0.1 the running of the simulation is facilitated and it comes back to equilibrium much sooner, following a perturbation.

The program listing for the model (see Table 2) consists of three columns of information. Each program step is numbered,

and the computations follow this ordered sequence. Note that there are 96 program lines (all calculators mentioned in this paper have sufficient capacity to accomodate it). The second column indicates the particular calculator keys which have to be pressed to record the program. The third column is simply a code which identifies these keys according to their location on the HP-97 keyboard; this information is often useful in troubleshooting programs.

TABLE 2

Program Listing for the Model of Figure 1

Step	Key Entry	Key Code
ØØ1	LBLA	21 11
	DSP1	-63 Ø1
	Ø	ØØ
	STOØ	35 ØØ
ØØ5	1	Ø1
	5	Ø5
	STO1	35 Ø1
	.	-62
	1	Ø1
Ø1Ø	4	Ø4
	STO2	35 Ø2
	1	Ø1
	STO3	35 Ø3
	2	Ø2
Ø15	Ø	ØØ
	STO4	35 Ø4
	1	Ø1
	STO5	35 Ø5
	LBLB	21 12
Ø2Ø	RCL1	36 Ø1
	PRTX	-14
	3	Ø3
	÷	-24
	RCL2	36 Ø2
Ø25	÷	-24
	2	Ø2
	8	Ø8
	.	-62
	7	Ø7
Ø3Ø	-	-45
	RCLØ	36 ØØ
	-	-45
	RCL4	36 Ø4
	RCL5	36 Ø5
Ø35	÷	-24
	PRTX	-14
	.	-62
	Ø	ØØ
	7	Ø7
Ø4Ø	x	-35
	÷	-24
	STO7	35 Ø7
	PRTX	-14
	5	Ø5
Ø45	-	-45
	X>Ø?	16-44
	GTOb	22 16 12
		-62

Step	Key Entry	Key Code
	1	Ø1
Ø5Ø	ST-4	35-45 Ø4
	GTOC	22 13
	LBLb	21 16 12
	.	-62
	1	Ø1
Ø55	ST+4	35-55 Ø4
	LBLC	21 13
	RCL4	36 Ø4
	RCL5	36 Ø5
	÷	-24
Ø6Ø	RCL7	36 Ø7
	x	-35
	PRTX	-14
	STO6	35 Ø6
	9	Ø9
Ø65	8	Ø8
	-	-45
	X<Ø?	16-45
	GTOa	22 16 11
	RCL6	36 Ø6
Ø7Ø	5	Ø5
	÷	-24
	1	Ø1
	9	Ø9
	GTOD	22 14
Ø75	LBLa	21 16 11
	RCL6	36 Ø6
	1	Ø1
	Ø	ØØ
	Ø	ØØ
Ø8Ø	÷	-24
	.	-62
	3	Ø3
	8	Ø8
	LBLD	21 14
Ø85	-	-45
	RCL3	36 Ø3
	$X^{\rightleftarrows}Y$	-41
	-	-45
	.	-62
Ø9Ø	Ø	ØØ
	6	Ø6
	x	-35
	ST+1	35-55 Ø1
	SPC	16-11
Ø95	GTOB	22 12
	RTN	24

The graphs shown in Figures 2 and 3 are the results of two simulation runs of the model represented by the block diagram of Figure 1. Each set of four plotted points, representing the values of each of the four graphed variables at one point in time, is one complete iteration or solution of the simulation. There are approximately 45 solutions in all in the one simulation run of Figure 2 which required almost 4 minutes to complete. In simulating this model the HP-97 can output about 12 complete iterations per minute on printed paper tape; two of these are shown in Figure 4. But to obtain the graphs of Figures 2 and 3, the printed numerical data must be transformed graphically as follows. On a piece of ordinary graph paper coordinate axes are set up for each of the output variables and in ranges sufficient to cover the changes expected. Then, one by one, each recorded value is plotted on its corresponding graph until all 4 values in one completed iteration have been plotted. Then the data representing the next solution is plotted, etc.

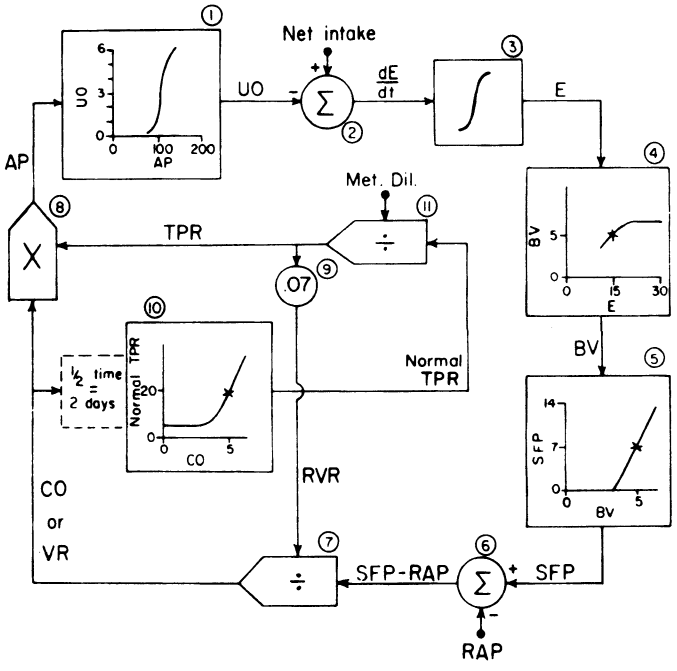

Fig. 1. Systems analysis of the renal and fluid volume system for arterial pressure control (Reprinted from Guyton: *Textbook of Medical Physiology*, 5th Ed., W. B. Saunders Co.).

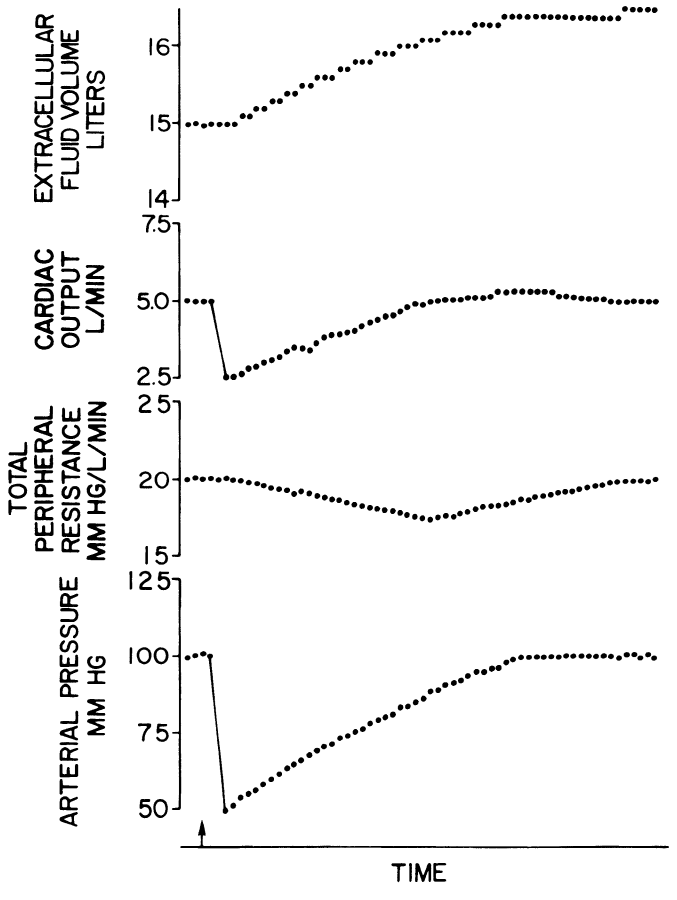

Fig. 2. Simulation of events associated with the production of mild hypertension coincident with a slight evelation of the extracellular fluid volume. At the time indicated by the arrow, the simulation was momentarily interrupted by pressing the "run/stop" key on the calculator keyboard. While stopped, the net intake of fluid (Block 2) was changed from normal to 4 times normal. The simulation resumed running when the R/S key was again pressed.

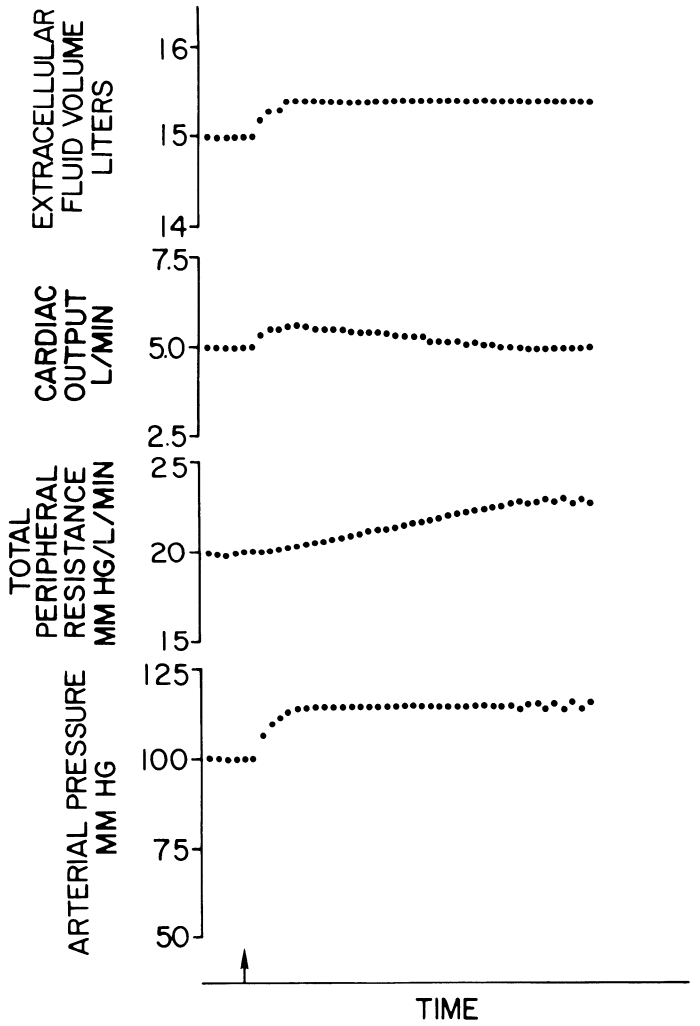

Fig. 3. Simulation of acute heart failure and the chronic compensatory events which follow it. At the time indicated by the arrow, the simulation was interrupted and right atrial pressure (Block 6) was increased from its normal value of zero mmHg up to 3.5 mmHg. Pressing the calculator's R/S key caused the simulation to resume.

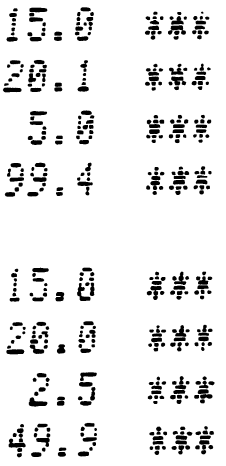

Fig. 4. A portion of the HP-97 printed paper tape with output data. The numbers correspond to the results of two successive iterations which occurred at the time indicated by the arrow in the graph of Figure 3. Reading from the top: E= 15.0, TPR = 20.1, CO = 5.0, and AP = 99.4. This order is repeated in the next iteration.

The simulation shown in Figure 3 took a little longer to achieve a new steady-state than did that of Figure 2. Approximately 60 iterations occurred, taking about 5 minutes to complete the run. During this time about 250 values were recorded automatically by the printer. Rather than being printed automatically, it is possible to have the computations output instead on the calculator's lighted display so that they can be written down by the operator. But this method of recording is not practical when a large amount of data is being generated or very long computation times are anticipated.

The HP-97 printing calculator can easily satisfy the first of Dr. Ingram's arguments about using computers in teaching. I have found it to be highly reliable and very easily transported between home, office or anywhere. The usual airport surveilance magnetometers will not harm the calculator or the programs stored on magnetic cards, but the latter can be accidentally erased if subjected to strong magnetic fields.

Because the HP-97 has a list price of $750 it might not be within everyone's means to acquire it. Another programmable calculator, the model HP-19C, lists for only $225 and has an unusual combination of features. In contrast to the HP-97, the HP-19C is a pocket-sized calculator. It has only about one-half of the programming capacity of the HP-97, but this is sufficient to simulate a model the size of that shown in Figure 1. Other features of the HP-19C include a built-in thermal printer, full range of scientific functions, and a "continuous memory." This latter feature means that the programs are retained in memory indefinitely when the calculator is turned off. Not only are the programs retained, but the contents of the storage and display registers are retained, also. All of these features are found in a surprisingly compact package.

And Hewlett-Packard has just introduced a new calculator which might appeal to many users due to its versatility. The new HP-41C is a pocket-sized programmable with about 300 lines of "continuous" program memory. The memory can be expanded many-fold using separate plug-in memory modules which are available as an accessory. Other accessories are peripheral devices which can be added at any time; these include a magnetic card reader (for pre-recorded programs), a thermal printer, and a unique "wand" which reads printed bar codes similar to those found on food and sundries packages. The manufacturer claims this latter feature makes it fast and easy to load a variety of inexpensive software.

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ELEMENTARY ASPECTS OF IONIC EQUILIBRIA

(A self-instructional package)

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PREFACE

This self-instructional package has been used by medical students and graduate students at the University of Virginia for 4 years and has been revised twice in response to student feedback. It was written because the author found it difficult to efficiently communicate the basics of ionic equilibria in a lecture format. Our students work through this package prior to the scheduled lecture on this subject and then the class time is used for discussion and questions and to present more advanced examples of ionic equilibria in biological systems.

The package deals only briefly with osmotic aspects of the Gibbs-Donnan Equilibrium. The reasons for this are that the package primarily deals with ionic equilibria and not osmosis and that the package is now about the right length for most students to complete in one sitting.

The tone of the package is informal and even "slangy." Our students have responded favorably to the informality, the purpose of which is to enhance the fun of learning and not to patronize the student.

The author would welcome comments from teachers and, especially, students who use this package.

INTRODUCTION

Ions are of great importance in the function of all the cells of the body. Ions are vital in controlling the action of enzymes; divalent ions (Ca^{++}, Mg^{++}) are especially important in this regard. The concentration of Ca^{++} regulates the onset and the intensity of muscle contraction. The distribution of Na^+ and K^+ across the cell membranes of muscle cells results in the resting membrane potential that is vital for the excitability of these cells. The movements of Na^+ and K^+ in response to changing membrane permeabilities causes the action potential. The purpose of this unit is to help you learn about ions in equilibrium across cell membranes and the use of the principles of equilibria. You will understand certain aspects of cellular function in these terms and this will provide a basis for your subsequent study of ion flows across cell membranes.

OVERVIEW AND OBJECTIVES

This package will help you to learn the meaning of ionic equilibria. First you will study the concept of the "electrochemical potential" of an ion and how you can use this concept in understanding the energetics of ion movement. Next you will learn about the Nernst Equation that describes mathematically some consequences of chemical equilibrium. Finally you will consider the Gibbs-Donnan Equilbrium, a cellular equilibrium characterized by certain ions being in equilibrium across the plasma membrane.

Your objectives in using this package are:

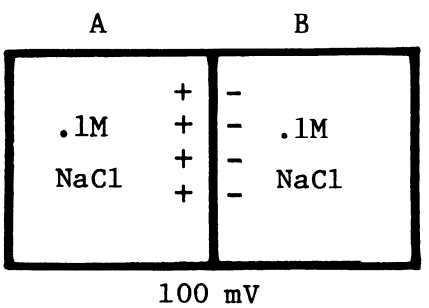
I. You will learn the definition and some of the uses of the concept of the *electrochemical potential* of an ion.
   A. You will remember the equation that *defines* electrochemical potential (μ) of an ion.
   B. You will use the definition of μ to calculate the difference in μ ($\Delta\mu$) of an ion across a membrance.
   C. You will be able to know from the value of $\Delta\mu$ whether energy is required for a given ionic flow or whether energy can be produced by that ionic flow.

II. You will learn the *Nernst Equation* that describes the equilibrium of an ion across a membrane.
   A. You will remember the Nernst Equation
   B. You will be able to recognize different phrases that are synonymous with or that imply that the distribution of an ion on the two sides of a membrane *satisfies the Nernst Equation.*
   C. You will be able to *use* the Nernst Equation to calculate the electrical potential (voltage) difference across a membrane or the ratio of ionic concentrations on the two sides of a membrane for an ion in equilibrium across the membrane.

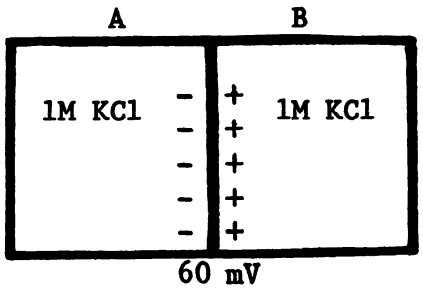
III. You will learn that the *Gibbs-Donnan Equilibrium* involves one ionic species to which the membrane is *impermeable.*
   A. You will be able to calculate the following properties of a Gibbs-Donnan Equilibrium: The final concentrations of all the ionic species involved on both sides of the membrane and the transmembrane electrical potential difference (voltage).

