

# THE AMERICAN PHYSIOLOGICAL SOCIETY

Founded in 1887 for the purpose of promoting the increase of physiological knowledge and its utilization.

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# The Physiologist

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

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## PROPOSED BYLAWS AMENDMENTS TO BE VOTED ON AT SPRING BUSINESS MEETING

Amendments will be presented for consideration by the membership at the Spring Business Meeting in Dallas as recommended by Council. Current Bylaws are published in their entirety on pages 1 – 3.

To dignify the designation of "Retired" member, the amendment to be considered is :

### ARTICLE III. Membership

SECTION 6. ~~Retired~~ Emeritus Members. A regular member or associate member, who has reached the age of sixty-five (65) years and/or is retired from regular employment may, upon application to Council, be granted ~~retired~~ emeritus status

The proposed amendment for Student membership resulted from a proposal to amend the Bylaws that was tabled at the 117th Business Meeting (April 1977). The following amendment to be considered is:

### ARTICLE III. Membership

SECTION 7. Student Members. ~~Any Graduate students who is actively engaged in physiological work as attested to by two regular members of the Society and who have completed their preliminary examination for the doctoral degree provided they are a residents of North America. No individual may remain in this category for more than five years/, without reapplying.~~

This Bylaw is intended to open Student membership to all predoctoral students, including undergraduates where appropriate when such students are significantly engaged in physiological work and wish to become identified with the activities of the Society and its members.

CONSTITUTION AND BYLAWS  
(Adopted April 1953, as amended April 1977)

CONSTITUTION

ARTICLE I. *Name*

The name of this organization is THE AMERICAN PHYSIOLOGICAL SOCIETY.

ARTICLE II. *Purpose*

The purpose of the Society is to promote the increase of physiological knowledge and its utilization.

BYLAWS

ARTICLE I. *Principal Office*

SECTION 1. The Society shall have its principal place of business at 9650 Rockville Pike, Bethesda, Maryland 20014. The Central Office shall house all activities delegated to the employees of the Society.

ARTICLE II. *Corporate Seal*

SECTION 1. The corporate seal of the Society shall be a circle surrounded by the words, THE AMERICAN PHYSIOLOGICAL SOCIETY. The seal shall also show the founding date and the date and place of incorporation.

SECTION 2. The Executive Secretary-Treasurer shall have custody of the seal. It shall be used on all official documents requiring it, and shall be placed on the documents by the Executive Secretary-Treasurer upon approval by Council.

ARTICLE III. *Membership*

SECTION 1. The Society shall consist of regular members, corresponding members, honorary members, associate members, retired members, student members, and sustaining associates.

SECTION 2. *Regular Members.* Any person who has 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.

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.

SECTION 4. *Honorary Members.* Distinguished scientists of any country who have contributed to the advance of physiology shall be eligible for proposal as honorary members of the Society.

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.

SECTION 6. *Retired Members.* A regular member or associate member, who has reached the age of sixty-five (65) years and/or is retired from regular employment may, upon application to Council, be granted retired member status.

SECTION 7. *Student Members.* Graduate students in physiology who have completed their preliminary examinations for the doctoral degree provided they are residents of North America. No individual may remain in this category for more than five years.

SECTION 8. *Sustaining Associates.* Individuals and organizations who have an interest in the advancement of biological investigation may be invited by the President, with approval of Council, to become sustaining associates.

SECTION 9. *Nominations for Membership.* Two regular members of the Society must join in proposing a person for regular membership, corresponding membership, honorary membership, associate membership, or student membership, in writing and on forms provided by the Executive Secretary-Treasurer. In the nomination of corresponding members, a corresponding or honorary member of the Society may substitute for one of the regular members in proposing a person for corresponding membership. The Membership Committee shall investigate their qualifications and recommend nominations to Council. Council shall nominate members for election at the Spring and Fall meetings of the Society. A list of nominees shall be posted for consideration by the members attending the meeting two days prior to the Business Meeting at which the election occurs.

SECTION 10. *Election of Members.* Election of regular members, corresponding members, honorary members, associate members, and student members shall be by secret ballot at Spring and Fall Business Meetings of the Society. A two-thirds majority vote of the members present and voting shall be necessary for election.

SECTION 11. *Voting.* Only regular members shall be voting members. Corresponding, honorary, associate, and retired members shall have the privilege of attending Business Meetings of the Society but shall have no vote.

ARTICLE IV. *Officers*

SECTION 1. *Council.* The management of the Society shall be vested in a Council consisting of the President, the President-Elect, the immediate Past-President, and four other regular members. The terms of the President and of President-Elect shall be one year. The terms of the four additional Councillors shall be four years each and they shall not be eligible for immediate reelection except those who have served for two years or less in filling interim vacancies.

A quorum for conducting official business of the Society shall be five of the seven elected members of Council.

The Chairman of the Publications Committee, the Chairman of the Finance Committee, and the Executive Secretary-Treasurer are ex officio members of the Council without vote. The Council may fill any interim vacancies in its membership. Council shall appoint members to all committees.

SECTION 2. *President.* A person shall serve only one term as President, except that if the President-Elect becomes President after September 30 he shall continue as President for the year beginning the next July 1. The President shall chair all sessions of the Council and Business Meetings of the Society and shall be an ex officio member of all Committees without vote.

SECTION 3. *President-Elect.* The President-Elect shall serve as Vice-President of the Society and as official secretary of the Council. Should he have to function as President prematurely, the Council shall select from among its own members an official secretary.

SECTION 4. *Election of Officers.* Nominations for President-Elect and for members of Council will be made by mail

ballot on forms provided by the Executive Secretary-Treasurer, before February 1 of each year. Each member may nominate no more than one candidate for each office. If a member wishes to nominate a certain person for President-Elect and for Council he must nominate that individual for each position. The ten candidates that receive the highest number of nominating votes will appear on the appropriate ballot for President-Elect or for Council.

Election of the President-Elect and members of Council will be made by mail ballot on forms provided by the Executive Secretary-Treasurer, prior to April 1 of each year. Each voting member must indicate on the ballot his rank preference for all of the candidates on each ballot. The ballots will be counted according to the Election Plan. Two ballots, one for President-Elect and one for Council will be mailed together. The results of the election will be announced at the Spring Meeting of the Society and the newly elected officers will take office on July 1 following their election.

SECTION 5. *Executive Secretary-Treasurer.* The Council shall be empowered to appoint and compensate an Executive Secretary-Treasurer who shall assist it in carrying on the functions of the Society including the receipt and disbursement of funds under the direction of the Council. He shall be responsible for management of the Central Office of the Society under general supervision of the Council.

#### ARTICLE V. *Standing Committees*

SECTION 1. *Publications Committee.* A Publications Committee composed of three regular members of the Society appointed by Council shall be responsible for the management of all of the publications of the Society. The term of each member on the Publications Committee shall be three years; a member may not serve more than two consecutive terms. The Council shall designate the Chairman of the Committee who shall be an ex officio member of the Council, without vote. Council is empowered to appoint and compensate a Publications Manager who shall assist in carrying out the functions of the Publications Committee under the supervision of the Executive Secretary-Treasurer. The President, Executive Secretary-Treasurer and the Publications Manager shall be ex officio members of the Publications Committee, without vote. The Committee shall have the power to appoint editorial boards for the Society's publications. The Committee shall present an annual report on publications and policies to the Council for approval and present an annual budget coordinated through the Executive Secretary-Treasurer, to the Finance Committee for its approval and recommendation to Council.

SECTION 2. *Finance Committee.* A Finance Committee, composed of three regular members of the Society appointed by Council, shall receive the total coordinated budget proposals annually from the Executive Secretary-Treasurer and shall determine the annual budgets, reserve funds and investments of the Society, subject to approval by Council. The term of each member of the Finance Committee shall be three years; a member may not serve more than two consecutive terms. The Council shall designate the Chairman of the Committee who shall be an ex officio member of the Council, without vote. Council is empowered to appoint and compensate a Business Manager who shall assist in carrying out the functions of the Finance Committee under the supervision of the Executive Secretary-Treasurer. The President-Elect, Executive Secretary-Treasurer, the Chairman of the Publications Committee, and the Business Manager shall be ex officio members of the Finance Committee, without vote.

SECTION 3. *Membership Committee.* A Membership Committee, composed of six or more regular members of the Society appointed by Council, shall receive and review processed applications for membership and make recommendations for nomination to the Council. The term of each member of the Membership Committee shall be three years; a member shall not be eligible for immediate reappointment. The Chairman of the Committee shall be designated by the Council.

SECTION 4. *Education Committee.* An Education Committee, composed of five or more regular members of the Society and representatives of such other societies as may be designated by the Council appointed by Council, shall conduct such educational, teaching and recruitment programs as may be required or deemed advisable. The term of each member of the Education Committee shall be three years. The Chairman of the Committee shall be designated by the Council. The Executive Secretary-Treasurer may act as Executive Director of the educational programs with approval of the Council. The Committee shall present an annual report to the Council and an annual budget through the Executive Secretary-Treasurer to the Finance Committee for its approval.

SECTION 5. The Council may appoint such special and other standing committees as it deems necessary or that are voted by the Society. The Council may name regular members of the Society as representatives to other organizations whenever it deems such action desirable.

SECTION 6. *Term of Office of Chairman.* The Chairman of a standing committee may serve one full term in that capacity in addition to any consecutive term as a committee member limited by other provisions of these Bylaws.

#### ARTICLE VI. *Dues*

SECTION 1. *Annual Dues.* The annual dues for regular members, corresponding members, associate members and student members shall be determined by the Council and shall be paid in advance of July 1. Honorary members and retired members shall pay no membership dues.

SECTION 2. *Non-payment of Dues.* A regular member, corresponding member, associate member or student member whose dues are two years in arrears shall cease to be a member of the Society, unless, after payment of his dues in arrears and application to the Council, he shall be reinstated at the next meeting by vote of the Council. It shall be the duty of the President-Elect to notify the delinquent of his right to request reinstatement.

SECTION 3. *Retirement.* A regular member, corresponding member, or associate member who has been granted retired membership status is relieved from the payment of dues but retains the other privileges of his former membership status, except voting privileges.

#### ARTICLE VII. *Financial*

SECTION 1. *Society Operating Fund.* The Society Operating Fund shall consist of all funds, other than Publication Operating Funds and Publication Contingency and Reserve Funds, restricted or unrestricted, uninvested or invested, short or long term. The Executive Secretary-Treasurer shall be the responsible agent to the Council with signatory powers. Signatory powers may be delegated to the Business Manager by the Executive Secretary-Treasurer.

SECTION 2. *Publications Operating Fund.* The Publications Operating Fund shall consist of all funds that involve receipts, expenses, short-term investments relating to the

annual receipts, disbursements and continuing operation of the Society's publications. The Executive Secretary-Treasurer shall be the responsible agent to the Council with signatory powers. Signatory powers may be delegated to the Publications Manager and/or the Business Manager by the Executive Secretary-Treasurer.

**SECTION 3. *Publications Contingency and Reserve Fund.*** The Publications Contingency and Reserve Fund shall consist of the long-term capital investments of publication earnings. The Executive Secretary-Treasurer, with advice from the Finance Committee, shall have discretionary and signatory powers, except for withdrawals. Authority for any withdrawal from this fund shall require the following five signatures: 1) The Chairman of the Publications Committee (Alternate, the senior member of the Committee); 2) The President of the Society (Alternate, the President-Elect); 3) The Executive Secretary-Treasurer (Alternate, the Publications Manager); 4) and 5) Any two members of Council. The Finance Committee shall not recommend to Council the expenditure of any of this capital fund for non-publication purposes without the consent of the Publications Committee. The Finance Committee shall be responsible for the separate investment of the reserve fund for publications; any capital gains from such investment shall accrue to the fund (capital losses will, however, reduce its value). Any dividends, interest or income, other than capital gains, from this invested fund may be used for emergency support of any of the activities of the Society, including publications, as determined annually by the Council but the primary goal shall be to increase the investment capital.

**SECTION 4. *Fiscal Year.*** The official fiscal year shall be from January 1 through December 31.

**SECTION 5. *Audit.*** All statements of net assets and related statements of income, expenditures and fund capital shall be audited annually by an independent auditing firm.

**SECTION 6. *Bonding.*** All persons having signatory powers for the funds of the Society shall be bonded.

## **ARTICLE VIII. *Publications***

**SECTION 1.** The official organs of the Society shall be the American Journal of Physiology, the Journal of Applied Physiology, Physiological Reviews, the Journal of Neurophysiology, The Physiologist, and such other publications as the Society may own. All publications shall be under the jurisdiction and management of the Publications Committee unless otherwise designated by the Council. The names of the journals and publications may be changed by the Council on recommendation from the Publications Committee and any publication may be dropped by Council on recommendation from the Publications Committee.

## **ARTICLE IX. *Meetings***

**SECTION 1. *Spring Meeting.*** A meeting of the Society for transacting business, electing officers and members, presenting communications, and related activities, shall ordinarily be held in the Spring of each year.

**SECTION 2. *Fall Meeting.*** A Fall meeting of the Society shall be held at a time and place determined by the Council for presenting communications, electing members, and for transacting business except for the election of officers and adoption of amendments to the Bylaws. Under exceptional circumstances Council may cancel such a meeting.

**SECTION 3. *Special Meetings.*** Special meetings of the

Society or of the Council may be held at such times and places as the Council may determine.

**SECTION 4. *Quorum.*** At all Business Meetings of the Society fifty regular members shall constitute a quorum.

**SECTION 5. *Parliamentary Authority.*** The rules contained in Roberts Rules of Order, Revised, shall govern the conduct of the Business Meetings of the Society in all cases to which they are applicable and in which they are not inconsistent with the Bylaws or special rules of order of the Society.

## **ARTICLE X. *Society Affiliations***

**SECTION 1.** The Society shall maintain membership in such organizations as determined by Council.

## **ARTICLE XI. *Regulations***

**SECTION 1. *General Prohibitions.*** Notwithstanding any provision of the Constitution or Bylaws which might be susceptible to contrary interpretation:

- a. The Society is organized and operated exclusively for scientific and educational purposes.
- b. No part of the net earnings of the Society shall or may under any circumstances inure to the benefit of any member or individuals.
- c. No substantial part of the activities of the Society shall consist of carrying on propaganda, or otherwise attempt to influence local, state or national legislation. (All activities of the Society shall be determined by Council). The Society shall not participate in, or intervene in (including the publishing or distributing of statements) any campaign on behalf of any candidate for public office.
- d. The Society shall not be organized or operated for profit.

**SECTION 2. *Distribution on Dissolution.*** Upon lawful dissolution of the Society and after payment of all just debts and obligations of the Society, Council shall distribute all remaining assets of the Society to one or more organizations selected by Council which have been approved by the United States Internal Revenue Service as organizations formed and dedicated to exempt purposes.

## **ARTICLE XII. *General***

**SECTION 1. *Records.*** All official records, archives and historical material shall be held in the Central Office in the custody of the Executive Secretary-Treasurer.

**SECTION 2. *Procedures and Customs.*** The Society shall maintain a current Operational Guide detailing the procedures and current customs of the Society operations as well as the duties and responsibilities of officers, committees, and major employees. The Operational Guide shall be maintained current by the Executive Secretary-Treasurer as determined by the Council.

## **ARTICLE XIII. *Amendments***

**SECTION 1. *Presentation.*** Amendments to these Bylaws may be proposed in writing, by any regular member, to Council at any time up to three months in advance of the Spring Meeting, or at a Business Meeting of the Society. Such proposed amendments must be presented in writing at the following Spring Business Meeting for action by the Society.

**SECTION 2. *Adoption.*** These Bylaws may be amended at any Spring Business Meeting of the Society by a two-thirds majority vote of the regular members present and voting.



Henry Cuthbert Bazett was named President-Elect at the Detroit meeting of the Society in April 1949 and assumed office as President after the 1950 meeting in Atlantic City. Unfortunately, he is the only President who never presided at a meeting of the Society. On the way to the International Congress in Copenhagen in July 1950, he died of a heart attack on the boat. His term of office was short but he served the Society as President-Elect for one year, as member of the Council for two years, and as a member of the Board of Publication Trustees for six years. His tragic death is, therefore, all the more reason for including him in this historic account of the Society Presidents.

Dr. Bazett was born in Gravesend, England, June 25, 1885, and was educated at Oxford where he received a B.A. in 1908, M.B. and B.Ch. in 1911, M.S. in 1913, M.D. in 1919, and L.R.C.P. and F.R.C.S. in 1911. He received an honorary D.Sc. from Western Ontario in 1945. After various appointments in England and an experience as medical officer in the Army during the First World War, he came to this country as Professor of Physiology at the University of Pennsylvania in 1921, the position which he held at the time of his death. He received the Cheselden Medal from St. Thomas Hospital in 1911, the Military Cross of Great Britain in 1915, Officer of the Order of the British Empire in 1915, and Commander in 1946. He was a member of the Canadian Committee on Aviation Medicine Research from 1941 to 1943 and President of the Philadelphia Physiological Society in 1924. He was interested in decerebrate animals, temperature control, circulation, and blood volume. He must have learned from Haldane his tolerance for drastic experiments on himself for he had thermocouples inserted into himself at various depths and in every available blood vessel (except, he insisted, the internal carotid artery) in order to record the temperature gradients.

The sensation of cold was another of his interests. In that connection, he once related to the writer an account of one of his experiences as a medical officer in the British Army. During the first battle of Ypres, he suffered an attack of acute appendicitis. He

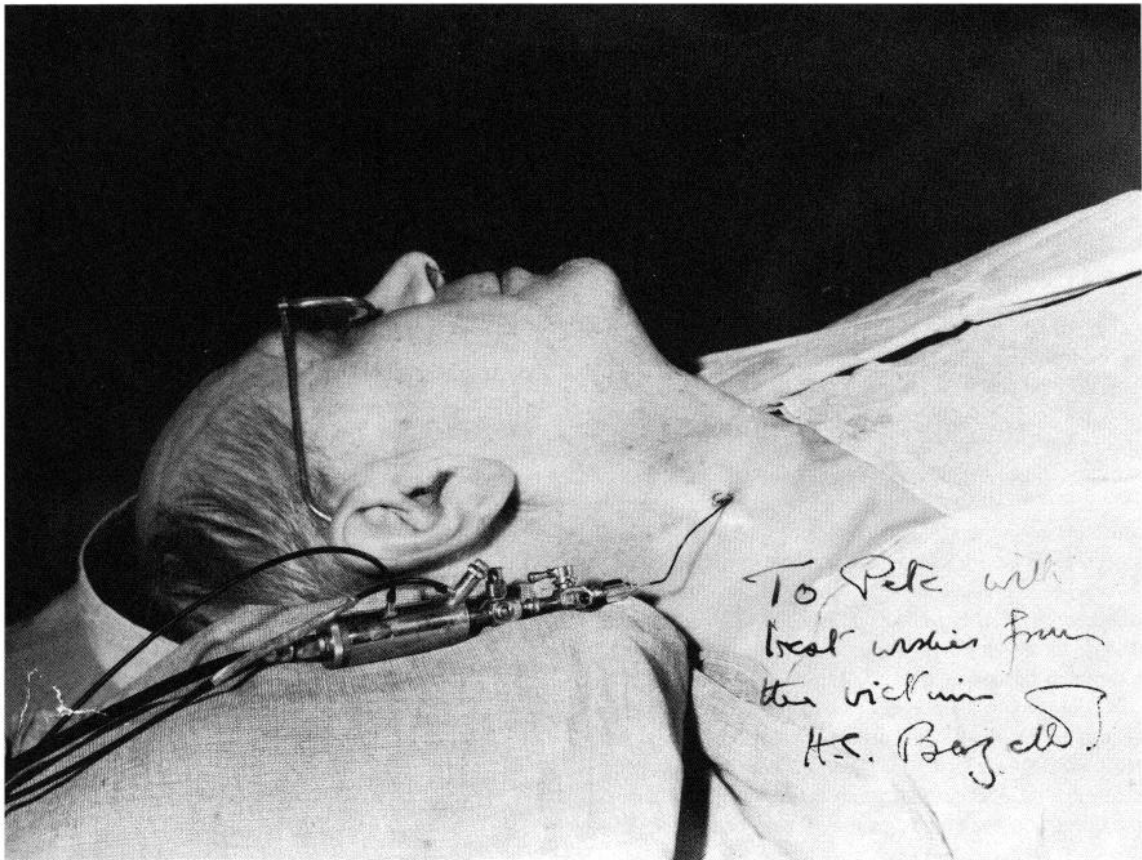
was operated on in a tent at the front and the appendiceal abscess was drained. He was not expected to survive and the number of wounded to be evacuated was so great that he was left unattended in the unheated tent until he was found by a friend belonging to the same medical unit who had him transferred to a base hospital. Bazett regarded this as a fine experiment on the effects of cold on shock.