PRACTICE CYCLE #1

INPUT: Earlier you learned that if an uncharged molecule is distributed unequally across a membrane to which it is permeable, the substance will diffuse from the side where it is more concentrated to the side where it is less concentrated. In considering *ions,* however, you also need to know if there is an electrical potential (voltage) difference across the membrane. This is because an ion bears a *charge* and is therefore affected by an electrical field as well as a concentration difference. Consider the situation diagrammed below. There is no difference in the concentrations of NaCl on the two sides of the membrane. Thus no net flow of either Na^+ or Cl^- will occur by the sort of diffusion we discussed previously (due to random thermal motions of the ions). Note, however, that there is a voltage difference (100 millivolts, abbreviated mV) between the two chambers with side A being positive with respect to side B and side B negative with respect to side A. A positive ion (a cation like Na^+) will tend to be repelled from the positively charged chamber and attracted to the negatively charged chamber. A negative ion (an anion like Cl^-) will tend to be repelled from the negatively charged chamber and attracted to the positively charged chamber.



PRACTICE: The diagram below shows two solutions separated by a membrane. There is an electrical potential (or voltage) difference between the two chambers the magnitude and direction of which are indicated in the diagram.



In which direction will K^+ tend to flow due to diffusion?

1. _____A to B,_____B to A,_____no net flow

In which direction will K^+ tend to flow due to the electrical potential difference?

2. _____A to B,_____B to A,_____no net flow

In which direction will Cl^- tend to flow due to the electrical potential difference?

3. _____A to B,_____B to A,_____no net flow

FEEDBACK: Did you check no net flow for Question 1? That is right because in the absence of a concentration difference of K^+ between chambers A and B, no net flow by diffusion will take place.

Did you say that K^+ will tend to flow from B to A due to the electrical potential difference? Good! This is because a positively charged ion will be repelled from the positively charged chamber and attracted to the negatively charged chamber.

The answer to Question 3 is A to B. Since Cl^- has opposite charge to K^+ the force exerted on Cl^- by the electric field will be opposite in direction to that on K^+. In other words, Cl^- will be repelled from the negatively charged chamber and attracted to the positively charged chamber.

PRACTICE CYCLE #2

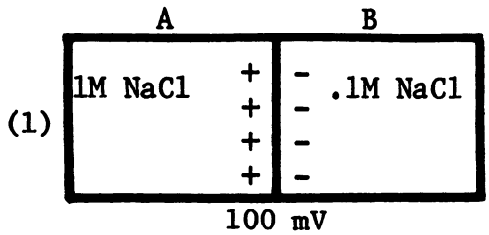
INPUT: In considering ion flow in the presence of a concentration difference for that ion *and* an electrical potential difference, we need to consider both of these factors in deciding which way the ion should flow. If there is a concentration difference tending to cause K^+ to flow from chamber A to chamber B and *also* an electrical potential difference tending to cause K^+ to flow from A to B, these tendencies will be additive and a flow of K^+ from A to B will occur that is larger than that caused by the concentration difference alone or by the electrical potential difference alone. If, on the other hand, the concentration difference of K^+ tends to make K^+ flow A to B, but the electrical potential difference tends to cause K^+ to flow from B to A, then we have opposing tendencies. In order to say whether a net flow of K^+ will occur, and if so, in which direction we need to be able to compare quantitatively the strength of the opposing tendencies (the "concentration force" versus the "electrical force").

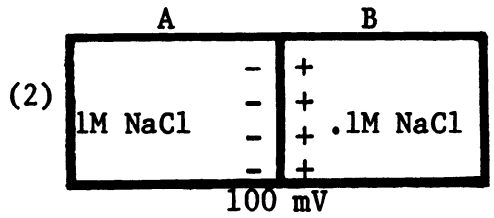
PRACTICE: The diagrams below show two solutions separated by a membrane permeable to Na^+. In each case, can you tell which direction Na^+ will tend to flow?

1) _____A to B,_____B to A,_____can't tell.

2) _____A to B,_____B to A,_____can't tell.

FEEDBACK: Did you check A to B for example 1? Very Good! Clearly the concentration of Na^+ being higher in A makes Na^+ tend to flow from A to B. Note that the excess electronegativity in chamber B also tends to cause Na^+ to flow from A to B because opposite electrical charges attract. If you checked *can't tell* for example 2, you are right! As in 1, the concentration difference tends to make Na^+ flow from A to B. But now the electrical field is reversed, so that this force tends to cause Na^+ to flow from B to A. Not knowing which tendency is larger, you can't tell which direction Na^+ will flow!





PRACTICE CYCLE #3

INPUT: You can see from the last example that we are in need of a way to compare the tendency of an ion to flow due to a difference in *concentration* and the tendency to flow due to an *electrical potential difference.* Since electrical potential difference (ΔE) is measured in volts and concentration difference (ΔC) is measured in moles/liter, it is not clear how you can compare the two tendencies or forces. The fathers of physical chemistry defined a quantity known as the *electrochemical potential of an ion* (μ) that will help you out of your dilemma! μ for an ion, say Na^+, is defined by

$$\mu Na = RT \ln C_{Na} + zFE$$

where R is the gas constant, T is the absolute temperature (in °K), ln C_{Na} is the natural logarithm (log to the base e) of the sodium concentration (C_{Na}), z is the charge number for the ion (+1 for Na^+, -1 for Cl^-, +2 for Ca^{++}, etc.), F is Faraday's number (96,500 coulombs/mole), and E is the electrical potential (for example in volts). Now the *electrochemical potential difference* ($\Delta\mu$) across a membrane is simply the difference between μ on side A and μ on side B.

$$\Delta\mu = \overset{A}{\Delta}Na - \overset{B}{\mu}Na, \text{ so}$$

$$\Delta\mu Na = RT \ln C^A_{Na} + zFE_A - (RT \ln C^B_{Na} + zFE_B)$$

$$= RT (\ln C^A_{Na} - \ln C^B_{Na}) + zF (E_A - E_B)$$

PRACTICE: Remember from your old days in algebra class that $\ln_x - \ln_y = \ln x/y$ and change the last equation for $\Delta\mu Na$ into a nicer form

$$\Delta\mu Na = \_\_\_\_\_$$

FEEDBACK: Did you obtain

$$\Delta\mu Na = RT \ln (C^A_{Na}/C^B_{Na}) + zF (E_A - E_B)?$$

If so, great. If not, it isn't terribly important at this point. What is important is that this last equation tells you exactly how to add up the tendency for Na^+ to flow because of the concentration

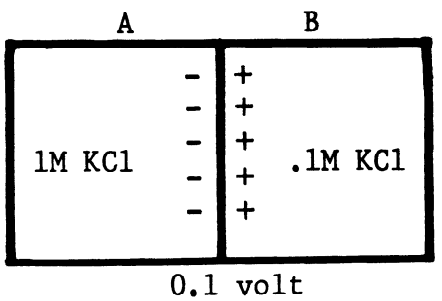
difference (this is the first term on the right hand side) and the tendency for Na^+ to flow due to the electrical force (the second term on the right hand side).

If $\Delta\mu_{Na}$ is positive (this means $\mu^A_{Na} > \mu^B_{Na}$) the net tendency will be for Na^+ to flow from A to B. If $\Delta\mu_{Na}$ is negative ($\mu^B_{Na} > \mu^A_{Na}$), then Na^+ will tend to flow from B to A in the net sense. Net flow will occur from where the electrochemical potential (μ) is higher to where it is lower.

PRACTICE CYCLE #4

INPUT: To put what you just learned into slightly different terms, RT ln C_A/C_B can be thought of as the *"concentration force"* tending to make the ion move from A to B and $zF(E_A-E_B)$ can be regarded as the *"electrical force"* tending to make the ion flow from A to B. If either term turns out to have a negative value, this tells you it really makes the ion tend to flow from B to A. Thus both the magnitude and direction of each "force" is given. If the "concentration force" and the "electrical force" are equal in magnitude, but opposite in sign, $\Delta\mu = 0$. This is interpreted as meaning that the concentration force and the electrical force are equal and opposite, so that the net force on the ion is zero. $\Delta\mu = 0$ means the ion has no overall tendency to flow in either direction.

PRACTICE: Given the situations described in the sketch below, let's plug in the numbers we know into the equation defining $\Delta\mu_K$.



$$\Delta\mu_K = RT\ln(C^A_K/C^B_K) + zF(E_A - E_B)$$

$z = +1$ for K^+. Since side A is electrically *negative* with respect to side B, $E_A - E_B$ must be a *negative* number.

So

$$\Delta\mu_K = RT \ln (1/.1) + F(-0.1)$$

(Recall that ln x is positive if $x > 1$.)

1. Use the signs of the terms in the $\Delta\mu_K$ equation to tell which way the "concentration force" and the "electrical force" tend to make K^+ flow.

a) "concentration force": ____A to B, ____B to A, ____no force

b) "electrical force": ____A to B, ____B to A, ____no force

2. If you knew how to calculate the magnitude of each term how would you decide the *direction* of net K^+ flow?

FEEDBACK: 1) Did you say a) "conc. force": A to B and b) "elec. force": B to A? That's super! Note that this result coincides with the result you obtained in Practice Cycle #2 by using more ordinary reasoning. If you missed this one, here is how you might have gotten the right answer:

a) "conc. force" = $RT \ln C^A_K/C^B_K = RT \ln 10$. R,T, ln 10 are all positive numbers. Thus "conc. force" must be positive and thus denotes A to B tendency.

b) "electr. force" = $z_K F(E_A - E_B) = (+1)F(E_A-E_B)$. F is positive, $E_A - E_B = -0.1v$ so that "electr. force" is negative and thus denotes B to A tendency.

2) If you knew how to calculate the magnitude of each term, you could decide whether $\Delta\mu$ is positive (A to B flow), negative (B to A flow) or zero (no net flow). If you got *either* of these correct, you're doing well!

PRACTICE CYCLE #5

INPUT: The last example showed you that in order to tell the direction of net ion movement you need to be able to calculate the magnitudes of the "conc. force" and the "electr. force," as well as their direction. You shall *soon* develop that computational ability. It is worthwhile for you to learn to do this for another reason. If $\Delta\mu_K$ is positive, this means that K^+ will tend to flow spontaneously from A to B, if you want to force K^+ to flow the other direction you must do work on the K^+ ions! As you will see soon *the units of $\Delta\mu$ are energy/mole* and $\Delta\mu$ represents the amount of work you must do to move 1 mole of K^+ ions against the tendency to flow from A to B spontaneously. If we allow K^+ to flow according to the forces acting on it and it flows from A to B (since $\Delta\mu_K$ is positive) it is theoretically possible to harness the energy lost by the K^+ ions in flowing from higher to lower μ to do some other sort of work!

Since the dimensions of $\Delta\mu$ are energy/mole any of the various energy units can be used. Most commonly, however, μ is expressed as calorie/mole or joule/mole. We will use joule/mole in this package since these units are most convenient for our purposes.

$$\Delta\mu = RT \ln(C_A/C_B) + zF(E_A - E_B)$$

We will see that with the proper units for the various quantities in this expression, the "concentration force" [$RT \ln(C_A/C_B)$] and the "electrical force" [$zF(E_A - E_B)$] both come out in units of joule/mole and thus can be added and subtracted.

Considering first the "concentration force" recall that R = 8.3 joule/mole °K and T(°K) = 273 + °C. RT thus is in terms of joule/mole. Since $\ln(C_A/C_B)$ is dimensionless, the whole "concentration force" term has units of joule/mole.

Now look at the "electrical force" term. F is the number of coulombs of charge on a *mole* of univalent ions and z is the charge number of the ion in question. Then zF is the number of coulombs of charge per mole of the ion in question. The units of $(E_A - E_B)$ are volts. Thus the units of the "electrical force" term are coulomb · volt/mole. You may not recall from college physics that coulomb x volt = joule. Having been reminded of this you can see that the units of $zF(E_A - E_B)$ are joule/mole as well when E is expressed in volts.

Now that we know that (with R in joule/mole °K and E in volt) the "concentration force" and the "electrical force" both have units of joule/mole, we know that it is kosher to compare their magnitudes directly to determine which way an ion will flow in the net sense.

Before proceeding to a computational example, let's make things a bit easier for ourselves. With our decimal number system it is often more convenient to work with log (logarithm to the base 10) rather than ln (logarithm to the base e). (A table of logarithms to the base 10 is provided just before the Post-test.) Recall that $\ln x = 2.3 \log x$. Recasting the expression for $\Delta\mu$ now gives

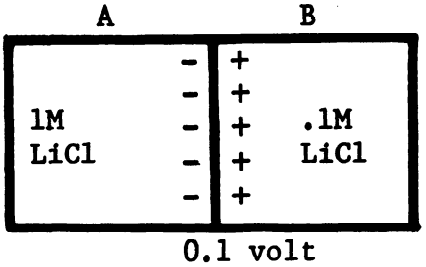
$$\Delta\mu = 2.3\ RT \log (C_A/C_B) + zF(E_A - E_B)$$

Now let's put all this stuff to work!

PRACTICE: For the example shown below calculate the magnitude and the sign of $\Delta\mu$. R = 8.3 joule/mole.

When Li^+ flows from A to B.

_____work is required_____we can *obtain* work.



FEEDBACK: Since the "concentration force" and the "electrical force" are oppositely directed, you cannot answer the question before you compute $\Delta\mu$. Did you determine that work is required to move Li^+ from A to B? If so, you should be pleased. If not, consider the following

$$\Delta\mu_{Li} = 2.3\ RT \log (C^A_{Li}/C^B_{Li}) + zF(E_A - E_B)$$

Note that since side A is *negative* with respect to B, $E_A - E_B$ is negative.

Putting in numbers

$$\Delta\mu_{Li}\ (2.3)(8.3)(300) \log 10 + (1)(96{,}500)(-0.1)$$

$$= 5727 \text{ joule/mole} - 9650 \text{ joule/mole}$$

"conc. force" "electr. force"

$$= -3923 \text{ joule/mole}$$

Now you can get the answer to whether or not energy is required to move Li^+ from side A to side B in one of two ways:

1. $\Delta\mu^A_{Li} = \mu^A_{Li} - \mu^B_{Li}$ is *negative.* This means that μ^B_{Li} is larger than μ^A_{Li}. So Li^+ will flow spontaneously from B to A. Thus to make Li^+ flow from A to B we must do work.
2. The "conc. force" tends to cause Li^+ to flow from A to B. The "electr. force" tends to cause Li^+ from B to A. The "electr. force" is greater in magnitude than the "conc. force." Thus Li^+ will flow spontaneously frome B to A. Thus to cause Li^+ to flow from A to B requires that work be done. Note that the amount of work required to cause 1 mole of Li^+ to flow from A to B is 3923 joules.

PRACTICE CYCLE #6

INPUT: Remember I promised you would learn something about ionic equilibrium? With what you just learned as background, this will be a snap. For an ion to be in equilibrium across a membrane, $\Delta\mu$ across the membrane must be zero. This will happen when the "conc. force" and the "electr. force" on the ion are equal and opposite, so that the net force on the ion is zero. Under such conditions there will be no net flux of the ion.

$\Delta\mu = 0 = RT \ln(C_A/C_B) + zF(E_A - E_B)$ leads to (algebra)

$[E_A - E_A] = -(RT/zF) \ln(C_A/C_B) = (RT/zF) \ln(C_B/C_A)]$

(Remember that - ln x/y = ln y/x)

This is the *Nernst Equation,* named after the great German physical chemist Nernst. *Please note that it is neither more nor less than a statement of electrochemical equilibrium ($\Delta\mu = 0$). This equation holds only if equilibrium exists for the ion in question.*

PRACTICE:

Statement: The distribution of X^- across the membrane "satisfies" or is consistent with the Nernst Equation. Please check the statements below which are synonymous with or implied by that statement.

1. _____we do not know which direction X^- will flow
2. _____X^- will show no net flow
3. _____$\Delta\mu_X$ is positive
4. _____$\Delta\mu_X$ is negative
5. _____$\Delta\mu_X = 0$
6. _____There is no transmembrance voltage
7. _____There is no "conc. force" on X^-
8. _____The "conc. force" is equal and opposite to the "electr. force" on X^-
9. _____X^- will flow from high μ to low μ
10. _____The flow of X^- will obey Fick's First Law.

FEEDBACK: Did you check 2, 5, and 8? Good! $\Delta\mu_X = 0$ (answer 5) is the definition of equilibrium. Since the statement said the Nernst Equation is satisified, you know you are dealing with an equilibrium situation. An ion at equilibrium has no net force on it: so that "conc. force" + "electr. force" = 0 as you said for answer 8. With no net force there will be no net flow (answer 2). The other answers are either ruled out by the correctness of 2, 5, and 8, or have nothing to do with the original statement. Wonderful? Now, you will get to see what the Nernst Equation is really good for!

PRACTICE CYCLE #7

INPUT: Since the Nernst Equation, you just told me, is a statment of the fact that the "concentration force" is equal and opposite to the "electrical force," I know that you know you can use the Nernst Equation as written

$$E_B - E_B = RT/zF \ln(C_B/C_A) = (2.3RT/zF) \log(C_B/C_A)$$

to calculate the value that the *transmembrane voltage must have in order to just balance the concentration force* that is caused by the difference between C_A and C_B.

You can also turn Nernst on his ear, thusly

$$\log(C_B/C_A) = (zF/2.3RT)(E_A - E_B)$$

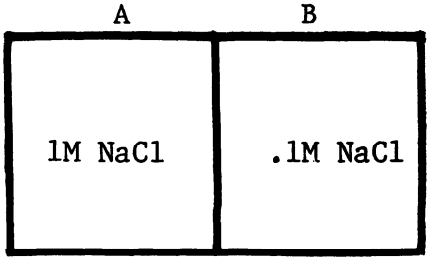
Now you see if we know $E_A - E_B$, we can calculate the *concentration ratio* C_B/C_A that will set up a "conc. force" just equal and opposite to the "electr. force" created by $E_A - E_B$.

To make things a bit easier, you should know that 2.303RT/F at room temperature (25°C) equals about 60 mV (.06 v). So at room temperature

$$\boxed{E_A - E_B \doteq (60 \text{ mV}/z) \log_{10}(C_B/C_A)}$$

Let's consider two examples. In the situation diagrammed below, what potential difference must exist between A and B in order that Na+ will be in equilibrium (the "electrical force" must be equal and opposite to the "concentration force").

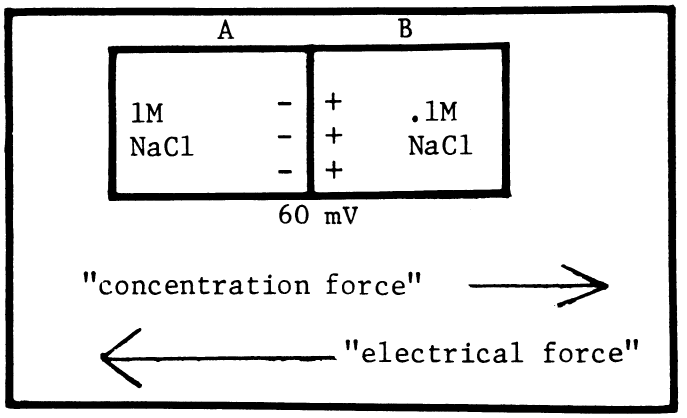
Since equilibrium is to exist, the Nernst Equation is applicable



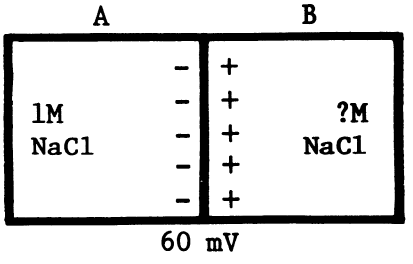
$$E_A - E_B = \frac{60mV}{z_{Na}} \log \frac{C^B_{Na}}{C^A_{Na}} = \frac{60mV}{+1} \log \frac{.1}{1}$$

$$= 60mV \log \frac{1}{10} = -60mV \log 10 = -60mV$$

This says that $E_A - E_B$ is *minus* 60 mV. Thus A is *negative* relative to B. Check this out with reference to the diagram below. The "conc. force" tends to cause Na^+ to flow from A to B, so if equilibrium is to exist the "electr. force" must cause Na^+ to flow from B to A. If A is negative relative to B, Na^+ will be attracted to A and repelled by B, so flow due to the "electrical force" will tend to occur from B to A as required. You see that in using the Nernst Equation you get the correct sign for $E_A - E_B$ (if you do the algebra right). But you can also obtain the correct sign for $E_A - E_B$ from the sort of reasoning we just applied.



Now let's use the Nernst Equation to find the *equilibrium concentration* of an ion. In the example below, what will be the



equilibrium concentration of Cl^- in chamber B? Solving the Nernst Equation for log C_B/C_A we obtain

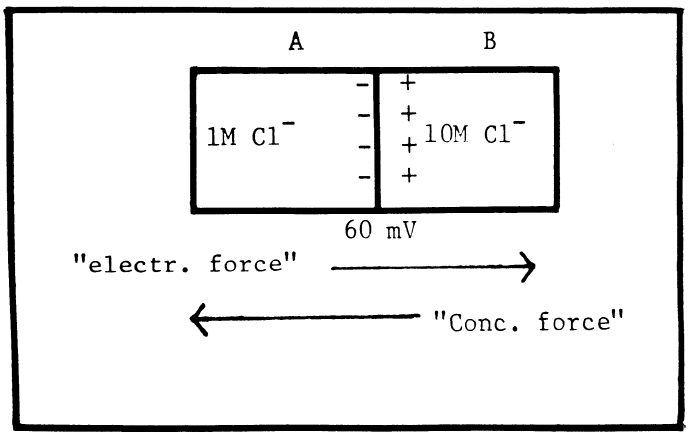
$$\log C^B_{Cl} / C^A_{Cl} = z_{Cl} (E_A - E_B)/60mV$$

$$= -1(-60mV)/60mV = +1$$

So $\log C^B_{Cl}/C^A_{Cl} = 1$, taking the antilog of both sides we get

$C^B_{Cl}/C^A_{Cl} = 10$

Since $C^A_{Cl} = 1M$, $C^B_{Cl} = 10M$. Let's see if this makes sense. Since side A is negative with respect to B and since Cl^- bears a negative charge, the "electr. force" will tend to cause Cl^- to flow from A to B. Thus for equilibrium to exist the "concentration force" must tend to cause Cl^- to flow from B to A. That is C^B_{Cl} must be greater than C^A_{Cl}, as we found. By now you probably have got the message that a 60 mV potential difference is just sufficient to balance a 10 fold concentration difference of a univalent ion, and vice versa, provided the "electr. force" and "conc. force" are in opposite directions.



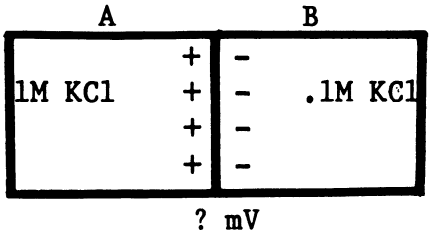
PRACTICE: Refer to the sketches below:

1) Calculate $E_A - E_B$ if Cl^- is in equilibrium across the membrane.

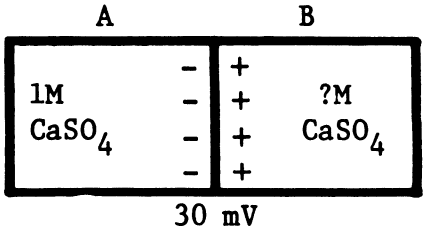
_____

2) Compute Ca^{++} conc. on side B if Ca^{++} is in equilibrium across the membrane. _____

(1)



(2)



FEEDBACK: Did you get +60 mV for 1) and 0.1M for 2)? Wow! If not, here's how you might have done it:

1) $E_A - E_B = (60mV/z) \log C_B/C_A$

$= (60mV/-1) \log .1/1 = -60mV \log 1/10 = 60mV \log 10/1$

$= 60mV$ (Since this is positive, A is positive with respect to B)

2) $\log C_B/C_A = (z/60)(E_A - E_B)$

$= (2/60)(-30) = -1$

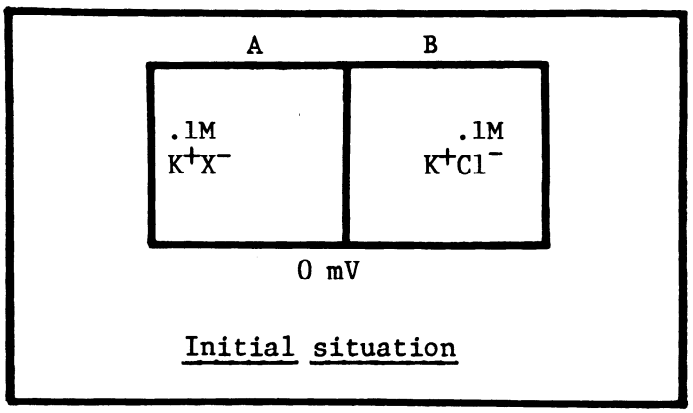
so $\log C_A/C_B = 1$, and $C_A/C_B = 10$

Since $C_A = 1M$, $C_B = 0.1M$

PRACTICE CYCLE #8

INPUT: You have worked hard to get to this point in the package, right? What for? You are now in a position to learn about the Gibbs-Donnan Equilibrium. This is a special sort of ionic equilibrium that obtains when one of the ions involved cannot cross the membrane separating A from B because the membrane is impermeable to that ion, but is permeable to water and the other ions in the system. Consider the situation shown below. The membrane has the properties just described and X^- is the impermeable ion. There is no electrical force just yet. X^- cannot

flow, K^+ has equal concentration in A and B and thus won't flow. Cl^- has greater concentration in B than A and thus will flow from B to A. This results in transferring negative charges from B to A, so that a transmembrane potential (A negative with respect to B) will be set up. Cl^- will flow until this electrical potential results in an "electr. force" that is opposite in direction to the "conc. force."



PRACTICE:

1. Will the flow of Cl^- ever stop?_____yes,_____no
2. When_____(what will characterize the condition under which net Cl^- flow will stop, if it will stop).

FEEDBACK: Did you answer: 1) yes and 2) when $E_A - E_B \doteq (60mV/-1) \log_{10} C_B/C_A$ (or some equivalent statement). If you got these both you should be pleased with yourself! 1) Since as Cl^- flows a countervailing "electr. force" builds up progressively and the "conc. force" progressively diminishes, the forces will ultimately balance. 2) When the "electr. force" is equal and opposite to the "conc. force" the flow of Cl^- will stop. This is expressed by the Nernst Equation

$$E_A - E_B = (60mV/-1) \log (C^B_{Cl} / C^A_{Cl})$$

PRACTICE CYCLE #9

INPUT: Remember that $E_A - E_B$ (A negative) that built up as Cl^- flowed from B to A in the last example. Consider what that voltage will do to K^+. It will create an "electr. force" to move K^+ also from B to A and there is initially no "conc. force" to oppose this "electr. force." Note that as K^+ flows, an oppositely-directed "conc. force" will build up. So that it appears that K^+ must ultimately stop flowing too! There is one more principle that will help us to deal with this situation: The Principle of Electroneutrality. This principle says we cannot separate charges across the membrane. However many Cl^- ions flow from B to A, the same number of K^+ ions must flow from B to A as well. (In reality the numbers of ions that flow may be slightly different, but it will be on a scale that is chemically insignificant. For example the degree of separation of charge across a nerve cell membrane is of the order of 10^{-12}M, while ionic concentrations are at least 10^{-3}M). Now you can use the knowledge that the ionic flows of Cl^- and K^+ are equal, plus the knowledge that *both* must ultimately attain equilibrium to learn more about this situation. Now if both K^+ Cl^- must attain equilibrium, then at equilibrium *both* of these ions must satisfy the Nernst Equation or equivalently $\Delta\mu = 0$ for each ion.

For K^+ at equilibrium: $E_A - E_B = (60mV/1) \log (C^B_K/C^A_K)$

For Cl^- at equilibrium: $E_A - E_B = (60mV/-1) \log(C^B_{Cl}/C^A_{Cl})$

PRACTICE: Use the fact that both Cl^- and K^+ attain equilibrium, so that both must satisfy the Nernst Equation to derive a relationship among the concentrations of Cl^- and $K+$ in A and B at equilibrium.

FEEDBACK: If you got $C^A_K\ C^A_{Cl} = C^B_K\ C^B_{Cl}$, you are correct!

Here's how:

K^+ satisfies Nernst $=> E_A - E_B = (60mV/1) \log (C^B_K/C^A_K)$

Cl^- satifies Nernst $=> E_A - E_B = (60mV/-1) \log (C^B_{Cl}/C^A_{Cl})$

$= (60mV \log (C^A_{Cl}/C^B_{Cl})$

Now there can only be one value of $E_A - E_B$ at equilibrium. Thus these two expressions must be equal:

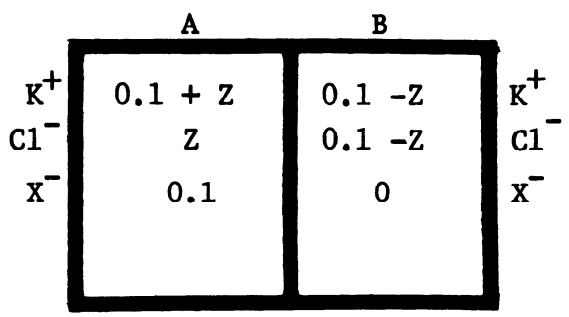
$60mV \log (C^B_K/C^A_K) = 60mV \log (C^A_{Cl}/C^B_{Cl}) => C^B_K/C^A_K = C^A_{Cl}/C^B_{Cl}$

cross multiplying $=> C^A_K\ C^A_{Cl} = C^B_K\ C^B_{Cl}$. This is called the *Donnan Relation.*

PRACTICE CYCLE #10

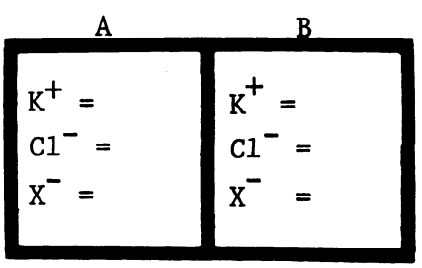
INPUT: You can now use your new friend the a) Donnan Relation plus your old buddy the b) Electroneutrality Principle to really define the equilibrium situation.

If you assume that A and B have equal volumes and that the flow of Cl^- from B to A reduces the concentration of Cl^- in B by Z, then the concentration of Cl^- in A must increase by Z. *Electroneutrality* says the *same* amount of $K+$ must flow from B to A so that the changes in concentration of $K+$ in B and A are the same. See the diagram to the right. Now, you also know that these equilibrium concentrations of $K+$ and Cl^- must also obey the *Donnan Relation.*



PRACTICE: Set up the *Donnan Relation* and find out the final equilibrium concentrations of $K+$ and Cl^- in A and B.

Z = ?



FEEDBACK: Did you get the Donnan Relation to look like

(0.1 + Z) (Z) = (0.1 - Z) (0.1 -Z)?

If you remembered how to solve a quadratic equation, you got Z = 0.03333..... Using this value for Z and the top diagram we obtain:

	A	B
K^+	0.133...	0.0666...
Cl^-	0.033...	0.0666...
X^-	0.1	0

Thus using the two things you learned, namely the Donnan Relation and Electroneutrality Principle, you were able to find the equilibrium concentrations of all the ions involved in this Gibbs-Donnan situation!

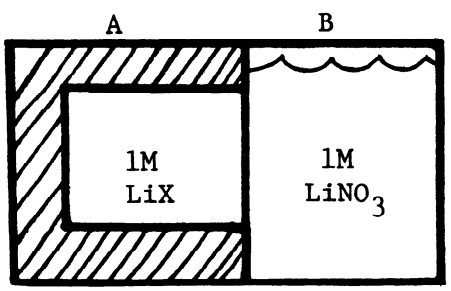
You should note one more aspect of the Gibbs-Donnan "Equilibrium." While the permeable ions have come to equilibrium, water has not. Note in the last table that the total concentration of ions on side A is 0.16666... compared with only 0.1333.. in B. Besides, there is 0.1 M X^- on side A and none on side B. Thus the total concentration of osmotically active solutes is greater on side A than on side B. Water will tend to flow from B to A unless it is restrained, for example by making the chambers airtight and incompressible or by providing a pressure on chamber A to just counterbalance the osmotic imbalance.

PRACTICE CYCLE FOR *OVERALL* OBJECTIVE

INPUT: I believe you can see now that understanding the Gibbs-Donnan Equilibrium involves *most* of the principles we have learned. If you can put all of this together at once, you can feel that you have really mastered the basics of ionic equilibria. In the practice below try as much as possible to work with first principles in mind (to refresh your mind about these principles).

PRACTICE: The membrane is permeable to everything but X^-. We have just filled A and B with the solutions shown. Chamber A (and the membrane) are *rigid*. 1) Calculate the final concentrations of all species.

2) Calculate $E_A - E_B$



FEEDBACK: 1) Did you obtain these results? Great!

	A	B
Li^+	1.333...	0.666...
NO_3^-	0.333...	0.666
X^-	1.0	0

2) Did you get $E_A - E_B$ = -18mV? Fine!

If you got all of these, you should be pleased.

1) Here's showing you how: Let y be the NO_3^- concentration change.

$$(1 + y)(y) = (1 - y)^2 \Rightarrow y = .3333$$

This allows us to compute all ion concentrations:

	A	B
Li^+	1 + y	1 - y
NO_3^-	y	1 - y
X^-	1	0

Both NO_3^- and Li^+ satisfy the Nernst Equation, so

2) You may use either to get

$E_A - E_B = 60mV/+1 \log_{10}(.6666/1.3333) = -60mV \log_{10}2 = -18mV$

Table of logarithms to the base 10

Number	log
0.01	-2
0.1	-1
1	0
2	0.3
3	0.48
4	0.6
5	0.7
6	0.78
7	0.85
8	0.9
9	0.95
10	1
100	2
1000	3

POST-TEST

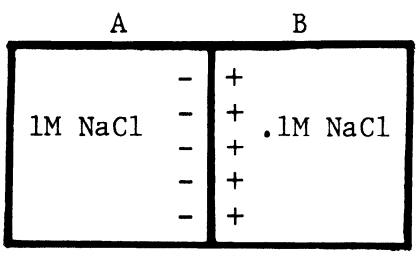
1. Write down the equation that defines *the electrochemical potential of the ion* X^-. Label the "concentration term" and the "electrical term".
2. Chambers A and B are separated by a membrane permeable to Na^+ and Cl^-. The chambers contain the concentrations of Na^+ and Cl^- shown and $E_A - E_B$ is as indicated below. *Calculate* $\Delta\mu_{Na}$ and $\Delta\mu_{Cl}$ across the membrane in units of joule/mole.

   R = 8.3 joules/°K-mole
   T = 303°K

   $$\ln y = 2.3 \log_{10} y$$

   F = 96,500 coul/mole

   coul x volt = joule

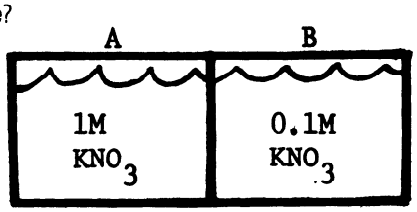


3. Given the situation in problem 2, is energy required to cause Cl^- to move from B to A or can energy be obtained when Cl^- flows from B to A?
4. Na^+ is in equilibrium across a membrane. The electrochemical potential of Na^+ on one side is 2700 joule/mole. Calculate the electrochemical potential of Na^+ on the other side.
5. Write down the Nernst Equation.