Even in his last years he was quite vigorous and the writer remembers very clearly an early morning swim with him at the hotel in Augusta during the Fall meeting in 1949. As President-Elect, he was in high spirits and was diving repeatedly with great enthusiasm and enjoyment. The writer also served with him for six years on the Board of Publication Trustees under the chairmanship of Walter Meek and learned to value highly his companionship and his good judgment.

Dr. Bazett was one of the leaders in bringing about the organization of the International Union of Physiological Sciences and was an official delegate to the meeting in Copenhagen for the purpose (although he did not live to attend this meeting). He was also chairman of the Society's Committee on Scientific Aid and had collected over \$600 and many books and some equipment for distribution to needy physiological laboratories in Europe. The following year, the collection was continued (by Dr. Walter Root, who succeeded him as chairman) "in honor of Dr. Bazett" and an additional \$2,000 was collected. This committee was eventually discontinued but it served a very important purpose and many foreign laboratories profitted by Dr. Bazett's inspired efforts on their behalf. His enthusiasm for good causes was infectious and he was highly respected by his colleagues as his election to the presidency amply testifies.

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Taken from "History of the American Physiological Society, The Third Quarter Century, 1937-1962" by Wallace O. Fenn.



Between 1949 and 1950, when this picture was snapped, the human arterial system was plumbed extensively within Henry Cuthbert Bazett's physiology department at the University of Pennsylvania. There were then no federally mandated committees to mastermind human research. One simple policy, that investigators and subjects were one and the same, required only that there must be one more investigator than was needed to investigate.

Dr. Bazett insisted that he was more curious about his own cardiovascular system than he was about those of his juniors. Our trio (Hugh Fitzpatrick, Truman "Nipper" Schnabel, Jr., and I) of that great, but sadly last, year with Professor Bazett held a different view. He really wanted to instill in us the sense of responsibility that comes with inserting a long catheter into another human being's arteries, and we were especially moved by the fact that this subject was our chief and an internationally

famous one at that. It should be recalled that not only were these procedures not commonplace, but indeed hardly had they been done at all. We were pleased that no catheter was ever set free and lost within an artery; however, one fast-acting hemostat did catch one catheter, together with Dr. Bazett's brachial nerve, between its blades.

Stimulated curiosity, investigative strategy, excitement, challenge, and admiration were everyday experiences of all who had the privilege of beginning their careers with that great physiologist and friend. It also was a time that ushered in a golden period of national zeal for basic physiological investigation. Bazett saw the financial support for research turn from severe austerity to the beginning of adequacy, and he predicted its tidal nature. (Lysle H. Peterson)

[I am especially pleased to have the privilege of submitting this picture and a brief accompanying note about Cuthbert Bazett. Although this is not going to be the usual type of picture, it will certainly capture the whole philosophy of his professional life, which was to participate as the subject in virtually every experiment in which he was involved. There is the well-known series of experiments involving the definition of temperature receptors in which he used his prepuce in order to create a controlled temperature differential across the skin. We also utilized minute thermocouples mounted in 1 mm intravascular catheters to measure the temperature differentials in the peripheral veins. Again, we were all subjects, but he was always the first.

I was a medical student in those days and developed the small intra-arterial and intravenous catheters. I was indeed fortunate as a medical student to have Cuthbert Bazett give me a laboratory and make me feel part of the department and team.]

Lysle H. Peterson, M.D.  
Professor of Physiology  
University of Texas Health  
Science Center  
Houston, Texas

In the Spring of 1979 the first volume, entitled *The Heart*, in the revision of the *Handbook of Physiology* section on circulation will be published. Examination copies will be available at the Dallas meeting of the Society. Look for a brochure in the mail, so that you can order a copy at Society member discount prices.

What follows is taken from the preface to this first volume, Robert Berne, Editor, and Nick Sperelakis, Associate Editor. It indicates the aims and contents of the revised section and the first volume.

The first edition of the *Handbook of Physiology* section on *Circulation* appeared between 1962 and 1965. This publication of the American Physiological Society consisted of three volumes that covered many aspects of the physiology of the heart and circulation. Since that time knowledge has advanced slowly in some areas of physiology, more quickly in others. Meanwhile the total body of information has grown almost exponentially, making it increasingly difficult to organize and meld old and new data to provide the reader with a comprehensive, critical appraisal of cardiovascular physiology. Nevertheless, the aim of the revised second *Handbook* section, retitled *The Cardiovascular System*, is to accomplish these goals and produce authoritative reference works with extensive bibliographies. The book will be useful to students of physiology at all stages of study, to professional physiologists, and to interested scientists in related disciplines. The utility of the *Handbook of Physiology, Circulation* has been proved by its continued and ongoing use by many investigators and teachers, a condition the editors hope will also be true for this revision.

*The Cardiovascular System* will consist of five volumes on the heart, vascular smooth muscle, the microcirculation, the peripheral and organ system circulation, and cardiovascular pathophysiology. It is anticipated that these volumes will be published within the next three to four years and will cover all aspects of cardiovascular physiology.

The first volume in the section on the cardiovascular system is entitled *The Heart*. It consists of twenty-five chapters that provide a broad coverage of normal cardiac function. The volume is divided into seven sections: 1) Development and Morphology of the Heart, 2) Electrophysiology, 3) Cardiac Contraction, 4) Neural Factors in Cardiac Function, 5) Humoral Factors in Cardiac Function, 6) Myocardial Metabolism, and 7) Myocardial Blood Supply. The section on morphology includes three chapters on the embryology, cellular interactions, and biochemical changes during development of the heart, one chapter on gross morphology and histology, and one chapter on cardiac ultrastructure. The section on electrical activity contains chapters on the origin of the resting potential, electrogenesis of the action potential and automaticity, conduction of the action potential, excitation and the electrocardiogram, and electromechanical coupling. The section on cardiac contraction includes five chapters on the heart as a pump, mechanical properties, force-interval relationship, elastic properties of the myocardium, and control of cardiac performance. The section on neural factors contains five chapters on neural control, baroreceptor regulation, chemoreceptor regulation, cardiac reflexes, and central nervous system influences. The section on humoral factors consists of a single chapter on adrenergic and cholinergic mechanisms in the regulation of myocardial contractility. The section on metabolism of the heart includes three chapters that consider cardiac energetics, carbohydrate and fatty acid metabolism, and protein metabolism. The last section describes the coronary circulation.

Edited by: Alfred P. Fishman  
Eugene M. Renkin

Pulmonary edema generally becomes evident clinically only when excess water has spread beyond the confines of the interstitial spaces to flood the alveoli. At this stage, the pathogenetic mechanisms responsible for the accumulation of the excess water are generally difficult to unravel.

During the past decade, it has become possible to take a closer look at the early stages of pulmonary edema. The use of electron microscopy has clarified the fine structure of the alveolar-capillary membrane and biochemical studies have defined many aspects of the surfactant layer that lines the alveolar epithelium. Improvements in the technique of right-heart catheterization have allowed ready access to the pulmonary circulation, permitting estimation of pulmonary venous pressures. Technological advances have simplified the determination of hemodynamic and osmotic pressures in the pulmonary circulation, making it possible to assess the applicability of Starling's law of water exchange. Methods for gaining access to the lymphatic drainage of the lungs in experimental animals have made it possible to measure water and protein turnover in the lungs. In addition, pulmonary function laboratories have begun to provide practical approaches to the early detection of excess water in the lungs with techniques for determining pulmonary compliance and closing volumes.

Once techniques were developed to study the pulmonary and lymphatic circulations and the elements that comprise the alveolar-capillary barrier were understood, it became possible to examine the turnover and accumulation of water and proteins in the lungs in terms of contemporary anatomical, physiological, physical, and chemical concepts. This volume presents, with particular emphasis on pulmonary edema, a comprehensive discussion of the mechanisms involved in the exchanges of water and solutes across biological membranes and in the distribution and accumulation of water within tissues. Not only does it depict the recent progress in the study of this disorder, but it also presages advances to be anticipated in the years ahead.

This volume, the third in the Society's Clinical Physiology Series, contains 18 chapters arranged in three sections:

- Ultrastructure and Functional Bases for Exchange of Water and Protein (microscopic architecture of capillary and alveolar epithelium; interstitial matrix; transport pathways)
- Fluid Accumulation in Lungs (pathways; accumulation matrix; distribution; role of lymph)
- Excess Water in the Lungs (mechanical influences; oxygen toxicity; adult respiratory distress syndrome; high altitude effects).

The book contains many electronmicrographs, faithfully reproduced on quality paper.

Members of the Society may purchase copies from the Bethesda Office when it becomes available early in 1979. Look for a brochure and order form in the mail at that time. The price to members of APS is \$24 (\$30 to non-members).

discipline. You understood that the Federation could become a voice for experimental science in the United States, in a growing political arena. You foresaw the need for scientists to participate in a set of communications processes. I can remember many a long evening in which the Board said you nay. I never did quite understand how you put up with us. I thought that many times you must have gone home and had several drinks to quiet the anger which must certainly have welled up as your best-laid plans were put back in the ice box again. And most of those plans nevertheless, have become reality over the course of time . . . The Federation is a tribute to you as a planner, dreamer, schemer, conniver and organizer."

Without question the vision and leadership of Milton O. Lee was the major contributing factor to the growth and influence of the Federation of American Societies for Experimental Biology and its rise to national eminence.

Milton Lee's contributions to the American Physiological Society were not unrecognized by its officers and members. Although no glowing statements were made at the time of his retirement, there was no question that he had developed a pattern for the growth of the American Physiological Society and on which his successors, Drs. Daggs and Reynolds, have so successfully built to make the American Physiological Society preeminent in the world of science.