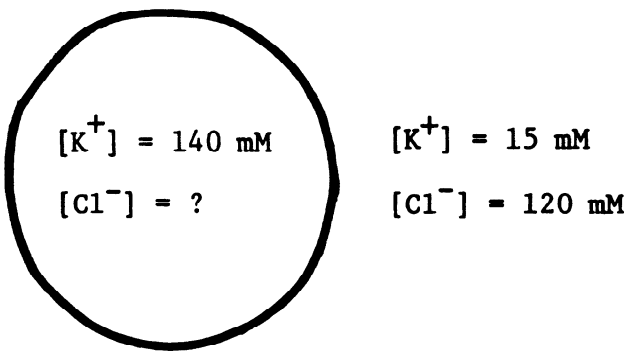
6. Check the statements below that follow from the statement:
X^- satisfies the Nernst Equation

___ a. X^- may or may not be in equilibrium
___ b. X^- is in equilibrium
___ c. there is no net force on X^-
___ d. μ_X on one side = μ_X on the other
___ e. The "electr. force" on X^- is equal and opposite to the "conc. force"
___ f. there is neither a conc. gradient X^-, nor is there a voltage across membrane
___ g. no net flow of X^- will occur
___ h. X^- may tend to flow in either direction spontaneously
___ i. The flow of X^- will follow Fick's First Law
___ j. X will flow down its electrochemical potential gradient.

7. Chambers A and B are separated by a membrane, as shown below. If K^+ is in equilibrium across the membrane, what is the value of $E_A - E_B$ (get correct sign). Which side is positive?

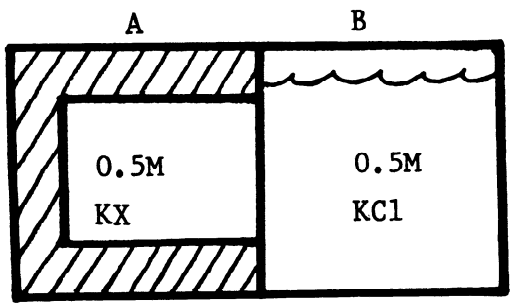


8. K^+ is in equilibrium across the membrane of the cell shown below. If Cl^- is also in equilibrium, what is the intracellular chloride concentration?



9. A membrane permeable to K^+, Cl^-, and H_2O separates chambers A and B. The membrane is impermeable to X^-. We place solutions of the indicated composition in A and B. Chamber A and the membrane are rigid. *At equilibrium* what will be

a. The concentrations of all ionic species in A and B?



membrane and the walls of chamber A are strong and rigid

b. The transmembrane voltage, $E_A - E_B$?

c. Will a hydrostatic pressure exist in A at equilibrium that exceeds the pressure in B?

10. Did you find this material interesting?

11. Do you believe this material will help you to understand cellular physiology?

POST TEST ANSWERS

1. $\mu^x = RT \ln C^x + ZFE$
2. $\Delta\mu_{Na}$ = 0
   $\Delta\mu_{Cl}$ = 11, 574 joule/mole
3. ✓ energy required, ___ no energy required
4. 2700 joule/mole
5. $E_A - E_B = (RT/ZF)\ln(C_B/C_A)$ (or equil. form)
6. ___a ✓c ✓e ✓g ___i
   ___✓b ✓d ___f ___h ___j
7. $E_A - E_B$ = -60MV ___A is positive ✓B is postive
8. 12.86 mM intracellular Cl^-
9.

	A	B
a. K^+	0.666...	0.333...
Cl^-	0.166...	0.333...
X^-	0.5	0

   b. $E_A - E_B$ = -18mV (be sure to include sign)
   c. yes
10. ✓yes, ___no
11. ✓yes, ___no

ENDOGENOUS PYROGEN PHYSIOLOGY*

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The physiological mechanisms by which fever is produced in man and experimental animals have, for many years, intrigued medical practitioners and basic physiologists. Body tissue do not normally contain transferable fever-producing substances. If, however, phagocytic cells are activated by certain stimuli, they may synthesize pyrogenic factors of endogenous origin. First recognized about three decades ago, these endogenous substances were found to initiate the onset of fever if injected into a suitable assay animal (1-5). A variety of factors are produced and released from circulating leukocytes or tissue macrophages when these cells are stimulated either by pyrogenic substances or by engaging in phagocytic activity. Although initially called granulocytic or neutrophilic pyrogen, the fever-producing factors of cellular origin are now generally known as endogenous pyrogen, or EP.

The entire field of body temperature regulation has been stimulated by the recent discovery that many cold-blooded animal species increase their internal body temperatures as a purposeful response to an experimental inoculation of pathogenic bacteria (3-5). Cold-blooded animals (and some infant mammals) increase their internal temperature by moving to a warmer environment. This for of "behavioral" fever is analogous to the development of clinical fever during the course of infectious or inflammatory processes in man.

These exciting discoveries and the additional demonstrations that fever may be of benefit in terms of host survival have led to a renewed interest in fever and its underlying mechanisms. This interest is evidenced, in part, by the fact that the American Physiological Society has sponsored two recent symposia on this topic (4-5).

Hormone-Like Role of EP

It is now widely accepted that a variety of infectious microorganisms or inert substances are able to "turn on" or activate certain pyrogen-producing body cells, stimulating them to release EP. This mediating substance then moves via the blood stream to initiate the onset of fever through its ability to stimulate hypothalamic temperature-regulating centers. As depicted in Figure 1, this entire system meets the concept of a hormone-like control mechanism. The individual pyrogen-producing cells are analogous to the cells in endocrine glands which release well known hormones. EP in turn produces its effect on a distant target tissue, i.e., certain neurons within the central nervous system. EP is believed to alter the "set point" of a thermostat-like control mechanism located in temperature-regulating areas of the anterior hypothalamus. This stimulus promptly initiates complex physiological responses mediated via efferent neural pathways to peripheral skeletal muscles and blood vessels. Dermal vasoconstriction and muscular shivering occur as a consequence, leading to an increase in the production and retention of heat within the body. Hormonal responses may also be involved.

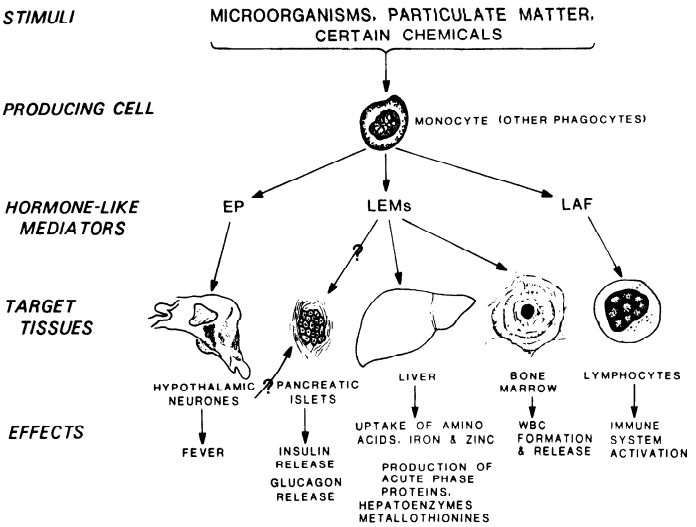

Fig. 1 Diagrammatic concept of the interrelationship between the many possible forms of endogenous mediators released from monocytes or other phagocytic cells following their activation. A multiplicity of responses in target tissues are initiated by EP, LEM, and LAF (See text).

The Molecular Nature of EP

Despite much effort by many laboratories during the past three decades, no one is yet able to provide an exact structural formula for this important mediator. Rather, much of the available information about EP has been derived by exclusion. EP is generally thought to be a small protein with a molecular weight of 13,000 to 15,000 daltons. Pyrogenic EP species with larger molecular weights have been identified and it is postulated that some EP may circulate as a dimer or a trimer. Various attempts to concentrate and purify EP have shown that as little as 30-50 ng of purified EP can produce 1.0°C fever in a test rabbit. However, pyrogenic fractions have been purified to the point that they no longer exhibit a chemical reaction for protein, and it is therefore possible that EP may contain carbohydrate or lipid components.

EP is thought to have three sulfhydryl groups and it can be inactivated by heat or high pH. The febrile effects of EP are not species-specific. EP does not produce tolerance in the manner of bacterial endotoxin and the molecule is poorly immunogenic.

Assay of EP

All studies of EP are complicated by the need to quantitate the activity of this substance with relatively crude bioassay procedures. Traditionally, this has been done using rabbits carefully selected for their propensity to develop a reproducible febrile response pattern when they are tested. This form of bioassay requires relatively large amounts of pyrogen and the assay alone can consume major portions of any product emerging from fractionation and purification procedures.

Mice may be employed as bioassay animals (4) and a procedure for cannulating the lateral ventricle of the brain of rats for bioassay purposes has been described (6). Both the mouse and the chronically cannulated rat require far smaller quantities of EP

* Tutorial Lecture presented at the 1979 Fall Meeting in New Orleans.

than rabbits to produce a satisfactory assay. Bioassay systems are difficult to use, must be carefully standardized, and require sufficient numbers of test animals to be statistically valid. Bioassays are also susceptible to the contamination of any test sample by ubiquitous bacterial endotoxins. Endotoxin must be excluded with great care from any crude or purified preparation of EP that requires testing.

An alternative radioimmunoassay procedure has been described (7) but is of limited availability because of the great difficulty in producing highly purified EP and specific high-titer anti-EP immunoglobulin.

Cellular Production of EP

Only certain types of body cells are capable of producing and secreting EP. The EP-producing cells of healthy normal subjects or experimental animals have the capacity for phagocytizing particulate matter and all are thought to be of bone marrow origin. None of these cells are of the lymphoid series.

The EP-producing cells that normally circulate within the blood stream include neutrophils, eosinophils, and monocytes. The EP-producing cells usually located within tissues include macrophages, Kupffer cells, and other cells of the reticuloendothelial system. Several varieties of cultured tumor cells spontaneously produce EP *in vitro*. Tumor cell lines presently known to produce EP include cultured human histiocytic lymphoma cells, Hodgkins disease cells and renal carcinoma cells, and the mouse histiocytic and myelomonocytic tumor cell lines.

Table 1 lists a large variety of pyrogenic substances (including both living organisms and nonviable substances) known to stimulate the release of EP from phagocytic cells. Viable or killed microorganisms can generally initiate cellular EP production and release by stimulating an initial episode of phagocytic activity. In addition, many nonviable substances can also activate cellular EP-producing and -releasing mechanisms when studied under *in vitro* conditions that do not require phagocytosis. The molecular mechanisms leading to a physiological activation of EP-producing cells remain unclear. However, these mechanisms may involve some interaction between a stimulating substance and a receptor on the exterior surface membrane of EP-secreting cells. As shown in Table 2, the production and release of EP is influenced by the source and type of producing cell as well as by the conditions used for *in vitro* production.

Table 1. Pyrogens that stimulate EP release.

A. *Living Organisms*
- Viruses
- Bacteria
- Fungi
- Plasmodia
- Other Microorganisms

B. *Nonviable Substances*
- Bacterial endotoxins
- Bacterial exotoxins
- Pyrogenic steroids
- Lymphokines
- Poly I:Poly C. Other polynucleotides
- Antigen-antibody complexes
- Antigens that stimulate delayed dermal hypersensitivity
- Particulate matter
- Bleomycin
- Colchicine
- Muramyl dipeptide
- Nonorganic substances

Table 2. Cellular EP Production

Cell Source	Cell Activation	EP Production	EP Release
Peripheral Blood	None occurs in vivo	Requires energy expenditure Blocked by fluoride	Delayed several hours
	Required in vitro	Requires protein synthesis Blocked by actinomycin Blocked by puromycin Confirmed by tagged amino acid incorporation	Prolonged, 4-12 hours
Sterile Exudates	Occurs in vivo	Occurs in vivo	Spontaneous but brief
		Protein synthesis not required in vitro	Optimal in 0.9% saline
			Inhibited by: K^+ and Ca^{++} ions -SH group inhibitors
Cultured Tumors	None required	Spontaneous	Spontaneous
		Continuous	Continuous
		Prolonged	Prolonged

Early studies generally dealt with EP species released *in vitro* from already-activated cells contained in sterile exudates. Activated human cells can be obtained from sterile exudate fluids found in some acutely inflamed joints. In laboratory animals, exudate cells can come from subcutaneous sterile abscesses previously induced by phlogistic agents or from peritoneal cavity exudates induced by an earlier intraperitoneal injection of an irritant, such as 2% shellfish glycogen solutions. The latter method has generally been used in rabbits to obtain the largest quantities of pyrogen-producing cells.

Exudate cells are activated during their accumulation *in vivo* and are probably releasing EP at the time they are collected. If placed in sterile physiological saline, these cells release EP spontaneously and promptly, but for a period of only several hours. Peritoneal exudate cells show no requirement for protein synthesis following their collection, although EP synthesis undoubtedly takes place within the exudate cells while they are being mobilized *in vivo.*

The *in vitro* release of EP from sterile exudate cells is maximized by holding them in physiological saline at 37°C, but is inhibited if $K+$ or $Ca++$ are added to the media. EP release may be a regulated phenomena involving the exterior cellular membrane. This is suggested by the reversal of $K+$ inhibition which is observed following the addition of ouabain as well as $K+$ to the incubation medium.

A different set of circumstances holds if white blood cells are obtained from whole blood and then studied *in vitro.* Circulating blood leukocytes are not activated *in vivo* and demonstrate no spontaneous *in vitro* release of EP. When whole blood neutrophils, eosinophils, or monocytes are studied, they must first be activated by inducing them to engage in phagocytic activity or by stimulating them with endotoxin. In contrast to sterile exudate cells, EP-producing cells obtained from whole blood require an initial period of protein synthesis after the cells are activated. This protein synthesis can be blocked by puromycin or actinomycin. Production of EP can also be blocked by inhibiting cellular energy expenditure with fluoride. The occurrence of *in vitro* protein synthesis has been confirmed by using radioactively tagged amino acids which are incorporated into EP prior to its release.

Studies with whole blood leukocytes are of special value, for the molecular processes required for EP production can be differentiated from those governing EP release. Unlike the findings in sterile exudate cells, the release of EP from whole blood leukocytes occurs over a prolonged period. Release does not begin until several hours after *in vitro* activation and then it continues for almost a day. In contrast to its synthesis, EP release

from whole blood leukocytes appears to be independent of energy expenditure, since it is not blocked by fluoride.

In combination, these data suggest that circulating white blood cells do not contain stored EP. This concept is in keeping with earlier studies which consistently failed to demonstrate the presence of preformed transferrable pyrogenic substances in these cells. Thus, the production of EP within circulating leukocytes requires the conventional molecular mechanisms for synthesizing new protein, including the expenditure of cellular energy, the nuclear transcription of genetic information and the *de novo* synthesis of protein by ribosomes.

Few details are yet known about the molecular aspects of EP production in cultured tumor cells. Since pyrogen output by the tumor cells is spontaneous, does not require activation, and occurs continuously for prolonged periods of time, it has been speculated that a genome which controls EP production remains unrepressed and operates continuously. There are no reports of specific comparisons among the pyrogens produced by the different tumor cell lines.

Since the capacity for synthesizing new protein molecules is known to differ among various EP-producing cells, it is reasonable to expect that they would exhibit different abilities to produce EP. Neutrophils and monocytes are said to differ in their production of EP. Neutrophils are not activated by phagocytosis of latex beads although they do produce pyrogen after phagocytosis of viable or killed bacteria or after stiumlation with bacterial endotoxin. The monocytes, in contrast, can be activated by these latter stimuli as well as by the phagocytosis of latex beads. *In vitro* pyrogen production by neutrophils involves an early burst of protein synthetic activity, while the production of EP by monocytes occurs over a longer time period. Monocytes contain many more ribosomes than neutrophils, a fact reflected by their capacity to prduce 20- to 40-fold more pyrogen per cell than neutrophils. Monocytes may also release EP in a large molecular form as trimers. The EP produced by neurtrophils is said to be immunologically distinct from that produced by monocytes. Despite these reported differences, it is likely that some monocytes are present in neutrophil preparations used to generate EP. Both forms of EP have an equal capacity for stimulating a febrile response in assay animals.

Mechanism of EP Action

EP is believed to act in some manner upon temperature-regulating centers in the hypothalamus. In addition, close relatives of EP termed leukocytic endogenous mediators (LEM or EP/LEM), and lymphocyte activating factors (LAF) are produced and released concurrently from stimulated cells in a manner similar to that of EP (8). LEM (or EP/LEM) can account for the initiation of many physiologic effects in other target tissues including the liver, bone marrow, heart, and possibly the pancreas. LAF produced by macrophages can initiate immunological responses by lymphoid cells.

It is not known how EP crosses the blood-brain barrier, or precisely where or how it interacts with neurons in the hypothalamic area. Much current thinking is based on the fact that the pyrogenic activity of EP can be inhibited by antipyretic drugs, such as aspirin. Accordingly, the effects of EP on neurons are thought to be indirect, mediated locally via secondary neuroactive or neurotransmitter substances released within the brain itself. It has been postulated that EP may stimulate the formation of prostaglandin E_1 from arachidonic acid within the hypothalamus. It has also been suggested that other metabolites of arachidonic acid (thromboxanes or prostacyclins) may be the key neurotransmitter substances for fever production rather than a prostaglandin. These biologically active substances could lead to an increased local cellular activation of adenylate cyclase to cause cAMP formation within the neurons, or they could alter the local Ca^{++}:Na^{+} ratios. Although these are plausible concepts, the molecular neurophysiologic mechanisms operative within the thermoregulatory centers are exceedingly complex and have not yet been defined with certainty.