During the years Dr. Lee was engaged in research his contributions appeared in many prestigious journals and he presented papers at meetings in this country and abroad. At this time he also was consciously struggling with the problems of effective communication by and with scientists. His first efforts in this area occurred when he became the Managing Editor of Endocrinology and the Journal of Clinical Endocrinology. During World War II his interest in communication was heightened by his experiences as Nutrition Officer. His decision after the end of the war to accept the position of Executive Secretary of the American Physiological Society came only after considerable soul-searching with his collaborator and mentor, Dr. R. Hoskins. It was a decision resulting from his conclusion that biological scientists had arrived at a critical point in that their activities were at a high level but that their ability to communicate with society would be in need of encouragement and assistance.

He was a quiet, unassuming man who led by example rather than by fiat. His kindness, generosity and concern for others are well known to those who were fortunate enough to have worked with or for him. He took stands on many controversial issues, but even on such occasions his opponents admired him for his honesty and integrity. As Dr. Handler had said, many of his original ideas and stands, being somewhat ahead of their time, were finally adopted to the benefit of the Society. Society membership increased rapidly during his tenure and with it came increasingly pressing problems related to the dissemination of increased research activity. His initial responsibilities as Managing Editor of the American Journal of Physiology and Physiological Reviews expanded rapidly into including the Journal of Applied Physiology and the Journal of Neurophysiology. His attention in particular to the fledgling Journal of Applied Physiology illustrated most clearly his concern for advanced communications and his ability to perceive new ways in which to bring physiology into the main stream of research developments. The development of the outstanding Handbooks of Physiology were stimulated and fostered by his concern for communication. The growing pains of the Society led to many internal problems, which were deftly presented to the Council of the Society and to its membership. Dr. Lee was the calm force behind the solutions to these problems leading to unification and coherence in the Society's actions and decisions.

The American Physiological Society owes a great debt of gratitude to Milton O. Lee. Its successful development during the turbulent post-war years was assisted and stimulated by the quiet and persuasive work of one who was not only a good scientist but one who believed that Physiology had more to offer than its own advancement as a strong and vital discipline of the basic sciences. Dr. Lee gave us perspective and vision -- he encouraged the Society to become an essential element in the broad area of active involvement in society as a whole. The American Physiological Society regrets his passing but looks back at his accomplishments with pleasure and appreciation.

Dr. Lee is survived by his wife, Helen Mayhew Lee, 3388 Dartmouth Lane, Sarasota, and two sisters, Mrs. Ray Evans of Fort Lauderdale and Miss Doris Lee of Bradenton, Florida.

Memorial donations may be made to Suncoast Heart Association, Inc., Sarasota County Branch, P.O. Box 3341, Sarasota, Florida 33578.

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## HONORS AND AWARDS

The Institute of Medicine, established by the National Academy of Sciences for "the protection and advancement of the health of the public," elected 39 persons to a first term recently. Three APS members were recipients of this honor, their terms to begin January 1, 1979.

**Robert M. Berne**, Chairman and Charles Slaughter Professor of Physiology, University of Virginia School of Medicine.

**Stuart Bondurant**, President and Dean, Albany Medical College.

**Samuel O. Thier**, Chairman, Department of Internal Medicine, Yale University School of Medicine.

Two APS members have received awards for their research on the cardiovascular system from the Microcirculatory Society, Inc. Both recipients are faculty members at the College of Medicine and Dentistry of New Jersey.

**Francis P. Chinard**, was honored with the Eugene M. Landis Award of 1978 for his studies on capillary permeability in the lungs and kidneys and the development of a method to assess permeability.

**Walter N. Duran** was honored for his research on the exchange of substances, across the capillary walls of the cardiovascular system.

## PRESIDENT-ELECT'S TOUR

### Changes in Cuba

David F. Bohr

For my "President-elect's tour" I chose to return to scenes of my childhood. As a boy I spent five years in Cienfuegos, Cuba.

When I traveled there this past fall access to Cuba could only be had via Toronto, so that my trip from the U.S. to Havana was over 3,000 miles long, in contrast to the 100 mile boat ride from the southern tip of Florida to Havana that I used to take.

Amazing transitions have taken place in this island setting since the 20's, changes that largely have escaped our attention.

It was not surprising that our communication broke down 20 years ago when the new government of Cuba nationalized (a euphemism for "took over") American-owned power plants and sugar plantations. It was also not surprising that the Cuban government did this nationalizing as part of the overall corrective procedures for the oppressive situation that had made Cuba ripe for a revolution. Arthur Schlesinger, Jr., later White House Assistant to President Kennedy, reflected as follows about Batista's government: "The rapacity of the leadership, the corruption of the Government, the brutality of the police, the regime's indifference to the needs of the people . . . all these in Cuba as elsewhere, constitute an open invitation to revolution."

When Fidel Castro acquired power in January 1959, he rapidly took steps to consolidate his gains and to correct these bases for unrest. One of his approaches to consolidation was to develop citizen groups, Committees for the Defense of the Revolution: CDR. These Committees played an important role in thwarting the Bay of Pigs invasion in 1961. The CDR are still the grass roots organization through which information is disseminated and programs are implemented. Through an active CDR, public opinion is guided. Friendly Cubans who approached me on the streets told me "we know that the *people* of the U.S. are fine . . . it's just your imperialist government that is bad."

Very high on the action list of the new government was upgrading of education and health care delivery. Illiteracy (25 percent preceding the revolution) was vigorously attacked in 1961, the "Year of Education." Teachers were drafted, and groups of teenage "alphabetores" were instructed in the teaching of reading and writing, then sent out to live with farmers, and conduct classes in the rural neighborhoods to correct illiteracy. By the end of the year, illiteracy was reduced to three percent. Adult education programs are now widely used, in keeping with the country's stated goal--"Every worker a student and every student a worker."

An acute need for medical education developed when over half of the country's 6,000 doctors left Cuba following the Revolution. Before this, medical care could be afforded only by the wealthy; and now with the reduced number of physicians, the Socialist government hoped to make free medical care available to everyone. The new Ministry of Public Health was faced with the issue of choosing between delivery of health care through physicians' assistants, or development of a system which provided a sufficient number of physicians to carry out the program themselves. The latter was selected; and a medical education program was evolved which has increased the number of physicians in the island to over 10,000. This provides a higher physician to population ratio than we have in the United States. The Cuban Ministry of Health, however, states they will not be satisfied until their present ratio is greatly increased; they want a physician/population ratio of 1 to 500.

Medical education has not been short-changed in this process. Prior to entering medical school the student has seven years of primary (Fig. 1) and three years of secondary school (Fig. 2) followed by three years of pre-university school. Admission to medical school is highly selective--only about 20 percent of the applicants make it. It is based primarily on academic performance in the pre-university years; but consideration is also given to the applicants' work outside of school and socio-political activities.

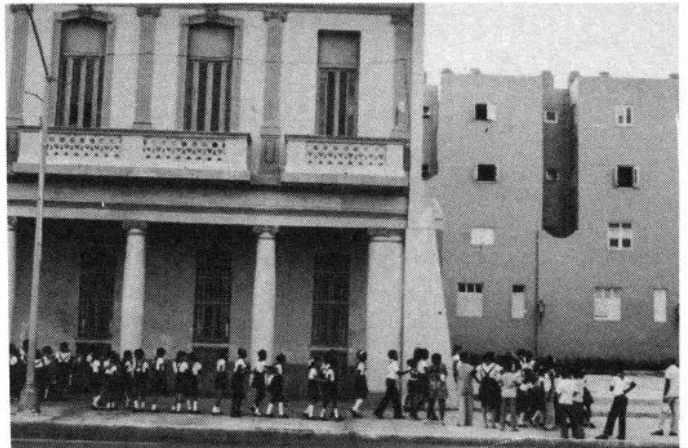


Fig. 1. School children in their uniforms in front of elementary school in Havana. Since the Revolution illiteracy has declined from 25% to 3%.

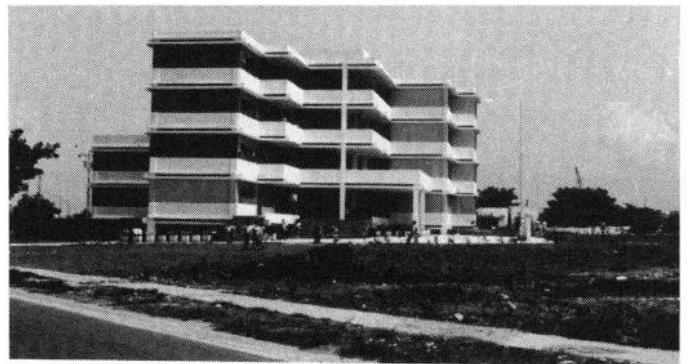


Fig. 2. A secondary school in a new suburb east of Havana.

Medical school is comprised of three two-year units. The first unit deals with normal structure and functions, the second with pathology and disease, and the third with patient care (Fig. 3). In addition to this classical medical curriculum, students must take courses dealing with social factors in health and disease, and their community orientation includes studies of Marxism/Leninism. Throughout the six years the student has periods of work compatible with his level of medical education. He may serve, for instance, as a sanitary engineer or a public health nurse.

All medical students are grouped in "brigades" of 25 to 30 members. Each brigade has responsibility for the success of each of its members. This relationship reflects the concept of social responsibility which is developed in all aspects of life in Cuba.

Following medical school, each graduate has three years of compulsory service in rural areas of Cuba. He may then specialize with three additional years of residency; 80 percent of doctors do specialize.

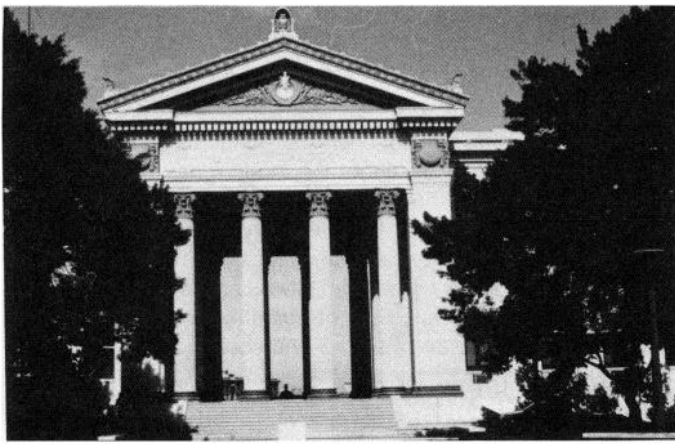


Fig. 3. University of Havana.