Most physiologists agree that any thermoregulatory control center within the hypothalamus must possess at least three major functional components (5). These include input receptors, a central neuroregulatory mechanism and output efferent pathways (Fig. 2). Input signals to the hypothalamus can come from hormone-like mediator substances as well as from a network of temperature-sensing neurons located throughout the brain and peripheral body tissues. These input signals appear to be coordinated within a thermoregulatory center in the hypothalamus which is variously termed the thermostat, comparator, integrator, or summing junction. Lastly, appropriate output responses must be formulated. The output signals may include both neuronal and endocrine mechanisms. These, in turn, would cause a peripheral increase in body heat conservation to produce a fever, or an increase in heat dissipation to cool the body.

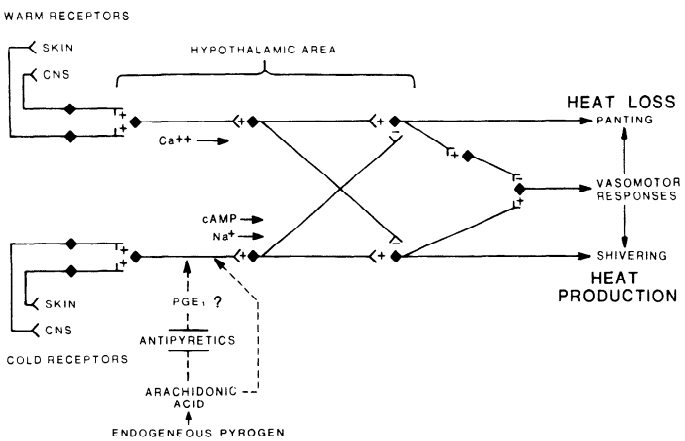

Fig. 2. Schematic concept of the hypothalamic thermoregulatory center based upon the Bligh model. Stimulatory impulses are +, inhibitory impulses are −. Neural pathways are shown as solid lines, humoral ones as dotted lines. Temperature sensing neurones from peripheral and CNS sites provide neural input into the hypothalamic centers. EP is thought to exert an indirect action via locally released mediators since a febrile response to EP is blocked by antipyretic drugs. Postulated neurones and synapses offer possible sites for the action of neurotransmitters, local mediators, monoamines and/or pharmacologic agents which influence the thermoregulatory mechanisms. A local increase in Ca^{++} ions leads to heat loss while an increase in Na^{+} ions leads to heat production. Cerebrospinal fluid concentrations of cAMP increase during EP-induced fevers (See text).

This integrated concept may involve more than one central control mechanism within the hypothalamus. As suggested by Satinoff (9), there may be two central thermostats, one which controls all behavioral thermoregulation while the other integrates all EP and neural thermosensory input signals. Alternatively, multiple thermostats may exist, with each type of input signal having its own regulatory mechanisms to generate a single type of output response. While these possibilities should be considered, most workers attempt to explain the hypothalamic regulatory center functions by means of a complex but unified integrating mechanism which is influeneced by all incoming signals. To obviate a theoretical requirement for the additional input of a constant reference signal, the system would need to possess multiple feedback loops from thermosensitive neurons.

The conceptual diagram shown in Figure 2 represents an extension of the neuronal model suggested by Bligh and Bacon (10) in which a variety of input signals and control mechanisms may be

integrated. Such a concept of the hypothalamic thermoregulatory center seems to be a useful one (5), although many of the details and uncertainties remain to be clarified. Neural messages from warm-sensing receptors located in peripheral or CNS sites are postulated to initiate a series of neuronal and neurotransmitter signals within the hypothalamus. After integration, the warm signals activate peripheral mechanisms leading to body heat loss. Simultaneously, through important neural crossover connections, warm input signals inhibit other pathways. Through such inhibition they depress body heat production. Cold input signals would have the opposite pair of effects, stimulating peripheral mechanisms to increase body heat production, and, at the same time, inhibiting heat loss mechanisms via a crossover pathway.

As suggested by this model, EP appears to stimulate thermoregulatory hypothalamic neurons in a manner of a cold input signal but only after additional secondary transmittors are released. Thus, EP is thought to act through the stimulation of other local mediators to achieve a resetting of the hypothalamic thermostat. It must also be remembered that an experimentally induced increase in Ca^{++} concentration in the cerebrospinal fluid leads to body heat loss while, in contrast, a localized CNS increase in Na^{+} leads to heat production. Regulatory mechanisms involving EP could, in concept, be directed toward the controls for regulating the concentration of these two cations and the ratio between them. Input stimuli that increase heat production have been shown to increase the concentrations of cAMP within the cerebrospinal fluid, so this may also be a key regulator. Still other studies suggest that the ability of mammals to generate a fever is ultimately dependent upon the presence of intact protein-synthesizing mechanisms within the brain. Much additional effort has been expended attempting to define the roles of other potential neurotransmitter compounds, including biologically active monoamines and a variety of pharmacological agents and drugs (11) that could play a role in thermoregulatory activities. Until these fundamental interrelationships can be clarified, the mechanisms by which EP initiates a hypothalamic response will remain conjectural.

Nonfebrile Actions of LEM (or EP/LEM)

A large number of nonfebrile physiologic and metabolic responses are known to begin shortly before or during fevers of infectious or inflammatory origin (12). These include hyperventilation with respiratory alkalosis, alterations in salt and water homeostasis, and measurable losses of nitrogen, potassium, phosphorus, and magnesium from the body. Many of these responses appear to be initiated by the hormone-like effects of LEM (or EP/LEM). The caloric energy to permit a febrile response is obtained primarily through the accelerated oxidation of carbohydrate and an increase in gluconeogenesis within the liver. This is made possible by the accelerated catabolism of somatic proteins, with flux of gluconeogenic amino acids from muscle to liver. The hormones that normally function to regulate body carbohydrate metabolism contribute to some degree in this response. Both insulin and glucagon are released in increased amounts from pancreatic islets. In addition to taking up more amino acids and producing more glucose, the liver also takes up and stores increased amounts of iron and zinc during febrile disease states. It rapidly begins to increase production and output of the entire group of "acute-phase reactant" plasma proteins. These include fibrinogen, haptoglobin, C-reactive protein, complement components, alpha-1 acid glycoprotein and ceruloplasmin, and in the rat, alpha-2-macrofetoprotein as well. The liver also accelerates its synthesis of a number of hepatocellular enzymes and hepatic metallothioneins, but it reduces the production of albumin. At the same time the bone marrow increases its production and output of phagocytic white blood cells.

It is possible that the key mediator for all of these widespread concomitant metabolic changes is EP itself. However, much evidence is at hand to suggest that many of these concomitant metabolic and physiologic events are initiated by closely related LEM species which are produced and released from phagocytic cells in a manner analogous to that of EP.

Bioassay of LEM (or EP/LEM)

Although it has not yet been possible to detect the presence of circulating EP in the serum or plasma of febrile human beings, LEM in plasma can be bioassayed in rats (13) by its ability to stimulate an abrupt decline in serum zinc and iron. LEM also stimulates an abrupt increase in the hepatic uptake of a nonmetabolizable amino acid, [^{14}C]cycloleucine, which is injected prior to the assay for use as an additional marker. The responses induced in assay rats become maximal within 6-9 hours after an intraperitoneal injection of a sample containing LEM. The magnitude of changes in assay rats are linearly correlated with the log-dose of administered LEM; changes fail to occur if normal human or animal plasma samples are tested. However, if human plasma is collected during fever due to bacterial, parasitic, and some viral infections or during active inflammatory bowel diseases, it can be shown to contain LEM. Longitudinal studies conducted throughout the course of typhoid fever in man showed the appearence of LEM in the plasma a day or two before the onset of fever. LEM disappeared only after fever had subsided (13).

Differences Between EP and LEM

Because identical techniques have been used to obtain EP, LEM, and LAF from stimulated rabbit peritoneal exudate cells, it remains possible that these may be identical substances (8). Partially purified preparations containing EP and/or LEM are able to stimulate *in vitro* colony formation in rat bone marrow cultures and fibrinogen synthesis in fetal rat hepatocyte cultures. Such findings show that a variety of body cells are targets for these mediators. Some preparations of LEM do not stimulate fever in assay rabbits. LEM does not adhere to glass as does EP, and LEM release from peritoneal exudate cells is not inhibited by the low concentrations of K^{+} shown to block EP release.

Arguments have been advanced (8) suggesting that the multiplicity of fever-related metabolic and physiological responses and the differences among these various responses during different kinds of infections and inflammatory diseases can best be explained by a large family of closely related mediators rather than by a single mediator. Nevertheless the present uncertainty concerning the relationships between EP and LEM can only be solved by side-by-side comparisons of pure preparations of each putative endogenous mediator in order to define their exact molecular compositions and biological activities.

Summary

When appropriately activated, mobile and fixed phagocytic cells can produce and release endogenous pyrogen and/or a variety of endogenous mediating substances into surrounding body fluids. The EP/LEM substances have hormone-like stimulatory effects upon distant body tissues. Although their molecular composition and nature of action at the cellular level remain undefined, these endogenous mediating substances appear to initiate or modulate fever as well as many of the generalized host metabolic and physiologic responses that accompany an infectious or inflammatory disease.

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BOOK REVIEWS

Common Medicines: An Introduction for Consumers. David J. George. W. H. Freeman & Co., San Francisco, 1979. 197 pp., illus., softbound, $6.00

This book is intended as an introductory text in pharmacology for the lay public. The principles of pharmacology which are presented, such as a trivial explanation of the cholinergic nervous system, require little or no scientific background and yet may aid the consumer in understanding the effects of drugs. On the other hand, understanding some of the mechanisms of action of specific drugs would require background in animal or cell physiology. Most of the major non-prescription medications are discussed, such as histamine/antihistamines, cough remedies, sleep-aids and laxatives. The few citations of drug interactions and precautions would probably be particularly valuable to the home pharmacist. The detailed chapter on antibiotics gives the reader a "feel" for antibiotic therapy, which he may or may not apply appropriately under conditions where a physician's judgement is warranted. A text such as this gives the lay person a little knowledge and awareness of drug use in our society, and hopefully would stimulate a cautious outlook on indiscriminate self-administration of drugs as medication.

Suzanne G. Laychock, Ph.D.
Medical College of Virginia

Handbook of Sensory Physiology: Vision in Invertebrates. Vol. VII/6. H. Autrum, Ed. Springer-Verlag, New York, 1979. 679 pp. illus. indices $176.00

This volume is part of Springer-Verlag's continuing series in sensory physiology; as in their other volumes on the vertebrate visual system this one is directed to areas of interest to researchers on invertebrate vision. The book begins with an introduction by Autrum of photosensory mechanisms from an evolutionary point of view and is followed by a discussion of photoresponses in protozoa as a model system for studying photobehavior. The emphasis in this chapter by D. Diehn is directed to the photoreceptor system for phototaxis of the protozoan algal flagellate *Euglena.* Two well developed chapters are devoted to discussions of extraocular photosensistivity; that is, photosensory processes that are initiated not through the eye. One is by M. Yoshida on dermal, nerve and brain photoreceptors as related to photobehavior. The other is a discussion by M. F. Bennett on extraocular photoreception in relation to circadian and migratory rhythmic photobehavior. These two chapters develop an area of research that is becoming of great interest to photobiologists. The remainder of the book is devoted to the eye. There are four chapters concerning the optics of invertebrate eyes; these are by W. H. Miller on intraocular filters, the physics of optical light gathering systems by A. W. Snyder, pseudo pupils by D. G. Stavenga, and a discussion by P. Kunze of the classical work going back to Exner on the optics of opposition and superposition compound eyes. The invertebrate visual cell electrophysiology is covered in some detail by M. Järvilehto. There are two interesting chapters; one on the spectral sensitivity of the eye and color vision by R. Menzel, and the other on pigments and physiology of invertebrate eyes by K. Hamdorf. The book concludes with how the techniques developed for genetics can be applied to isolate the mechanisms of the visual system of invertebrates which is demonstrated by M. Heisenberg.

In all, the text is well written and profusely illustrated with drawings, and numerous electron micrographs including scanning and transmission micrographs of the various eye structures and photoreceptors. These are very helpful in following the experiments described and the discussions that follow. There is an authors index to publications as well as to species and a subject index.

This volume does not cover all the diverse invertebrate species or their optics and photochemistry of the visual pigments, for much is yet to be discovered. Though the presentations by the various authors are directed to invertebrate visual and photoreceptor systems, comparisons are made to the visual system of vertebrates. On the whole, the book indicates the direction of the research and therefore serves as an invaluable reference source. The price is prohibitive for most students and researchers; nevertheless, it should be in the libraries for students and researchers interested in photobehavior and vision of invertebrates.

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INTERNATIONAL UNION OF PHYSIOLOGICAL SCIENCES

Dedicated to the advancement of Physiology for the welfare of mankind or all nations by the combined efforts and friendly cooperation of the physiologists of the world

NEWSLETTER

Volume 7 Number 2

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EDITOR'S NOTE

There is more to Physiology than producing, reading and publishing scientific papers. We realise this in the United Kingdom. Our Society started as a dining club and now, over one hundred years later, our nine annual meetings would be unthinkable without the dinner on the Friday evening. Physiologists are people, we get to know one another, gossip, sum up one another, in more or less kindly fashion, exchange views, not necessarily on matters physiological, discuss problems, air our prejudices: we are a national family and better physiologists as a consequence.

Such intimacy is possible in the small islands of Great Britain. It is far otherwise in the five continents of the world. The International Congress every three years does bring many physiologists together with considerable pomp and circumstance: the attendant satellites cater for special scientific interests. So do the standing Commissions, Committees and Workshops of I.U.P.S. But these also are restricted to special interests.

Inevitably far, far too few of the world's physiologists can get together every three years to see and be seen. How can we meet the needs of all physiologists and not confine our efforts to special interests?

There is only one way to do so, to bring the world physiologists together as a family. Scientific Journals are a dead loss in this respect, but another kind of journal can. "The Physiologist" of the American Physiological Society is an excellent example. It is a magazine unashamedly interested in physiologists as human beings. There are articles on the affairs of the American Physiological Society as a society, on current events, on past events, on the activities and interests of members past and present: there are letters to and from the Editor, book reviews, supplements, obituary notices. This is a publication for physiologists, it is about physiologists and physiology, primarily in America.

We need a publication to serve in similar fashion the physiologists of the world. This was to have been the role of the Newsletter when I.U.P.S. was young and full of enthusiasm in the brave new world of 1953. Now the President in his Message tells us that "for the time being at least the Newsletter as a separate issue will no longer be available." This last small effort is made possible by the goodwill of the American Physiological Society, of "The Physiologist" and of Dr. Orr E. Reynolds, its Editor.

Personally I do hope that in due course a time will come when, "by the combined efforts and friendly cooperation of the physiologists of the world," it will be possible to have a journal which will have as its prime function the binding of us together as a family. From personal experience as Editor of the Newsletter I know that we have the necessary goodwill and dedication. I had support from Corresponding Editors of the National Societies, from Chairmen of Commissions and Committees and from many others who submitted material for publication. Other members of National Societies willingly undertook the task of distributing copies of the Newsletter to the individual members of their Societies. To all these my thanks are due, I am deeply grateful.

R. C. Garry

The Physiologist, Vol. 23, No. 2, April 1980.

MESSAGE FROM THE PRESIDENT

Wallace Fenn was the driving force in establishing the IUPS Newletter, during his term (1962-1968) as Secretary of the Union. He repeatedly said that it should be in the hands of every physiologist in the world in order to achieve its greatest potential value. Under his Editorship the publication thrived, achieving a circulation of 7000 copies by 1965 after beginning with approximately 2000. The Editorship passed in 1965 to Jan Duyff who, because of illness, was able to publish only one copy (Vol. 2 no. 1) in April 1966. Council appointed James Stevenson as Editor in August 1968 and the journal received his typically enthusiastic attention. Eight editions appeared under his aegis before his sudden and untimely death in Zurich on 23rd July 1971 en route to the XXVth Congress in Munich. By this time 44 countries received copies they requested totalling approximately 7000 copies. Council appointed Arisztid Kovách as the new Editor in 1968 and despite his assuming the Secretaryship of the Union in October 1974 he was able to supervise the production of six editions before relinquishing the Editorship. The Hungarian Academy Press and Professor Kovách's colleagues were a great help to him during the period 1968-1977. The Council asked Emeritus Professor Robert C. Garry whether he would shoulder the task, and to its great satisfaction he agreed to do so. Readers of the Newsletter over the years will have appreciated his reports of activities of the Physiological Society - always characterised by wit and scholarship.

Quite typically, Robert Garry, aided only by his part-time Secretary Miss Margaret Paton, produced volume 7 no. 1 as the most formidable compilation so far issued. Indefatigable as ever he rounded up the corresponding editors from the different countries and quietly but firmly prevailed upon the Chairmen of the numerous Commissions to provide reports on their activities. Unfortunately, his continued activity has been halted because of the escalation of costs of printing and mailing, and for the time being, at least, the Newsletter as a separate issue will no longer be available. This was decided by Council at its London meeting in July 1979. At that meeting Council received the suggestion from Dr. Orr Reynolds, Chairman of the U.S. National Committee for IUPS and Executive Secretary/Treasurer of the American Physiological Society, that future issues of the IUPS Newsletter might be printed as a section of "The Physiologist." in five issues of eight pages each, annually at no cost to IUPS. He proposed that identity of the Newsletter should be maintained by a separate masthead and editor. Council welcomed this solution and decided that the present format of the Newsletter should be terminated at the end of year 1979 and that a two-page issue should be sent to Dr. Orr Reynolds by December 1979.

Council has asked me to convey our gratitude to Robert Garry for his devoted efforts and to thank Dr. Orr Reynolds for helping to preserve the message which Wallace Fenn so cherished as the purpose of the Newsletter.

Recent IUPS activities can only be summarized in this brief message. A highly successful Laboratory Teaching Workshop was held in New Delhi 17th-29th July 1978 run by Professor Surendra Manchanda. Thirty-one teachers from Indian Medical Colleges and eight such teachers from Iraq, Iran, Nigeria, Burma and Bangladesh participated. IUPS was fortunate in securing the help of Professor Ainslie Iggo (Edinburgh) and Dr. Ann Sefton (Sydney) in running this Workshop. A Winter School on the Neurobiology of Behaviour was held in New Delhi (19th February - 4th March 1979) with participants from Burma, Sri Lanka, Bangladesh and Afghanistan. Experts from India, Italy, Japan, U.K. and U.S.A. provided help, and IBRO, UNESCO, INS and many Indian National Organizations supported this programme.

Thanks to the enthusiasm of Professor Otto Hutter, Chairman of the IUPS Commission on Medical Physiology, it has been possible to arrange a small Workshop in Lagos, Nigeria, to operate in February 1980 in conjunction with the second meeting of the Nigerian Physiological Society.

Financial considerations have restricted the meetings of Executive and Council. A London meeting was held at The Middlesex Hospital, the Executive conferring on 7th July and the Council 8th - 10th July. Among the many items of agenda two may be referred to. First, proposed revision of the Constitution and By-Laws were discussed and will be presented for the approval of the General Assembly in Budapest at the XXVIIIth Congress. Second, proposals relating to the format of future Congresses submitted by John R. Pappenheimer were discussed at length and a Sub-Committee was formed to meet in Harvard on 21st-23rd November. Suggestions arising from the deliberations of this Sub-Committee (chaired by Dr. Pappenheimer) will be forwarded to Council and some of them will be submitted to the General Assembly.

Finally, the Budapest Congress arrangements proceed smoothly. Professor Thurau has paid two visits and I have made one to assist the Organizing Committee. Our Hungarian hosts have worked unsparingly and deserve our warmest thanks. There are over seven thousand prospective registrants. Fifty Satellite symposia (of which seventeen will be in Hungary) are scheduled - all held in Europe. I think that there will be much to look forward to.

Eric Neil
13th November 1979

OBITUARY NOTICES

CHARLES H. BEST 1899-1978

Rachmiel Levine contributes an admirable Obituary Notice of Charles Best to 'The Physiologist' for June 1978, Volume 21, pp. 43-44.

Best, an eminent physiologist and an outstanding benefactor of mankind by the part he played in the discovery of insulin, was the first President of the International Union of Physiological Sciences.

AREND BOUHUYS 1926-1979

Arend Bouhuys was a leading authority on Byssinosis: he died of a heart attack on June 15, 1979 aboard the Queen Elizabeth II. He was on his way to the University of Utrecht, The Netherlands, where he had recently been appointed Chairman and Professor in the Department of Physiology.

Bouhuys was well known for his work on the epidemiology of chronic lung diseases, especially for his studies on the cause and treatment of Byssinosis, an occupational hazard for workers in cotton mills: he campaigned vigorously for establishing, and strictly enforcing, satisfactory standards for dust-free atmospheres in cotton mills. He also made a major study of asthma. Altogether he was author of over 300 papers on diseases of the lungs and he was managing editor of "LUNG," an international journal on Lungs, Airways and Breathing.

Bouhuys was born in Deventer, the Netherlands, and received his basic training in Medicine in the University of Utrecht: he received the Doctorate in Medical Science from the University of Amsterdam in 1956: in 1959 he became Head of the Laboratory of Clinical Physiology in the University of Leiden.

In 1962 Bouhuys went to the United States as Assistant Professor of Physiology and Medicine at Emory University School of Medicine in Atlanta, Georgia. In 1964 he went to Yale to become Associate Professor of Epidemiology in the School of Medicine and also Fellow of the John B. Pierce Foundation Laboratory in New Haven. He was promoted in 1968 to the Chair of Medicine and Epidemiology at Yale.

Bouhuys was a member of many professional societies including the American Physiological Society: he was also a member of the I.U.P.S. Commission on Respiratory Physiology.

He was buried in his birthplace, Deventer, in the Netherlands.

Marjorie B. Noyes

GENICHI KATO

Professor Genichi Kato was a member of the Council of IUPS from 1959 to 1971. He was a member of the Japanese Academy, an honorary member of IBRO, of APS and of the Argentine Medical Association: he died on May 1, 1979 at the age of 89: he was born on February 11, 1890 in Niimi, Okayama, Japan.

Kato was internationally known for his theory of non-decremental conduction of nerve reported in 1923 at the second annual meeting of the Japanese Physiological Society.

When the twenty-third International Congress of Physiological Sciences met in Tokyo in 1965 Kato was President of the Congress: there were over 3,000 members from 46 countries.

A more complete obituary from a "farewell word" by Prof. Y. Tsukada at the Memorial Service in Keio University was published in *The Physiologist,* Vol. 22, No. 5, October 1979.

YAS KUNO 1882-1977

Professor Yas Kuno, a Member of the Japanese, Academy, passed away on December 30, 1977, at the age of 95. His breathing stopped very quietly and peacefully in the early morning during his sleep.

He was the oldest physiologist in Japan, had long been a leader in physiological research activity, and greatly influenced those who followed him. At this moment we would like to look back on his great achievements and contributions.

He was born on March 30, 1882, in Nagoya City, where he grew up. In 1903 he graduated M.D. from Aichi Medical College and the next year began to study physiology at the Tokyo Imperial University Medical Faculty under Professor Kenji Oosawa. His studies were soon interrupted by the Russo-Japanese War during which time he served as a military surgeon. In 1906 he returned to the Department of Physiology at Kyoto University Medical School.

In June 1911 he was appointed professor of physiology at the Medical School of South Manchuria. He studied physiology in Europe for 2 years (1913-1915) at the University of Leipzig and

then at University College London with E. H. Starling. In 1916 he was awarded the degree of Doctor of Medical Science (Ph.D.) by the Ministry of Education. In 1917 he was appointed professor of physiology at South Manchuria University Medical School.

In 1935 he again returned to Kyoto Imperial University Faculty of Medicine as Associate Professor and in 1939 was appointed professor of physiology at Nagoya Imperial University Faculty of Medicine when it was opened. In 1952 all Imperial Universities changed names and he was elected dean of the medical school of Nagoya University, serving until 1954. He retired from his Chair in 1955 and in January became Professor Emeritus. After retirement he lectured to medical students at Kyoto and Mie Prefectural Medical Colleges until 1965.

His contributions to physiology were enormous. His research on human perspiration started when he was in South Manchuria and his pupils still continue study in this field. When he began to study human perspiration nobody in the world had studied that subject. His works were completely original and he continued these studies for more than 50 years in South Manchuria, Kyoto and Nagoya. Under his guidance 60 pupils investigated the mechanisms of human perspiration and 160 papers were published including the mechanism of water metabolism. The experimental results, written in English, were published in two monographs: The Physiology of Human Perspiration (Churchill, London, 1934) and Human Perspiration (C. C. Thomas, Springfield, Illinois U.S.A., 1956). Among the more important results was the identification of two kinds of perspiration. One is "Thermal Sweating" which controls body temperature and the other is "Mental Sweating" which takes place only on the palm of the hand and the sole of the foot. The latter is adrenergic while the former is cholinergic. His hypothesis that the cholinergic innervation of the human sweat gland has developed from the adrenergic innervation in primitive animals was presented in his special lecture "The Mechanism of Human Sweat Secretion" at the closing session of the 23rd International Congress of Physiology in Tokyo in 1965. He probed into various aspects of sweating, including the mechanism of sweating, measurements of the amount of sweat, pathological sweating and so on, and thus opened the way to the study of sweating. He was indeed a pioneer in perspiration research. Modern textbooks of physiology include chapters on perspiration which reflect the work of Dr. Kuno and his pupils.

Professor Kuno also stimulated his pupils to study climatic physiology and endocrinology, both of which had been neglected by physiologists in Japan until that time. He trained several pupils who are now outstanding Physiologists in those specific fields. These include Prof. Korehiro Ogata, Hisato Yoshimura, Kentaro Takagi, Shinji Ito, Kokichi Ohara, Teruo Nakayama, and Akira Arimura among others. Almost all are now leading physiologists in Japan.

He attached importance not only to research, but also to publications, and founded the Japanese Journal of Physiology in 1951. He edited and sponsored that journal until 1970 at which time it was handed over to the Physiological Society of Japan and the University of Tokyo Press. He organized the Vitamin Society of Japan in 1944, and founded the Journal of Vitaminology. With his help, study in this field progressed remarkably.

During his service he was active on many important committies of the government and his university. In addition to his research activities he advised the Japanese government, as a member of the Science Council of Japan, to promote cooperation among scientists in various different fields. According to his advice the ministry of education organized a system of integrated scientific research groups that has since developed into the present organization which exists in Japan.

In international affairs he was elected a member of the permanent committee for the International Physiological Congress in December 1935 and served until 1953. When the International Union of Physiological Sciences was organized he was elected as one of the council members. At the same time he was a representative of the Japanese Union of Physiological Sciences, a liaison society between Japan and IUPS, and was Chairman of this society until 1959. In these and other ways he worked for the progress of international affairs for 24 years.

In 1941 he was awarded the Imperial Prize of the Japanese Academy for his excellent studies and was elected a member of the Japanese Academy in 1949. His studies also received global attention, so that he received honorary membership in the Physiological Society of Great Britain in 1952, the American Physiological Society in 1959 and the Physiological Society of the Federal Republic of Germany in 1960. Such brilliant honours are very rare in all the world as well as in Japan. He was further awarded the highest decorations of Japan, the Cultural Medal in 1963 for his cultural achievements, and the First Order of Merit in 1975.

I have described Dr. Kuno's outstanding professional contributions, but he has done more. He gave the world three sons who continue his contributions to mankind. The eldest son is ex-President of Keio University, the second is a professor of biochemistry in Kanazawa University, and the third son is a professor of physiology in the United States. He raised a very happy and productive family.

His motto was "the real aim of medicine is endless sympathy for the weakest persons."

Yasuji Katsuki

DAVID H. SMYTH, F.R.S.

David Smyth, Emeritus Professor of Physiology in the University of Sheffield, England, died in September 1979: he was 71 years of age.

David graduated first in Science and then in Medicine from Queen's University, Belfast, Northern Ireland. Later he went to University College, London, as Lecturer in Physiology and then, in 1946, to Sheffield as Professor.

For a time his interests were chiefly in the metabolism of carbohydrate and in intermediary metabolism. Later, however, he developed a personal, original and ingenious method to study absorption from the intestine. From the time of Waymouth Reid at the very beginning of this century, worth-while work on absorption from the gut had been bedevilled by the extreme delicacy of the epithelium of the intestine, especially in *in vitro* preparations. So David turned lengths of intestine inside out, everted them, to make sacs where the epithelium was ensured an adequate supply and tension of oxygen. This technique was most rewarding and yielded much information on absorption of monosaccharides and of amino-acids. In 1967 he was made a fellow of the Royal Society of London.

From time to time David contributed a "Personal View" essay to the British Medical Journal. His best known essay dealt with medical education. Up to the present time we have tended to regard instruction of the medical student as analogous to the building of a massive edifice, a process requiring ever increasing material and time: there has to be a solid foundation of

knowledge in the Basic Sciences, Mathematics, Physics, Chemistry and all the rest. Architects of such a curriculum would have the student of medicine middle aged before being licensed to practise.

David would have none of this. The medical student is a living growing plant not an inert mass of stone and lime. Let the student put up a few healthy essential green shoots nourished by a just adequate root system. Let him as soon as possible with safety begin to practise his profession in simple fashion. Should he wish thereafter to specialize in one of the many branches of Medicine let him put down, as need arises, a new root or roots in the basic science or sciences necessary for his specialty.

David served well the Physiological Society of the United Kingdom. He was a member of Committee, 1947-51, and editor of the Journal of Physiology, 1961-68, and had been the Society's Foreign Secretary for seven years at the time of his death. Until recently he had been Chairman of the British National Committee for Physiological Sciences.

He took a very active part in the work of the Research Defence Society and wrote a book on "Alternatives to Animal Experiments" of little comfort to antivivisectionists.

David was small in stature, quick in his movements and he retained the accent of his native land. He was bonhomous but he could be loudly critical of inefficiency and muddle. Trenchancy of speech was softened by almost continuous hilarity. He will be sadly missed in our own national society and a major loss to the International Union of Physiological Sciences.

R. C. Garry

IN MEMORIAM, MOHAMED TALAT, President of the Egyptian Society of Physiological Sciences

Professor Dr. M. Talat founded the Egyptian Society of Physiological Sciences: he died in 1977 at the age of 71.

He graduated MB ChB from the Egyptian School of Medicine in 1928: from University College, London he received his B.Sc. in 1932: from Cambridge University his Ph.D. in 1935. In 1975 he was honoured by the Award of the Country.

He had 104 publications to his credit in Egyptian and International Journals. For more than 50 years he was associated with the University of Cairo where he was Professor of Physiology in the Faculty of Medicine. In 1954 he was Chairman of the Physiology Department and Vice-Dean of the Medical Faculty. He was also founder of the Physiology Department in the Faculty of Medicine in Alexandria University: he was a Member of the Egyptian Academy of Science.

He will be very much missed by his family, by his many friends and by his colleagues and by our Society. Few enjoyed such high regard.

A. H. Mohamed

IN MEMORIAM, HUSSEIN M. SAEID, Vice-President of the Egyptian Society of Physiological Sciences: he died in 1977 at the age of 66.

Professor Saeid founded the School of Plant Physiology in Cairo. He had the B.Sc. (Cairo) in 1933, Ph.D.(Cambridge) in 1937, D.Sc. (Cairo) and a Diploma from Imperial College, London. He was honoured by two Country Awards in Biological Sciences.

In 1965 he was one of the 15 UNESCO Members serving on a committee assessing biological resources. He had 63 publications in Egyptian and International Journals.

For more than 40 years he served the University of Cairo, Professor of Plant Physiology, Head of the Plant Physiology and Botany Department in 1950, Dean of the Faculty of Science for 6 years, Vice-President of Cairo University in 1964 and then Minister for Higher Education.

He was a Member of the Egyptian Academy of Science.

A. H. Mohamed

FRITZ VERZÁR 1886-1979

In the 93rd year of his life, on 13 March 1979, in Arlesheim by Basel, Fritz Verzár, Director of the Institute of Experimental Gerontology passed away. Previously he had been Head of the Department of Physiology in Debrecen, Hungary and later still Head of the Physiology Department in Basel, Switzerland. For more than 70 years he had devoted his whole life to Physiology and Experimental Biology.

Fritz Verzár was born in Budapest on 18 September 1886. He followed in his father's footsteps and qualified in Medicine in his native town. While still a student the secrets of living things so aroused his interest that he started his first research work in the Anatomy Department of M. Lenhossek. Later he worked in the Pharmacology Department of G. Mansfeld and later still in F.

Tangl's Department of Pathological Physiology. Verzár's first publication appeared when he was only 21 years old. After graduation he worked in J. Bernstein's laboratory in Germany: then he went to England to Cambridge to work with Joseph Barcroft. Verzár had many interests, new problems fascinated him and to their solution he brought unusual working capacity. In his lifetime he published 20 books and more than 400 scientific papers.

At the age of 32 Verzár was made the head of the Pathophysiological Department in the Medical Faculty of Debrecen University: after a few years he became Head of the Physiology Department as well. At this time he was studying the nature of excitation and the laws governing the propagation of nerve impulses. He proved the existence of afferent fibres from the heart. He managed to record nerve impulses by use of a string galvanometer. Later he turned his attention to nutrition and to endocrinology. He paid special attention to the interaction between hormones and vitamins with special reference to that between the adrenal cortex and the vitamin B complex. He also worked on the movements of the villi of the intestine and on absorption from the intestine, especially of sugars.

Verzár shouldered an important administrative task when, in 1926, it was decided to establish the Hungarian Biological Research Institute at Tihany. Verzár became the first Director of the Institute. He also organised the Hungarian Physiological Society: the first meeting took place in 1931 at Tihany.

In 1930 the University of Basel invited Verzár to become head of their Physiology Department. Verzár accepted, little thinking that this move would mean a break with his native Hungary. In Basel he continued to work on absorption and on the adrenal cortex. In 1936 appeared his well-known book "Absorption from the Intestine." His co-author was Jean McDougall who was to become his second wife. During this period he showed that, after removal of the adrenal cortex, cats and rats could be kept alive for a long time by administration of deoxycorticosterone. This work was summarised in a new book "Die Funktion der Nebennierenrinde."

After World War II Verzár was active in the work of WHO and of FAO. The Governments of Peru and Bolivia sought his expert advice and he helped to organise preclinical teaching in Caracas.

At the age of 70 Verzár retired from the University of Basel. He then turned his attention to the study of old age. He established and directed for 20 years the Experimental Institute of Gerontology in Basel: this was supported by the pharmazeutical industry in Switzerland. Verzár was active in developing research in Gerontology, he and his co-workers studied the senescence of collagen: he founded the journal "Gerontology."

During his life time Verzár received many honours. The Medical University of Debrecen conferred an honorary doctorate: in 1973 he became an honorary member of the Hungarian Academy of Sciences by election.