Much of the students' clinical training and service takes place in the polyclinics (Fig. 4) which form the primary setting for delivery of health care in Cuba. These clinics are distributed throughout the island, one for every 40,000 population. Each is completely staffed with the essential medical specialists and ancillary personnel, and facility for the delivery of health services (Fig. 5). Through the CDR the people of Cuba are encouraged to make use of the polyclinics for preventive medicine. Currently the 10,000,000 population of Cuba makes 40,000,000 visits to the polyclinics per year.

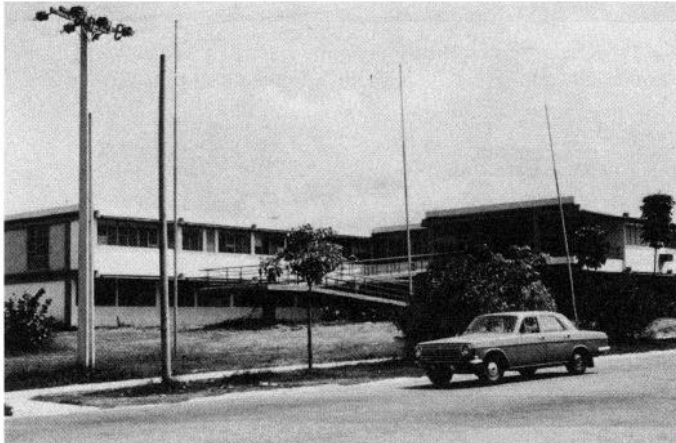


Fig. 4. A new polyclinic near Havana. Each polyclinic gives complete, free, outpatient service to 30 to 50 thousand people. There are approximately 200 of these located strategically throughout the island.

All of this is free. Even the medical student is subsidized through medical school (Fig. 6). He leaves his education days with a strong motivation to contribute to the social welfare and health of the Cuban people. He must sign an oath not to enter private practice (although it is not against the law) because, from the patients' point of view, paying for a private physician amounts to being penalized for being sick.

The enormous cost of this level of health care delivery and this support of education was certainly obvious (Fig. 7). I commented to my host that taxes must certainly be high to pay for it. "What taxes?" was the reply. "If more money is needed, the Government increases the price of tobacco and sugar we sell abroad." He did not mention a sizable subsidy for the Cuban economy that has come from Russia.

Research in basic and clinical science is developing. Publications appear in a series of "Revista Cubanas" in Medicine, Surgery, Pediatrics, and Ob-Gyn. Abstracts of publications are written in English, French, and Russian. I was most impressed by

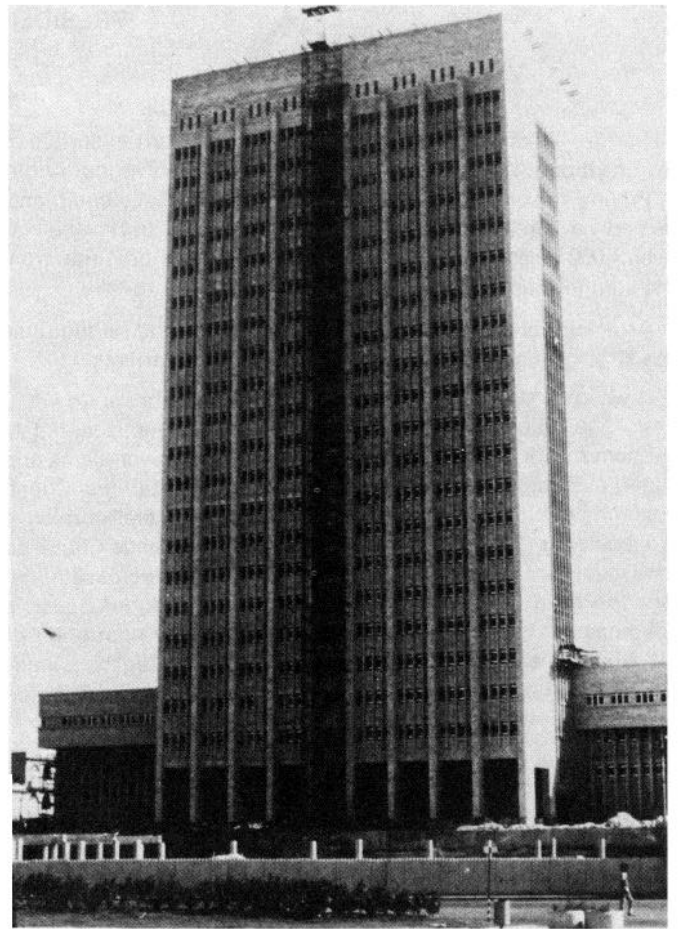


Fig. 5. New general hospital in Havana. It will be open for patients in 1980. Before the Revolution Cuba had 3 teaching hospitals, all in Havana. There are now 54 located throughout the island.

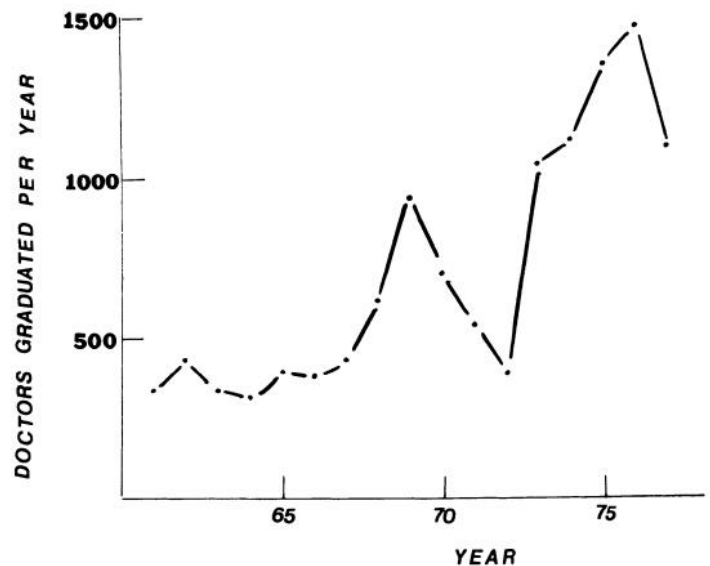


Fig. 6. Number of MD's graduated per year. (Data from *Ministerio de Salud Publica de Cuba: Informe Anual*, 1977)

an epidemiological study that is now being carried out on management of hypertension. The entire populations of two similar polyclinic areas in different parts of the island were surveyed for hypertension. In each, the incidence in the population over 15 years of age was approximately 17 percent. All patients with hypertension in both polyclinic areas were told of their

diagnosis. In the "reference" or control polyclinic area the patients were merely told that they should have their disease treated but initiative for pursuit of treatment was left to the patient. In the "test" polyclinic area, compliance with prescribed treatment was energetically pushed by personnel of the polyclinic. Notices sent by mail, house calls, and even peer pressure through the CDR are employed to insure compliance with the antihypertensive therapy. This is an important study which will evaluate the efficacy of rigidly controlled therapy on the reduction of the complication of hypertension. It is carried out with little added cost in the highly organized existing system for delivery of health care.

Gráfico 18  
CONSULTAS MEDICAS  
1963-1976

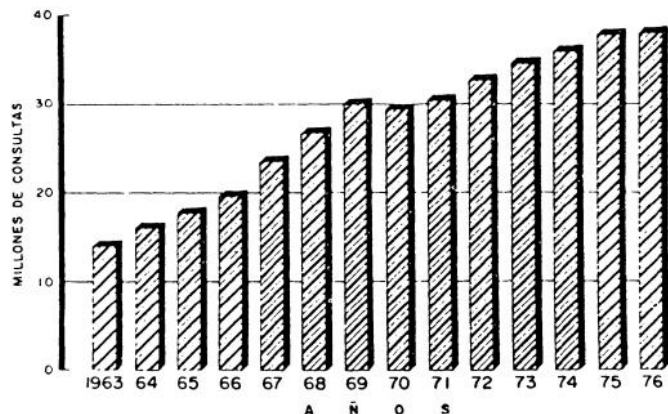


Fig. 7. Medical consultations per year. On the average each Cuban now visits his polyclinic four times per year. The frequency of dental visits is increasing even more rapidly. (Reprinted from *Ministerio de Salud Publica de Cuba: Informe Anual, 1977*)

Physiology in Cuba is an active profession in both teaching and research. All physiologists are medical school graduates. These graduate students must subsequently complete a three-year program of study and research in physiology to qualify for a junior faculty position. Senior faculty positions require a higher academic degree which is achieved by a minimum of three more years of research and dissertation defense.

I talked to Doctor F.R. Dorticos, President of the Cuban Physiological Society, about establishing channels through which physiologists in our two countries could get together. We discussed the possibilities of our societies having joint meetings and of Cuban Physiologists training in the United States. I told him that I would explore both.

I would like very much to see arrangements made for future joint meetings of the American Physiological Society and the Latin American Society of Physiological Sciences. Subsequently, in Mexico City I discussed this possibility with Dr. Garcia Ramos, President of that Society and with Dr. Hugo Aréchiga, President of the Mexican Physiological Society. We considered trying to have such a meeting in Havana, but Dr. Garcia Ramos expressed concern that physiologists from some Latin American countries probably could not attend. It would be more realistic to have a joint meeting of only the Mexican, Cuban and American physiological societies in Havana. Another realistic possibility is for our Society to invite all members of the Latin American Society of Physiological Sciences to join us at our Fall meeting in San Diego in 1982.

Regarding the training of Cuban physiologists in this country, I told Dr. Dorticos that I thought appropriate settings in our country could be found. I would appreciate hearing from members of our Society who would be interested in participating in this mechanism for reestablishing relations with physiologists in Cuba.

Fidel Castro and the Revolution have certainly given education and health care to the Cuban people (Fig. 8). Educators and doctors in Cuba are justifiably proud of what they have accomplished (Fig. 9).

Gráfico 5  
MORTALIDAD POR TUBERCULOSIS  
1959-1977

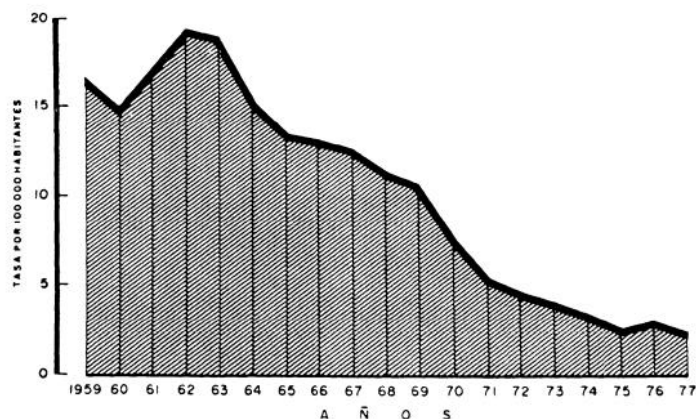


Fig. 8. Incidence of death due to tuberculosis. All measurements of health care in Cuba indicate that it is steadily improving. (Reprinted from *Ministerio de Salud Publica de Cuba: Informe Anual, 1977*)



Fig. 9. A government building in Havana. There is extensive propaganda in Cuba against imperialism, the profiteering by one country at the expense of another.



Fig. 10. A street in Havana. These are typical residences and autos, Michigan vintage of the 1950's. It is atypical to see this many cars in one place.

Even Cuba's most ardent supporter does not claim that life on the island approaches being Utopia. The country does have near 100% employment, but to the superficial observer, the economy is clearly an unsurmounted hurdle. Housing is poor, manufactured items are in scarce supply, clothing is rationed, and very few people have their own automobiles (Fig. 10). Yet it is a setting in which dramatic changes have occurred leading to the development of very extensive education opportunities and to a health care delivery system that is excellent. I believe that physiology in Cuba has a promising future.

## GRADUATES OF PHYSIOLOGY TRAINING PROGRAMS

Franklyn G. Knox, M.D., Ph.D.  
Secretary Treasurer  
Association of Chairmen of  
Departments of Physiology

The Association of Chairmen of Departments of Physiology (ACDP) conducts an annual survey of Departments of Physiology and addresses data of interest to physiologists in general. Data in regard to faculty positions were reported in an earlier issue of *The Physiologist*. In the present report, data concerning students completing programs by June 30, 1978, are presented. The data represents responses from 102 physiology departments participating in the survey.

As summarized in Table I, 106 students of physiology received Ph.D. degrees and 65 students completed postdoctoral training in physiology. Most individuals had secured positions at the completion of the training program. The distribution of minority students is also indicated in the table.

In Table II the disciplines represented by these students are categorized, utilizing the International Union of Physiologic Societies specialty code (IUPS). In 1978, the IUPS specialty code was not included in the questionnaire itself, whereas the discipline was requested. Future questionnaires will utilize the IUPS specialty code and this may effect the details of the response. In particular, the categorization of general physiology may receive a different response.

The Association of Chairmen of Departments of Physiology hope that this data are of use to the membership of the American Physiological Society.

TABLE I

### STUDENTS COMPLETING PROGRAMS BY JUNE 30, 1978

|                   | Predoctoral |        | Postdoctoral |        |
|-------------------|-------------|--------|--------------|--------|
|                   | Male        | Female | Male         | Female |
| Minority          |             |        |              |        |
| Black             | 1           | 2      | 2            | 0      |
| Other             | 2           | 5      | 18           | 4      |
| Non-minority      | 56          | 6      | 31           | 3      |
| Need Positions    |             |        |              |        |
| Yes               | 12          |        | 6            |        |
| No                | 81          |        | 56           |        |
| TOTAL IN PROGRAMS | 106         |        | 65           |        |

TABLE II

Disciplines represented by  
Predoctoral students receiving Ph.D. degrees in  
Physiology for the year ending June 30, 1978

| IUPS Specialty<br>Code | Discipline                    | # of Individuals |
|------------------------|-------------------------------|------------------|
| 12                     | Endocrine                     | 13               |
| 16                     | Gastrointestinal              | 2                |
| 25                     | Neurosciences                 | 19               |
| 32                     | Respiration                   | 2                |
| 24                     | Muscle & Exercise             | 7                |
| 08                     | Cardiovascular                | 13               |
| 30                     | Renal                         | 6                |
| 17                     | General Physiology            | 17               |
| 13                     | Energy Metabolism, Temp. Reg. | 1                |
| 07                     | Blood                         | 3                |
| 09                     | Cellular & Tissue             | 5                |
| 05                     | Biophysics                    | 2                |
| 04                     | Biochemistry                  | 2                |
| 02                     | Anatomy & Embryology          | 4                |

Postdoctoral students completing a fellowship for the year  
ending June 30, 1978

|    |                               |   |
|----|-------------------------------|---|
| 05 | Biophysics                    | 5 |
| 25 | Neurosciences                 | 9 |
| 17 | Physiology                    | 9 |
| 12 | Endocrines                    | 9 |
| 24 | Muscle & Exercise             | 5 |
| 09 | Cellular & Tissue             | 4 |
| 13 | Energy Metabolism, Temp. Reg. | 1 |
| 22 | Microbiology                  | 1 |
| 08 | Cardiovascular                | 9 |
| 07 | Blood                         | 4 |
| 31 | Reproduction                  | 2 |
| 04 | Biochemistry                  | 2 |
| 27 | Pathology                     | 2 |
| 32 | Respiration                   | 2 |

## SYMPOSIUM IN HONOR OF DR. DAVID BRUCE DILL

A Symposium *Life, Heat and Altitude* will be held to honor Dr. David Bruce Dill on his 88th birthday.

The Symposium will be held at the Environmental Protection Agency Auditorium on the campus of the University of Nevada, Las Vegas, on May 15, 16, and 17.

On May 15, the subject of presentations will be: *Advances in Adaptations to Heat*; on May 16, *Advances in Adaptations to Altitude*; and on May 17, *Advances in Aging*.

For further information please contact: Dr. M. K. Yousef, Biological Sciences Dept., Univ. of Nevada, Las Vegas, Las Vegas, NV 89154 (702) 739-3390 or Dr. S. M. Horvath, Institute of Environmental Stress, University of California, Santa Barbara, CA 93106 (805) 961-2350.

**Newsletter for Comparative Physiology Section  
of the  
American Physiological Society**

The joint fall meeting APS/ASZ (DCPB) was held 22-27 October, 1978 in St. Louis, Mo. On 25 October, the first meeting of the Comparative Physiology Section (CPS) of APS was held. A brief report on past activities of the joint APS/ASZ Task Force on comparative physiology was delivered by Task Force chairman, Frank Conte. Dr. Conte stated that the Task Force had served its purpose and would be discharged.

Dr. Conte introduced the newly elected members of the CPS steering committee:

|                 |                      |
|-----------------|----------------------|
| Counselor 1     | Frank Conte          |
| Counselor 2     | Bill Dawson          |
| Counselor 3     | Knut Schmidt-Nielsen |
| Program Officer | Bruce Umminger       |
| Secretary       | Rod McNabb           |

**Publications:** Various representatives spoke about publication outlets available to comparative physiologists. These included American Journal of Physiology; Regulatory, Integrative and Comparative Physiology; Journal of Experimental Zoology; Physiological Zoology; Journal of Comparative Physiology; Thermobiology; The Physiology Teacher. Two themes seemed to predominate in these remarks: a) Each journal is working at reducing publication delay (most of which occurs with author's revisions and/or the review process), and b) There is a need for greater numbers of possible reviewers.

**Programs:** Bruce Umminger thanked Ann Kammer for her past service as program officer. He noted that a Spring meeting is scheduled for April 1979 in Dallas; Fall meeting 1979 is slated for New Orleans.

Discussion developed about possibilities for a newsletter, and it was agreed that CPS newsletters should be incorporated into issues of The Physiologist. Information will be correlated with ASZ newsletters.

***Survey of national needs in comparative physiology research:***

Jim Cameron presented a summary of results from the survey conducted last summer. On the whole, comparative physiology research receives significant funding only from NSF and NIH. For the fiscal year 1976, funds were lean from both agencies, although significant increases occurred in funds from both agencies by FY 1978. Both agencies funded about equal numbers of proposals, although the average award from NIH was nearly twice that from NSF (\$50-60 thousand versus \$30 thousand, respectively). Cameron also noted that non-medical school research on comparative physiology usually received about \$10 thousand less, per NIH grant, than did medical school based proposals. Overall, success seems to average about 55%. The survey could not give adequate information on funding from local sources, contract research awards and the extent to which comparative research is "boot-legged" on other grant funds.

Finally, respondents to the survey seemed to think that, yes, comparative physiology research is under-funded, but perhaps no more than all other areas of basic science. Our problems were perceived as part of a larger problem affecting the whole of the scientific community.

In the month of November, the APS office obtained a computer printout of the 204 names of APS members who designated comparative physiology as a primary or secondary research interest. It is hoped that these members can be called upon to serve as reviewers for journals and as sponsors for new members of

APS. Will APS members who have *not* already declared an interest, but wish to designate comparative physiology as one of their areas of expertise, please notify Frank Conte?

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**ANNUAL \$100,000 AWARD ESTABLISHED  
TO HONOR INVESTIGATORS IN MEDICAL RESEARCH**

New York, N.Y. January 8, 1979. A \$100,000 annual award for outstanding achievement in clinical research has been established by Mrs. Lita Annenberg Hazen, it was announced today. The Mount Sinai School of Medicine, designated by Mrs. Hazen to administer the program, is instituting an international search to choose the first recipient of the award.

An award committee of medical scientists and administrators, which designed the plan, describes it as unique among medical research awards. According to its terms, an annual \$50,000 prize will be given to a medical investigator whose major continuing research is judged to be scientifically significant and of superior quality. An additional award of \$50,000 will be granted to the investigator's institution in order to cover the costs of one or more research fellows, chosen through a competition, who will work with the prize-winner.

In announcing the award program, Dr. Thomas C. Chalmers, Dean of the School of Medicine and Chairman of the Hazen Award Committee, noted that the number of medical school graduates choosing clinical research as a career has been steadily decreasing. Chalmers cited an American Medical Association study which showed that physicians entering clinical research dropped by 27 percent in a recent four-year period.

"If further advances are to be made," Chalmers said, "the trend must be reversed. This demands a new focus on the researcher as role model and wider opportunities for training in clinical research. Such programs as the Hazen Award are needed to restore momentum in the field."

Nominations for recipients are to be submitted by June 15, 1979. Nominations are to be made through submission of the official nominating form by the proposer. The form is to be accompanied by the proposer's letter explaining in summary the significance of the nominee's work during the past five years. It is also to be accompanied by the nominee's curriculum vitae, a list of publications, and no more than three key papers related to his or her work. Personal applications for the award will not be considered.