A large number of students came under his sway, many subsequently were appointed to Chairs or senior research posts in Hungary and throughout the world. Verzár's scholarship and knowledge were outstanding and combined with that was deep love of humanity. This keeps the memory of his personality alive in the minds of his colleagues, of his research workers and of his students.

János Salánki
Tihany

Biology of the Chloride Cell:

Jean Maetz Memorial Symposium

In March 1980 a special issue of the bimonthly *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology* will be devoted to papers derived from a symposium on the "Biology of the Chloride Cell," which was held to honor the late Jean Maetz. The symposium focused on the integration of research information the function of the chloride cell, an acidophilic cell found in the gill epithelium and held to be the specific excretory (or secretory) unit responsible for the osmotic and ionic regulation of fish gills. The publication is divided into four sections on the anatomy, ultrastructure, physiology, and biochemistry of the chloride cell. Contents: Morphology of gill epithelia in fish. Gill arch of the mullet, *Mugil cephalus*. III. Rate of response to salinity change. Reconstruction of the gill from single-cell suspensions of the eel, *Anguilla japonica*. Tabular system membranes of teleost chloride cells: osmotic response and transport sites. Ion-secreting epithelia: chloride cells in the head region of *Fundulus heteroclitus*. Accessory cells in teleost branchial epithelium. Freeze fracture of the gill epithelium of euryhaline teleost fish. Polysaccharidic material in chloride cell of teleostean gill: modifications according to the salinity. Comparison of vertebrate salt-excreting organs. Kinetic studies of ion transport by fish gill epithelium. Ionic contributions to the potential and current across the opercular epithelium. Fish gill carbonic anhydrase: acid-base regulation or salt transport? Role of Na-K-ATPase in chloride cell function. Cl^--HCO_3^--ATPase in the gills of rainbow trout: evidence for its microsomal localization. Ion exchanges through respiratory and chloride cells in freshwater- and seawater-adapted teleosteans. Role of C-4 pathway in crustacean chloride cell function.

Contributors to this special issue, which was organized by F.P. Conte and edited by B. Schmidt-Nielsen, are:

P. Laurent • S. Dunel • F.E. Hossler • N. Naito H. Ishikawa • C.W. Philpott • K.J. Karnaky, Jr. S.R. Hootman • C. Sardet • M. Pisam • J. Maetz L.B. Kirschner • D.H. Evans • K.J. Degnan J.A. Zadunaisky • M.S. Haswell • D.J. Randall S.F. Perry • F.H. Epstein • P. Silva • G. Kormanik M. Bornancin • G. de Renzis • R. Naon • J.P. Girard P. Payan • F.P. Conte.

This publication may be purchased separately or received as part of your annual subscription to the journal.

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9650 Rockville Pike
Bethesda, Maryland 20014

Submit original and 7 copies of application and supporting documents.

APPLICANT'S LAST NAME _____

Date _____

THE AMERICAN PHYSIOLOGICAL SOCIETY
9650 Rockville Pike, Bethesda, MD 20014

MEMBERSHIP APPLICATION FOR:

- ☐ REGULAR
- ☐ CORRESPONDING
- ☐ ASSOCIATE
- ☐ STUDENT

CURRENT MEMBERSHIP CATEGORY; YEAR ELECTED _____

See Instructions

Name of Applicant: _____
First Middle Last

Mailing Address _____ Birth Date: _____

Citizenship: _____

Country of Permanent Residence:* _____

Telephone No.: _____

*Alien residents of North America attach 8 copies of Alien Registration Card or other evidence of intent to remain in North America.

1. EDUCATIONAL HISTORY

Dates	Degree	Institution	Major Field	Advisor

Doctoral Dissertation Title: (if any)

Postdoctoral Research Topic:

2. OCCUPATIONAL HISTORY

Present Position:

Prior Positions:

Dates	Title	Institution	Department	Supervisor

SPONSORS

#1. Name: _____

Mailing Address: _____

_____

_____

_____

Telephone No. Zip Code

#2. Name: _____

Mailing Address: _____

_____

_____

_____

Telephone No. Zip Code

I have read the guidelines for applicants and sponsors and this application and attest that the applicant is qualified for membership.

#1 Signature _____ #2 Signature _____

Each sponsor must submit an original and 7 copies of a confidential letter of recommendation to the Society, under separate cover.

(over)

APPLICANT'S LAST NAME _____

3. **DESCRIBE YOUR PHYSIOLOGICAL TEACHING** – What percent of your time/effort is spent in teaching Physiology?_____

Describe in the space provided your teaching of physiology including course descriptions (content, format); supervision of pre-doctoral and post-doctoral students; special contributions (films, textbooks, etc.).

4. **INTEREST IN THE SOCIETY** – List any APS Meetings attended by date and check the appropriate box for any papers.

SPRING (FASEB)			FALL (APS)		
Date	Presented	Coauthor	Date	Presented	Coauthor
_____	☐	☐	_____	☐	☐
_____	☐	☐	_____	☐	☐
_____	☐	☐	_____	☐	☐
_____	☐	☐	_____	☐	☐
_____	☐	☐	_____	☐	☐

List other scientific societies of which candidate is a member:

In the space provided state your interest in wanting to join the Society:

5. **SPECIAL CONSIDERATION** – Include any other contributions (Administrative, university, national service, awards and honors) that may be important to physiology.

6. **DESCRIBE YOUR RESEARCH** – What percent of your time/effort is spent in research?_____

Describe the fundamental physiologic questions in your research and how you have answered these questions. Limit the paragraph to the space provided.

7. **BIBLIOGRAPHY** – Attach a list of your publications under the following categories:
   1. Complete physiological papers, published or accepted for publication.
   2. Physiological abstracts (limit to ½ page).
   3. Other papers not primarily physiological (limit to ½ page).

The entire bibliography should not exceed 2 pages. Give complete titles and journal references with inclusive pagination. Use the bibliographic form found in the Society's journals. List authors in the order in which they appear in the publication.

INSTRUCTIONS FOR APPLYING FOR APS MEMBERSHIP

CURRENT APPLICATION FORMS

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

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

GENERAL INSTRUCTIONS

FOR ALL CATEGORIES:

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

The Bibliography must be submitted in the form found in the Society's journals. An example of the correct form is:

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

Send no reprints.

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

QUALIFICATIONS (Except Students):

The Membership Advisory Committee uses the following 5 categories in evaluating an application:

1. Educational History. Academic degree and postdoctoral training are evaluated and assessed with regard to how closely the applicant's training has been tied to physiology.
2. Occupational History. Particular emphasis is given to those applicants who have a full time position in a department of physiology, or are responsible for physiology in another department. Relatively high ratings are given to people with positions in clinical departments and to people functioning as independent investigators in commercial or government laboratories.
3. Contributions to the Physiological Literature. This category is of major importance. The applicant's bibliography is evaluated on the basis of publications in major, refereed journals which are concerned with problems judged to be primarily physiological in nature. Emphasis is given to papers published as the result of independent research. Special note is taken of publications on which the applicant is sole author or first author.
4. Interest in and Commitment to Teaching Physiology. This evaluation is based on: (1) the fraction of the applicant's time devoted to teaching, (2) publications related to activities as a teacher including production of educational materials, and (3) special awards or other recognition the applicant has received for outstanding teaching effectiveness.
5. Special Considerations. This category permits the Membership Advisory Committee to acknowledge unique accomplishments of an applicant. These might be excellence in a specific area, or unusual contributions to Physiology resulting from talents, interest or a background substantially different from the average.

SPONSORS:

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

Each sponsor should write an independent confidential letter about the candidate using the five categories listed above to evaluate the candidate.

CHECK LIST:

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

Executive Secretary
American Physiological Society
9650 Rockville Pike
Bethesda, Maryland 20014

SPECIAL INFORMATION AND INSTRUCTIONS

FOR REGULAR MEMBERSHIP

Bylaws of the Society:

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

IF ALIEN: Please attach a letter and 7 copies stating visa status and type of passport and giving evidence of intent to stay in North America.

Duties and Privileges:

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

FOR CORRESPONDING MEMBERSHIP

Bylaws of the Society:

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

Duties and Privileges:

1. Serve on Society Committees, Boards and Task Forces.
2. Serve as one sponsor of new Corresponding Members (One regular member must be sponsor of a new Corresponding Member).
3. Orally present or co-author a contributed paper and sponsor a non-member authored paper at the Fall scientific meeting.
4. Orally present or co-author one contributed scientific paper at the annual Federation meeting or sponsor one paper.
5. Receive The Physiologist.
6. Receive Federation Proceedings, Public Affairs Newsletters and annual Membership Directory.
7. Subscribe to handbooks and periodicals published by the Society at membership rates.
8. Register to attend scientific meetings of the Federation and the APS Fall meeting at member rates.

FOR ASSOCIATE MEMBERSHIP

Bylaws of the Society:

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

Duties and Privileges:

Same as for Regular Members except for the privilege of:

1. Holding Executive Office, or membership on certain committees.
2. Voting at Society Meetings.
3. Sponsoring New Members.
4. Receiving the Daggs Award.
5. Selection as Bowditch Lecturer.

FOR STUDENT MEMBERSHIP

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

Bylaws of the Society:

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

Duties and Privileges:

1. Present one contributed paper at the Fall Scientific meeting with the endorsement of the student's advisor.
2. Receive The Physiologist.
3. Subscribe to Handbooks and Periodicals at member rates.
4. Register to attend scientific meetings of the Federation and the APS Fall meeting at student rates.

SATELLITE SYMPOSIUM OF THE XVII INTERNATIONAL CONGRESS OF PHYSIOLOGICAL SCIENCES ON "CENTRAL INTERACTION BETWEEN RESPIRATORY AND CARDIOVASCULAR CONTROL SYSTEMS"

This Satellite Symposium was held in West Berlin just before the meeting of the International Congress in Paris in 1977. Host and Co-chairman of the Symposium was Professor Hans-Peter Koepchen, Institute of Physiology at the Free University of Berlin. The two other Chairmen were Professor Sidney M. Hilton, Department of Physiology, University of Birmingham, U.K. and Professor Andrzej Trzebski, Institute of Physiological Sciences, Medical Academy, Warsaw. Fifty-two participants from 15 countries read papers and took part in the discussion. The aim of the symposium was to bring together people working on central control of the cardiovascular and respiratory systems with special emphasis on overlapping areas and on the no man's land between specialised fields of research. This symposium was the continuation of previous meetings by the same people. There they had exchanged ideas and new facts. They had met in Warsaw in a Satellite Symposium of the XXV International Congress in Munich in 1971, in Tokyo during the International Congress in New Delhi in 1974. In between they met in an International Symposium on "Central Rhythms and Regulations" in West Berlin in 1972. In 1976 they had a Workshop in Heidelberg on "Nervous Cardiovascular Control." During these previous meetings it became more and more evident that it was necessary to devote a special symposium to the interaction of the two control systems which traditionally are treated separately.

There were five sessions, 24 papers were presented and these covered the following topics:-

"the central nervous basis for interaction between the cardiovascular and respiratory systems"

"the ventral surface of the medulla"

"inputs and the influence of the central nervous state on the responses to afferent stimuli"

Ample time was available for discussion and this was a good opportunity for informal presentation of new data and for airing of new personal views. After clarification of terms existing controversies and disagreements often proved to be of a semantic nature.

Cardiovascular effects produced by chemical and pharmacological stimulation of various areas of the ventral medullary surface provoked long discussion. Difficulties were encountered. Are the medullary chemosensitive areas primary and specifically related to the central control of respiration? On the other hand, have they more diversified functions related to the emotional defence reaction and to the general activating reticular system and to autonomic and to cardiovascular control?

Functional subdivision of the solitary tract nucleus as the main primary input for cardiovascular and respiratory afferent information was discussed. Also discussed were new facts on solitary and hypothalamic neurones sensitive to stimulation of atrial receptors. The specificity of the reticular neurones for cardiovascular and respiratory control was discussed in relation to new data on the frequencies of discharges from single reticular neurones with cardiac, respiratory and EEG frequencies. Important new ideas developed from various observations on the dependence of baroreceptor and chemoreceptor reflex responses on the phase of respiration. Confirmation of these findings, not only in different experimental animals but also in conscious man, showed that they are manifestations of basic functional interrelations between cardiovascular and respiratory control.

There was final round table discussion moderated by the three Chairmen in turn: there was ample opportunity for informal presentation of personal views and of new facts: this was most stimulating and gave rise to ideas for new research.

The Symposium made clear that the many nervous activities described represent something more than interaction between two separate control systems. Here is the expression of functional unity of a system serving adaptation to changing behavioural states. The apparent separation is due to the usual organization of groups of research workers and to conventional presentation in text books rather than to physiological reality. A new branch of Neurophysiology has emerged in recent years. This deals with the complex central nervous organization of cardiorespiratory and autonomic control. There is also close coordination with skeletomotor innervation: this is an aspect to be investigated in the future. The new approach is concerned more with analysis of features common to the entire system of adaptation than with analysis of each system separately. Those working in this new field have to be competent in Neurophysiology, in Cardiovascular physiology and in Respiratory physiology.

At the end of the Symposium many felt that this was the beginning of a promising field of Physiology: they hoped that the next International Congress would give an opportunity for a further Symposium to discuss research and to report findings.

H. P. Koepchen
A. Trzebski

REPORT FROM THE IUPS COMMISSION ON RENAL PHYSIOLOGY

A symposium on "Kidney and kidney hormones" took place in Sofia, Bulgaria, on 1-2 June 1978. This meeting was organized by the Physiological Societies of Bulgaria and of the German Democratic Republic. The outstanding organization was due to the devoted work of Professor N. Natcheff and Associate Professor O. Ikonomov and their co-workers.

Participants came from the German Democratic Republic, from the German Federal Republic, from Hungary, Rumania, Sweden, the Soviet Union and Czechoslovakia.

Three main topics were discussed:-

1 Homeostatic and transport functions of the kidney
2 Kidney hormones
3 The kidney and haemodynamics

On the programme were 8 invited lectures, 32 free communications and a few posters. The results of this advanced research work were greatly appreciated: so also was the fruitful collaboration between various groups. All participants thought it would be useful to plan similar symposia in the future.

A reception was organized for guests from each country. The Rector of the Medical University explained in detail the reformed centralized system of medical research in Bulgaria.

L. Takacs

REPORT OF IUPS REPRESENTATIVE ON ICLA

ICLA-INTERNATIONAL COMMITTEE ON LABORATORY ANIMALS
becomes
ICLAS-INTERNATIONAL COUNCIL FOR LABORATORY ANIMAL SCIENCE

At its General Assembly in the Netherlands this last August ICLA changed its title to ICLAS. The aims and activities remain largely the same.

In 1971 the Consultative Assembly of the Council of Europe put forward what is known as Recommendation 621. The recommendation deals with problems arising from use of live animals for experimental or industrial purposes. ICLAS has been considering this Recommendation for some considerable time; IUPS is obviously concerned. In addition ICLAS has other activities such as training in laboratory animal science, transport of laboratory animals, nutrition of laboratory animals, breeding of laboratory animals and conservation of primates.

Under ICLAS's constitution countries or states will be National Members each with a Representative on ICLAS: from 1980 each National Member will have to pay an annual subscription.

G. J. R. Hovell
Secretary-General of ICLAS
c/o Department of Physiology
Parks Road
OXFORD OX1 3 PT
UK

Mr. Hovell still represents IUPS on ICLAS.

REPORTS FROM CORRESPONDING EDITORS OF MEMBER SOCIETIES

AUSTRALIA

The 18th Annual General Meeting of the Society was held in Adelaide from August 28-30th, 1978 at Flinders University Medical Centre. At this meeting the Society introduced poster presentations for the first time and 11 posters were presented as well as 92 oral communications. A symposium on "Homeostasis" was arranged to commemorate the centenary of the death of Claude Bernard. Professor John B. West, University of California at San Diego, presented the APPS Invited Lecture on "Pulmonary Gas Exchange." In February 1979 the first Combined meeting with the Physiological Society of New Zealand was hosted by the Department of Physiology, University of Auckland, from February 24-26th. There was a full programme of papers and a symposium on "Control of the Circulation." The APPS Invited Lecture was given by Dr. E. A. Johnson, Duke University Medical Center on "The Genesis of the Cardiac Action Potential: Chemical and Electrical Considerations." These meetings were memorable both for their scientific content and the social events.

The Society now looks forward to the First Joint Meeting of the Australian Physiological and Pharmacological Society with the Australian Society of Clinical and Experimental Pharmacologists, University of Sydney from August 27-30th, 1979. It is planned to hold a symposium on "The Pharmacology and Sociology of Drug Dependence" and Professor Vernon Mountcastle, from The John Hopkins University, U.S.A., who will be visiting Australia at that time, has accepted our invitation to present the APPS Invited Lecture. The first meeting in 1980 will be hosted from May 12-14th, 1980, by the Department of Physiology in the University of Queensland.

The membership of the Australian Physiological and Pharmacological Society is now 370 ordinary members, 17 Sustaining members and 5 Honorary members.

Stella R. O'Donnell

BRAZIL

X CONGRESS OF BRAZILIAN PHYSIOLOGICAL SOCIETY

The Brazilian Physiological Society was founded in 1957 in Rio de Janeiro. Its first President was Professor Thales Martins, a well-known physiologist because of his work in endocrinology. In 1948 he and his colleague J. R. Valle received an international award from the "American Psychological Association" for their paper "Hormonal regulation of the micturition behavior of the dog," published in "The Journal of Comparative and Physiological Psychology" (41: 301-311, 1948).

The Society was reorganized in 1970, when a new statute was discussed and approved by the General Assembly, held in the city of Salvador during the annual meeting of the Brazilian Society for the Advancement of Science ("SBPC"). From 1970 to 1976 the Society was run by neurophysiologist Cesar Timo-Iaria (President), renal physiologist Gerhard Malnic (General Secretary), and nutritional physiologist Rebeca de Angelis (Treasurer). From 1976 to 1979 the Executive Comittee has been composed by cardiovascular physiologist Lineu Freire-Maia (President), neurophysiologist Fernando Pimentel-Souza (General Secretary), and nutritional physiologist Rocival L. Araujo (Treasurer). From 1970 to 1978 the Society organized 9 annual congresses as part of the meetings of the Brazilian Society for the Advancement of Science in the cities of Salvador (1970), Curitiba (1971), Rio de Janeiro (1973), Recife (1974), Belo Horizonte (1975), Brasilia (1976) and São Paulo (1972, 1977, 1978).

To celebrate 10 years of constant activity, the Society organized a separate congress of Physiology in the Department of Physiology and Pharmacology, Biomedical Institute, São Paulo University, São Paulo, from 9 to 11 April 1979. The local organizing committee of the X Congress of the Brazilian Physiological Society was composed by Professor Cesar Timo-Iaria, Pedro Guertzenstein and Oswaldo Lopes. At this meeting there was a total of 109 communications and 7 demonstrations, perhaps a number sufficient to warrant a short analysis of the present tendencies of Brazilian physiology. According to Prof. Timo-Iaria the several areas of Physiology were present in the Congress in different proportions, that is, neurophysiology (24.8%), comparative physiology (18.9%), endocrinology (17.6%), cardiovascular physiology (9.9%), nutrition (9.6%), respiratory physiology (5.1%), general physiology (4.5%), renal physiology (4.4%), blood (2.2%), gastrointestinal physiology (1.7%) and instrumentation (1.1%).

The following list of demonstrations also gives an idea of the type of research which some groups of Brazilian physiologists are presently doing:

1. Sodium outflow transients in the isolated toad's skin. L. H. Benevino & F. Lacaz-Vieira.
2. Constant current stimulus isolation unit: R. F. Marseillan.
3. Projecting and manufacturing some basic instruments for teaching and research in physiological sciences. C. Peres de Costa.
4. Acidification in the isolated and perfused kidney of the rat: C. R. Rubio, O. C. Mangili, G. Bento de Mello & G. Malnic.
5. On line measurements of fluid reabsorption in renal tubules: E. Malnic, C. R. Silva Neto, C. D. Stamopoulos & M. Mello Aires.

6. Effects of infusion of a hyperosmolar solution on the microcirculation of rats subjected to bleeding: I. T. Velasco, O. U. Lopes & M. Rocha e Silva Jr.
7. Involvement of derivatives of prostaglandins in aggregation of platelets; relevance and limits. B. B. Vargaftig, M. Chignard & J. Beneveniste.

The abstracts of communications and demonstrations were published in Portuguese. The Abstracts in English will appear in the second semester of 1979.

Professor Miguel R. Covian, from the Department of Physiology, Medical School, Ribeirao Preto, State of Sao Paulo, Brazil, and Member of IUPS Council, delivered an interesting lecture on "Role of the central nervous system in the regulation of sodium intake."

Professor Wilhelm Feldberg from Mill Hill, London, was to have been our special guest: but he was unable to attend. The Brazilian Physiological Society takes this opportunity to pay tribute to a great scientist, Dr. Feldberg, who trained many Brazilian Physiologists.

L. Freire-Maia

CZECHOSLOVAKIA

The scientific meetings of the Czechoslovak Physiological Society are held twice a year: in Bratislava, XLI, in February 1978: in Brno, XLII, in September 1978: in Prague, XLIII, in February 1979. Over 110 papers were read at each meeting and the scientific sessions were occupied by the following major topics:

activity of the higher nervous centres: ontogenesis of the Central Nervous System: neurochemistry: physiology of muscle fibers: interaction of circulation and respiration: renal physiology: thermogenesis: endocrinology and metabolism: methods used in physiology: physiology of work and exercise.

During these meetings special sessions and panel discussions were organised under the chairmanship of Professor A. Kucera, Olomouc, on the problems of teaching physiology in a medical school.

The Purkyne memorial lectures which opened the meetings were given by S. Tucek on "Biosynthesis of acetylcholine," by L. Jansky on "Nonshivering thermogenesis" and by Daria Zacharova on "The role of internal membrane systems on activation of muscle contraction." Summaries of the papers are published in English in "Physiologia Bohemoslovacca."

The Slovak Physiological Society, a branch of the Federal Czechoslovak Physiological Society, organizes regular bimonthly monothematic seminars with 4 to 5 lectures on recent results of research in the Physiological Institutes of Slovakia.

The tenth session of the Problem Commission of "Interbrain" took place in Smolenice near Bratislava in June 1978. The scientific part of the session dealt with the basic principles which regulate nervous systems at subcellular, cellular and intercellular level. Plans were drawn up for multilateral cooperation during the years 1979-1980.

A Centre for Physiological Sciences was established in the Slovak Academy of Sciences on January 1, 1979 in Bratislava. To form the Centre five Institutes were joined:

normal and pathological physiology: experimental endocrinology: experimental pharmacology: experimental surgery: neurobiology.

The Chairman of the Science Board for this Centre is Academician J. Zachar. The main programme of research by the scientific teams working in the Centre deals with membrane and intracellular receptors and channels for ions in membranes.

L. Macho

EGYPT

The Venom Research Project was initiated by Professor Dr. A. H. Mohamed in the Faculty of Medicine of Ain Shams University. Support was received from the National Institutes of Health at Bethesda, Maryland, U.S.A. Progress since 1962 has been so satisfactory that Ain Shams University has recently established a Venom Research Center still supported by the National Institutes of Health in Bethesda. This Center will support research in all Departments preparing improved polyvalent antivenins to protect those attacked in Egypt, in Africa and in the Middle East.

The chief collaboration is between the Department of Neurological and Communicative Disorders and Stroke at Bethesda and the Departments of Physiology, Pharmacology, Biochemistry, Immunology, Toxicology, Histopathology and Anatomy at Ain Shams University. Dr. Richard L. Irwin is the Director of the Department at the National Institute of Health, Dr. Ahmed Hassan Mohamed, who is a Physiologist, controls the Venom Research Project and directs the Venom Research Center.

The Egyptian Physiological Society now engages in all types of physiological activity, especially those activities, be they the physiology of man, of animals or of plants, which have a bearing on the welfare of the human population.

A. H. Mohamed

FINLAND

In 1977 the Finnish Physiological Society arranged five general assemblies in which 49 scientific lectures were given by foreign and Finnish physiologists. A special series of lectures on the Physiology and Pharmacology of the Circulatory System was held in Helsinki in May 1976 with 15 lectures and 63 participants. At the XXVII International Congress on Physiological Sciences in July 1977 in Paris the Society participated in the Symposium on Teaching in Physiology. The Finnish Physiological Society volunteered to arrange the 1986 International Congress on Physiological Sciences in Finland. In January 1978, in conjunction with the Finnish Medical Association, the Society organized a postgraduate training course in Circulatory Physiology in Helsinki. The course was supervized by Professor Leo Hirvonen, M.D. and Associate Professor Martti Hakumaki, M.D. members of the Society and over 100 practitioners and clinicians took part. In April 1978 the Finnish Physiological Society organized a meeting on Information in Sports Physiology at Kuopio University by our member Professor Osmo Hanninen, M.D. Over 30 press-editors and physiologists participated in the meeting.

In May 1978 the Society had its spring meeting at the Department of Physiology, University of Oulu (65°N). The program consisted of a discussion on intensive teaching in Physiology and scientific lectures. The Departments of Physiology and Pharmacology at Oulu University are organizing the XVIth Scandinavian Congress of Physiology and Pharmacology on 25-28 June 1979 in Oulu and about 500 participants are expected to attend the congress. In September the Society will arrange a meeting in

Tampere for young physiologists, at which short research reports from various areas of physiology will be presented.

In 1977 the Society also made a study of the research interests of Finnish physiologists: 16.7% were studying neurophysiology, 16.1% biology, 7.1% circulatory physiology or comparative physiology, 6.1% the environment, 5.4% muscle and exercise with less than 5% in each of the remaining areas.

Juhani Leppäluoto
Secretary

INDIA

The XXIV Annual meeting of the Association of Physiologists and Pharmacologists of India (APPI) was held in R.N.T. Medical College, Udaipur, Rajasthan, from December 27-29, 1978 with Prof. M. L. Gupta as Chairman and Professors K. P. Singh and L. K. Kothari as the Organizing Secretaries of the Conference. The highlights of the conference included the symposia on "Indigenous drugs in clinical medicine: problems and possibilities," "Human andrology," and "Technology of teaching basic medical sciences." In addition, a series of invited lectures, and over 180 Free-communications and poster sessions were held. The prestigious Maj. Gen. S. L. Bhatia Oration was awarded to professor K. N. Sharma, and D. R. Bajaj Research Prize for techniques to Dr. R. L. Bijlani.

The Membship of the A.P.P.I. stands at over 650 during the present year. Over 20 local chapters (branches) have been working in different cities of the country. The members periodically meet for scientific deliberations and the proceedings of these local branches are sent to the General Secretary, A.P.P.I. With the creation of an endowment for Subsistence Allowance Fund for younger scientists about 30 delegates were given subsitence allowance to enable them to attend the annual meeting.

During the year, a laboratory teaching workshop was organized in July in which about 40 participants from India and neighbouring regions participated. A Winter School on Neurophysiological and Neurochemical Correlates of Behaviour has also been organized from Feb. 19 to 28 followed by an International Symposium on Aggressive Behaviour held from March 1 to 4, 1979. The Faculty in the Winter School consisted of experts from U.S.A., U.K., Italy, and Australia besides from the host country.

It is planned to hold the Silver Jubilee meetings of A.P.P.I. in December 1979 in which an International Symposium is being planned to be organized.

K. N. Sharma

JAPAN

Establishment of the National Center for Biological Sciences: The National Center for Biological Sciences (President: Dr. Yasuji Katsuki) was established May 2, 1977, as the sixth of a series of cooperative organizations in Japan. The Center is responsible for integrating research in basic biology and physiology and of contributing to the development of academic research in cooperation with the Nation's Universities.

The Center, located in Okazaki City, Aichi Prefecture, consists of the National Institute for Basic Biology (Director: Dr. Masujiro Kuwahara) and the National Institute for Physiological Sciences (Director: Dr. Koji Uchizono).

A general characteristic of the Center is that both Institutes are involved to the same category of biological science, the fundamental study of life sciences. Therefore, the fact that they are located in the same area helps researchers to exchange information and opinions with each other for their mutual benefit and to widen their vision further. It is planned that the National Institute for Molecular Sciences, established in 1975 in the same area, will join the Center in the near future. These three Institutes will be reorganized as a general center for biological research, which is a new concept attempted for the first time in Japan. Those concerned are all eagerly looking forward to the results which are expected to affect greatly the future of academic organization in Japan.

The Center sponsors national and international symposia and supports national and international cooperative research programs. It is actively interested in academic interchange in the fields of basic biology and physiology. The Center is available for use by staffs of universities which are engaged in related research.

On request of universities, the Center cooperates in accepting and educating post-graduate students and postdoctoral fellows, not only within the nation but also from abroad.

The budget for 1977 and 1978 is ¥635,043,000, exclusive of personnel expenditure. The building will be completed in 1981.

The Objectives and Characteristics of the National Institute for Physiological Sciences: The Institute has as its ultimate object promotion of all aspects of human life activity, analysis of the natural laws of physiological functions and investigation of the functions of human beings and higher animals. The main subjects are divided into four project departments, consisting of 13 divisions as indicated below.

Department	Division
1 Molecular Physiology	1. Ultra Fine Structure
	2. Intracellular Metabolism*
	3. Neural Chemistry
2 Cell Organ System	4. Cell Membrane
	5. Functional Correlation
	6. Active Transportation*
3 Bio-Information	7. Neural Information
	8. Humoral Information
	9. Higher Neural Organization*
	10. Information Memory*
4 Bio-Regulation System	11. Higher Nervous Regulation
	12. Higher Humoral Regulation
	13. Biological System Technology

Of all, four divisions (marked *) are under visiting professorships. Besides these academic departments, there is a technical department consisting of various workshops to be used in common by the researchers. The division of Intracellular Metabolism (2. above), of Neural Information (7. above) and of Higher Nervous Regulation (11. above) started to function on April 1, 1978. The division of Ultra Fine Structure (1. above), of Cell Membrane (4. above) and of Higher Neural Organization (9. above) have been functioning since May 1977.

Y. Oomura

UNITED KINGDOM

On occasion the physiologists of the United Kingdom take time off to wonder where they are going. What will happen to the individual physiologist? And what's going to happen to the discipline he professes?

The physiologist is being diminshed both in his teaching and research, he is becoming sadly dependent on others.

In the not so distant past all the competent lecturer required was a large blackboard and a piece of chalk: if he were a Sybarite he equipped himself with coloured chalks. On rare occasions he indulged himself by showing a few large lantern slides mounted by himself.

Now the modern lecturer is furnished with a clutter of sophisticated audio-visual aids: a microphone is on the lecture desk, loud speakers hide in niches on the walls. A film camera stands by to photograph an experiment on the theatre floor for simultaneous display on the monitors which also grace the walls. The simple lantern of the past is replaced by a film projector, the place of the lantern slides is taken by film shot in the Department by a photographer on the departmental staff.

How much more does the listener and viewer learn by exposure to such an array of gimmickry? Some time ago Sir Lindor Brown, with characteristic impishness, showed an instructional film to his class. Immediately thereafter he handed out an examination question paper based on the film. The majority of the students had learned mighty little from the film.

Now what about the physiologist as research worker? Is he diminished also in this capacity? Once upon a time the physiologist was master of his work. From preparing solutions, fitting up apparatus, wiring simple electrical circuits, smoking the kymograph paper, supervising personally the progress of the experiment to the final varnishing of the kymograph paper he was in full and sole command.

Now the physiologist in his research capacity is a poor thing pathetically dependent on technicians and technologists. He buys off the shelf the stimulators and recorders which spew forth yards of paper. His apparatus is of a complexity wholly beyond his understanding, apparatus he cannot repair in an emergency. Of course he can comfort himself with the thought that his is the brain, his the knowledge, behind the design of the experiment. Nevertheless, in much of his activity he is a servile dependent creature, cribbed, cabined and confined by the capabilities of his equipment and by the expertise of his back-up staff.

What now is to be the fate of Physiology, the Discipline? Physiology is expanding and simultaneously being eroded. Sectional interests are proliferating, lusty, imperious offspring: they hive of, in the slang phrase, to do their own thing. As they go they filch from their parent, Physiology, and leave a sadly tattered spectre behind.

The Physiological Sciences are of vital importance for mankind in every walk of life. As long ago as 1972 our Society published a pamphlet "Physiology as an Education and as a Career." This booklet drew attention to the importance of a knowledge of Physiology for the welfare of mankind and, indeed, of the whole animal kingdom. If civilisation pays heed to physiological principles there will be less need for the therapy of Medicine. So here is scope for education, for teaching and for research.

However, a knowledge of integrated Physiology, not of specialist bits and pieces, is a simple need in Medical School. Who is going to do the teaching, where is it to be carried out?

So worried was our Physiological Society that it recently looked into this problem by appointing a "Commission on the future of teaching and research in Physiology in the U.K.." The Commission reported in a 15-page pamphlet which was discussed at a special meeting of our Society. What we were really asking was:

Is it desirable that a teacher of Physiology have a medical qualification?

In the United Kingdom the number of pre-clinical teachers with a training in Medicine is rapidly decreasing: pre-clinical work has not the emotional appeal of clinical work, neither has it the primitive satisfaction of care and rehabilitation of the sick. Pre-clinicians are not so well paid as clinicians. In these ways a medical qualification draws able individuals away from Physiology and consequently has a downright detrimental effect on Physiology.

But is a qualification in Medicine alone adequate for teaching and research in Physiology? The medical curriculum usually has a rather shabby foundation in the Basic Sciences: much time is spent in repetitive acquisition of dexterity and experience of little value to a physiologist. Nevertheless, the medical curriculum does give a valuable introduction to Pathology and Pharmacology both of major value to any physiologist. And an introduction to Pathology is not easily come by outside the medical curriculum.

But what is the reaction of the taught, of the medical students who still are in the majority in pre-clinical lecture theatre and laboratory? Be very sure that they know who among their teachers has had clinical experience and they set store by such experience. We heard of one ancient seat of learning where undergraduates demanded to be taught Physiology only by those with a medical qualification.

Recently an attempt has been made to give lecturers, without a training in Medicine, a crash course on the importance of physiological knowledge in the practice of Medicine. Is there not something faintly meretricious and objectionable in asking a teacher to colour up his discourse in such fashion? Is it desirable that he be expected to spell out to his pre-clinical class why it should take its pre-clinical studies seriously? A sorry state of affairs when we have to coax the young to learn.

Our Commission concluded "that physiology departments which teach medical students should have a substantial proportion, say 30-60%, of medically qualified members on their teaching staffs." Another significant recommendation was "the emphasis should be not on persuading medically trained people to become physiologists but on persuading physiologists and potential physiologists to obtain a medical qualification." Fair enough if one can envisage such a physiological trainee sweating it out in a conventional Anatomy Department.

We are saying then that Physiology still has a filial duty, but not complete subservience, to the Art of Medicine and Craft of Surgery which gave us birth as "The Institutes of Medicine" in the University of Edinburgh as long ago as 1724.

R. C. Garry

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