The Lita Annenberg Hazen Awards will be administered through the Mount Sinai School of Medicine of the City University of New York, One Gustave L. Levy Place, New York, NY 10029. Copies of the nominating form are available through the Office of the Dean.

## RENAL SECTION DINNER AND AWARD AT FASEB MEETING

The dinner will be held on Sunday, April 8 in the Oak Room of the Fairmont Hotel. Cocktails will be at 6:30 PM (cash bar) and dinner at 7:30 PM.

The speaker will be Dr. Sidney Solomon who is spending the current year with the National Science Foundation in Washington. The title of his talk is "Science funding, politics, society and you" and I'm certain that it will be a stimulating one for all of us.

In addition to Dr. Solomon's talk and a brief business meeting, the First Annual Awards for Excellence in Renal Research will be presented to young investigators for work reported at the last Fall Meeting of the American Physiological Society. We hope that these awards will grow to be an important stimulus to young workers in the field.

The cost of this year's dinner is \$17.00. This is a bit higher than we would like, but we have done our best to keep the price down while still obtaining reasonable arrangements. Tickets will be on sale in the registration area at the Federation Meetings until 4:00 PM, Saturday, April 7.

William H. Dantzer  
Secretary, Renal Section

## FULBRIGHT-HAYS AWARDS IN BIOLOGY

For more than thirty years the Fulbright - Hays program has provided opportunities for university lecturing and advanced research abroad. In recent years about 500 U.S. government awards per year have been made to American scholars and other professional--50 or more to specialists in one of the life sciences. The program, directed by the International Communication Agency, also includes awards to scholars from abroad for lecturing and advanced research at U.S. institutions.

Announcement of opportunities available to American scholars for 1980-81 will be published in March 1979. The general composition of the program involving about 100 countries is expected to be similar to that of recent years. Registration for personal copies of the announcement is now open to U.S. citizens with university or college teaching experience. Forms are available from the Council for International Exchange of Scholars, Suite 300, Eleven Dupont Circle, Washington, D.C. 20036.

Among the 1978-79 grants, 25 awards in animal and plant sciences were made to American scholars for work in Asia and the Pacific (10), Europe (10) and Latin America (5); 28 scholars from abroad will be in the U.S. from Asia and the Pacific (9), Europe (9), Latin America (2), Africa (5), and the Middle East (3). Grantee lists will be sent upon request. Nominations for 1979-80 awards are now being forwarded to the countries which programmed grants for announcement in the spring of 1978; most scholars receiving awards will be notified by February or March 1979.

## 1979 HARWOOD S. BELDING AWARD IN ENVIRONMENTAL PHYSIOLOGY

The Environmental, Thermal and Exercise Physiology section of the American Physiological Society will present the Annual Award to a graduate student at the Temperature Regulation Dinner during the Federation Meetings, April 1-10, 1979. The Award includes a prize of \$150.

### REQUIREMENTS

- 1) The graduate student applicant must plan to give the paper at either the 1978 Fall or 1979 Spring meetings of the APS. He or she must be first author on the abstract which is published in the *Physiologist* or the *Federation Proceedings*.
- 2) A requirement for receiving the Award is the attendance of the student at the Temperature Regulation Banquet. In case of illness he or she could still receive the Award by a vote of the Award Committee.
- 3) The typewritten copy of the presentation with illustrations should be submitted. Alternatively, a manuscript which is ready for publication may be submitted. Manuscripts must be received by *March 16*.

Manuscripts for the Belding Award should be mailed to:

Dr. Ethan R. Nadel  
John B. Pierce Foundation Lab.  
290 Congress Avenue  
New Haven, Conn. 06519

## AMMC ANNUAL MEETINGS

The Council of Academic Societies asked that the following schedules be published for the membership since many people need advanced notice of dates of future meetings.

| AMMC Annual Meeting |                      | CAS Bus. Mtg. |               |
|---------------------|----------------------|---------------|---------------|
| Wash., DC           | Nov. 3-11, 1979      | Wash., DC     | Nov. 5, 1979  |
| Wash., DC           | Oct. 25-30, 1980     | Wash., DC     | Oct. 27, 1980 |
| Wash., DC           | Oct. 31-Nov. 5, 1981 | Wash., DC     | Nov. 2, 1981  |
| Wash., DC           | Oct. 30-Nov. 4, 1982 | Wash., DC     | Nov. 1, 1982  |

# CONTRIBUTIONS TO THE AMERICAN PHYSIOLOGICAL SOCIETY

Last year the Society asked members for voluntary contributions in an effort to increase income without increasing dues. The response to the request was positive, and the following members had responded by press time. Their generosity is gratefully acknowledged.

|                        |                           |                         |                           |                        |
|------------------------|---------------------------|-------------------------|---------------------------|------------------------|
| Francis L. Abel        | Robert M. Bradley         | Theodore Cooper         | Gregory R. Ferrier        | Nathan B. Gross        |
| Ralph A. Ackerman      | Paul H. Brand             | Ethel Cosmos            | Benjamin G. Ferris, Jr.   | Roger Guillemin        |
| W. Ross Adey           | F. Norman Briggs          | La Val N. Cothran       | Michael Field             | Arthur C. Guyton       |
| Raymond P. Ahlquist    | Alvin Brodish             | James W. Covell         | William P. Fife           | Francis J. Haddy       |
| Cosimo Ajmone-Marsan   | Bernard N. Brodoff        | Benjamin G. Covino      | Clement A. Finch          | Howard B. Haines       |
| Qais Al-Awqati         | Chandler McC. Brooks      | Allen W. Cowley, Jr.    | V. A. Finch               | Charles L. Hamilton    |
| James K. Alexander     | George A. Brooks          | Eugene C. Crawford, Jr. | Martin J. Fisher          | Robert L. Hamlin       |
| Robert S. Alexander    | Harold L. Brooks          | Paul Cushman, Jr.       | Vincent J. Fisher         | Milton W. Hamolsky     |
| Mario Altamirano       | Ernest B. Brown, Jr.      | Esther Da Costa         | Robert S. Fitzgerald      | William Hansel         |
| Adelbert Ames III      | Kenneth T. Brown          | Joe M. Dabney           | Donovan E. Fleming        | James E. Hansen        |
| Max St. C. Amoss, Jr.  | Stanley J. Brumleve       | Willard M. Daggett      | Piero P. Foa              | Robert J. Hansen       |
| Lloyd L. Anderson      | Nancy L. R. Bucher        | Ivan E. Danhof          | Donald H. Ford            | Esther Hardenbergh     |
| Norman G. Anderson     | Ramon D. Buckley          | William H. Dantzer      | John G. Forte             | Alden H. Harken        |
| Orlando J. Andy        | Wilton H. Bunch           | George D. Davis         | Claude Fortier            | Alfred E. Harper       |
| Nicholas R. Anthonisen | John H. Burgess           | Hallowell Davis         | Harry A. Fozzard          | Fredric A. Harris      |
| Adrienne P. Applegarth | Landry E. Burgess         | Margaret A. Dawson      | John J. Franks            | Lura A. Harrison       |
| Octavio Aprigliano     | Ian E. Bush               | William D. De Hart      | Wallace G. Frasher, Jr.   | William M. Hart        |
| David T. Armstrong     | Leo K. Bustad             | Robert L. Dehaan        | Howard S. Frazier         | William J. Hatch       |
| Claude D. Arnaud       | Robert A. Butler          | Pierre Dejours          | Henry H. Freedman         | Joseph E. Hawkins, Jr. |
| Habeeb Bacchus         | Stephen M. Cain           | Jose Del Castillo       | Melvin J. Fregly          | Tibor Heim             |
| Michael D. Bailie      | Thomas B. Calhoon         | Ralph B. Dell           | Norbert Freinkel          | Lois J. Heller         |
| Praphulla K. Bajpai    | E. J. M. Campbell         | Duane Denney            | Edward D. Freis           | Ruth M. Henderson      |
| Oscar J. Balchum       | Leon Cander               | Joseph C. Denniston     | Walter H. Freygang        | Edwin Hendler          |
| William M. Balfour     | Jose L. Cangiano          | Reed Detar              | Robert M. Friedler        | Richard W. Heninger    |
| Bruno Balke            | Paul J. Cannon            | Joseph Di Salvo         | Julius J. Friedman        | Ann L. Henninger       |
| Nils U. Bang           | Edwin L. Carlson          | John N. Diana           | Robert H. Furman          | Julia F. Herrick       |
| Robert O. Banks        | Richard W. Carlson        | Richard L. Dobson       | Robert Galambos           | Michael L. Hess        |
| Clifford Barger        | David O. Carpenter        | Robert M. Donati        | William F. Ganong         | E. Arnold Higgins      |
| Samuel B. Barker       | Serge Carriere            | Thomas P. Dousa         | Joseph H. Gans            | John A. Hildes         |
| Thomas B. Barnett      | Sidney Cassin             | Philip Dow              | Duane L. Garner           | Stanley D. Hillyard    |
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| Ellen F. Barrett       | H. Mead Cavert            | Jeffrey M. Drazen       | Henry Gelband             | Mituhiko Hisada        |
| John N. Barrett        | Helene C. Cecil           | Leonard S. Dreifus      | Apostolos P. Georgopoulos | Peter W. Hochachka     |
| J. B. Basingthwaighte  | Alfred H. Chambers        | Robert E. Eckel         | Elisabeth C. Gerst        | Brian F. Hoffman       |
| D. V. Bates            | Cornelia P. Channing      | Richard W. Eckstein     | Menard M. Gertler         | Joseph F. Hoffman      |
| John W. Bauman, Jr.    | Christopher K. Chapler    | Henry F. Edelhauser     | Gerhard H. Giebisch       | Julien I. E. Hoffman   |
| Edward L. Beckman      | Jerome J. Chart           | Isidore S. Edelman      | Daniel L. Gilbert         | Frank J. Hohenleitner  |
| Mildred E. Behrens     | Robert T. Chatterton, Jr. | Charles Edwards         | Robert Gilbert            | Thomas F. Hornbein     |
| Paul M. Beigelman      | Reuben M. Cherniack       | Walter Ehrlich          | H. Earl Ginn, Jr.         | Barbara J. Howell      |
| Robert W. Berliner     | Shu Chien                 | Gilbert M. Eisner       | Jack M. Ginsburg          | Herbert N. Hultgren    |
| Robert M. Berne        | Francis P. Chinard        | Robert Elsner           | Ernest M. Gold            | Francis R. Hunter      |
| Joel Bitman            | Paul C. Churchill         | Joseph Engelberg        | Martin Goldberg           | Robert E. Hyatt        |
| Neville Bittar         | Richard L. Clancy         | Richard Engen           | Robert Goldstein          | Richard W. Hyde        |
| Joseph R. Blair        | Neville P. Clarke         | Alan N. Epstein         | Ramon R. Gonzales, Jr.    | Richard P. Imbruce     |
| Cynthia Blasingham     | James A. Clifton          | Howard H. Erickson      | Charles J. Goodher        | James M. Irish III     |
| Clark M. Blatteis      | Charles F. Code           | David N. Erwin          | Robert W. Gore            | Bela Issekutz, Jr.     |
| Jacob J. Blum          | Fredric L. Coe            | George M. Fanelli, Jr.  | Carl A. Goresky           | Felix A. Jacques       |
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| Robert F. Bond         | Clarence R. Collier       | Saul J. Farber          | Harris J. Granger         | Elsie E. Johnson       |
| Stuart Bondurant       | William D. Collings       | Donald S. Farner        | Alejandro E. Grassino     | J. Frederic Johnson    |
| Nicholas H. Booth      | Delwood C. Collins        | Lloyd C. Faulkner       | John Grayson              | David R. Jones         |
| Deepak Bose            | Joel S. Colton            | Eric O. Feigl           | Joseph Greenberg          | Gabor Kaley            |
| John C. Bowen          | James Conway              | Dale D. Feist           | Michael J. Greenberg      | George J. Kaloyanides  |
| William H. Boyd        | John S. Cook              | James M. Felts          | Clive V. Greenway         | Donald L. Kaminski     |
| Robert A. Brace        | Ian M. Cooke              | Vladimir Fencf          | Roger L. Greif            | John P. Kampine        |
|                        | Keith E. Cooper           | James L. Ferguson       | Arthur F. Grimm           | Kenneth J. Kant        |

|                      |                        |                         |                        |                           |
|----------------------|------------------------|-------------------------|------------------------|---------------------------|
| Merril B. Kardon     | Terry E. Machen        | Edward R. Perl          | Ewald E. Selkurt       | Ernest Urban              |
| Ronald L. Katz       | Peter T. Macklem       | Carl Pfaffmann          | Francois Sestier       | C. Robert Valeri          |
| William C. Kaufman   | Paul D. Maclean        | Eliot A. Phillipson     | Paulette E. Setler     | Heinz Valtin              |
| Hiroshi Kawamura     | Joseph H. Magee        | Richard N. Pierson, Jr. | John W. Severinghaus   | Hugh D. Van Liew          |
| Michael P. Kaye      | Michael Magno          | Roland N. Pittman       | Alan W. Sexton         | John C. Vanatta           |
| Homayoun Kazemi      | S.J. Majcherczyk       | George Polgar           | Robert E. Shade        | Arthur J. Vander          |
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| J. E. Kendrick       | John W. Manning        | Wilfrid Rall            | Jim L. Shields         | James H. Veghte           |
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| Richard E. Kerber    | Allyn L. Mark          | Walter C. Randall       | Arabinda K. Sinha      | Herman Villarreal         |
| Frederick W. L. Kerr | Julian B. Marsh        | Helen M. Ranney         | Otakar V. Sirek        | John H. K. Vogel          |
| Delbert L. Kilgore   | Norman B. Marshall     | Phillip L. Rayford      | William W. Sleator     | William C. Wagner         |
| Frederick King       | Donald K. Mathews      | Lawrence W. Raymond     | Arthur H. Smith        | Betty J. Wall             |
| Theodore M. King     | Steven E. Mayer        | E. Douglas Rees         | Curtis A. Smith        | John H. Walsh             |
| Daniel L. Kline      | Thomas V. McCaffrey    | Thomas J. Reeves        | H. Millard Smith       | Michael Wang              |
| Howard M. Klitgaard  | Willard L. McFarland   | David M. Regen          | Thomas G. Smith, Jr.   | O. Douglas Wangenstein    |
| Ernst Knobil         | James J. McGrath       | Theobald Reich          | Jan W. Snellen         | William H. Waugh          |
| Leon K. Knoebel      | James T. McIlwain      | Eugene M. Renkin        | Ray S. Snider          | Paul D. Webster III       |
| Thomas I. Koike      | Thomas J. McManus      | Donald W. Rennie        | Jonas Sode             | Norman W. Weisbrodt       |
| Samuel N. Kolmen     | Leena M. Mela          | Albert E. Renold        | Joseph E. Sokal        | Francis M. Weld           |
| Michael T. Kopetzky  | John P. Merrill        | John A. Resko           | Arthur K. Solomon      | N. T. Werthessen          |
| Ross C. Kory         | Joseph V. Messer       | Orr E. Reynolds         | Ralph R. Sonnenschein  | Clark D. West             |
| Philip Kramer        | David D. Michie        | David W. Richardson     | Frank E. South         | William L. West           |
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| Robert L. Kroc       | Charlotte M. Mistretta | Andre Robert            | Merrill P. Spencer     | John E. Whitney           |
| Ladislav Krulich     | Robert A. Mitchell     | David Robertshaw        | Kenneth R. Spring      | James T. Willerson        |
| William G. Kubicek   | George W. Molnar       | R. Paul Robertson       | Brian J. Sproule       | W. Lane Williams          |
| Albert L. Kunz       | James C. Moore         | Dudley F. Rochester     | Walter M. St. John     | J. Henry Wills            |
| Sherman Kupfer       | Donald P. Morgan       | Joe R. Rodarte          | Mildred T. Stahlman    | J. R. Wilson              |
| Neil A. Kurtzman     | Arnold M. Moses        | Terence A. Rogers       | Leah M. Staling        | Sabbo Woldring            |
| George H. Kydd       | Campbell Moses         | Ellis L. Rolett         | Isaac Starr            | Earl H. Wood              |
| Johannes A. Kylstra  | David R. Mouw          | Albert Roos             | Paul D. Stein          | Clinton N. Woolsey        |
| Yih-Loong Lai        | E. E. Muirhead         | Jerzy E. Rose           | Bernard G. Steinetz    | George W. Wright          |
| Barbara R. Landau    | Wolfram Nagel          | Fred Rosenthal          | Fred W. Stemler        | Robert D. Wurster         |
| Stanley Lang         | Paul Nathan            | James N. Ross, Jr.      | Nancy R. Stevenson     | F. Eugene Yates           |
| Maurice E. Langham   | Philip Needleman       | Harold H. Rotman        | P. Brian Stewart       | Edward L. Yellin          |
| Kathryn F. Lanoue    | Edwin M. Nemoto        | Aryeh Routtenberg       | Henry O. Stinnett      | Tada Yipintsoi            |
| N. Keroy Lapp        | Michael T. Newhouse    | Michael J. Rovetto      | Hubert L. Stone        | David B. Young            |
| Martin G. Larrabee   | Joseph E. O. Newton    | Paul C. Royce           | James C. Strand        | Byung P. Yu               |
| Parry B. Larsen      | Shih H. Ngai           | Elena Ruiz-Ceretti      | Denise J. Strieder     | Paul N. Yu                |
| Henry D. Lauson      | Charles S. Nicoll      | Mauricio B. Russek      | Cameron G. Strong      | Martin A. Zade-Oppen      |
| Richard W. Lawton    | Julian Niemetz         | Lester T. Rutledge      | Harold J. Swan         | Andrew A. Zalewski        |
| John K. Leach        | Thomas E. Nightingale  | Kiichi Sagawa           | William H. Sweet       | Claire E. Zomzely-Neurath |
| Alexander Leaf       | Edwin L. Nirdlinger II | Glenn W. Salisbury      | Ann Taylor             | Marjorie B. Zucker        |
| Don Lehmkuhl         | Sarah A. Nunneley      | Herbert A. Saltzman     | Henry L. Taylor        |                           |
| David E. Leith       | Robert E. Nye, Jr.     | Mohinder P. Sambhi      | Reginald M. Taylor     |                           |
| Jacob Lemann, Jr.    | George S. O'Brien      | William P. Santamore    | Robert E. Taylor       |                           |
| O. Robert Levine     | Dennis D. O'Keefe      | John A. Santolucito     | Henry Tedeschi         |                           |
| Matthew N. Levy      | John J. O'Neil         | Frederick Sargent II    | Louis E. Teichholz     |                           |
| Vladimir T. Liberson | Daniel H. Osmond       | Stanley J. Sarnoff      | Helen M. Tepperman     |                           |
| Frederick M. Liebman | Charles A. Owen        | Charles H. Sawyer       | Jay Tepperman          |                           |
| Thomas P. K. Lim     | Narendra B. Oza        | Mohammed M. Sayeed      | Paul E. Teschan        |                           |
| Ralph I. Lipman      | Max J. Paape           | John J. Sayen           | Rudolf Thauer          |                           |
| David M. Long, Jr.   | John B. Pace           | William B. Schallek     | Samuel O. Thier        |                           |
| William G. Lotz      | Peter K. T. Pang       | Harold P. Schedl        | John X. Thomas, Jr.    |                           |
| Ruy V. Lourenco      | John R. Pappenheimer   | Peter Scheid            | Charles M. Tipton      |                           |
| James H. Ludens      | Norman F. Paradise     | James M. Schooler, Jr.  | Richard B. Tobin       |                           |
| Kenneth D. Lukowiak  | Lloyd D. Partridge     | Harald Schraer          | Daniel C. Tosteson     |                           |
| Lorenz O. Lutherer   | David H. Pashley       | Lawrence P. Schramm     | Ignatius L. Trapani    |                           |
| Charles P. Lyman     | John W. Patterson      | Arnold Schwartz         | Theofilos J. Tsagaris  |                           |
| Peter R. Lynch       | Harry D. Patton        | Neena B. Schwartz       | Anastasios G. Tsakiris |                           |
| Donald M. Maccanon   | Anthony M. Perks       | Charles Seidel          | Jiri Turinsky          |                           |

## INSTRUCTIONS FOR APPLYING FOR APS MEMBERSHIP

At the April 1977 business meeting the proposed Bylaws Amendment for creating a new membership category for Students was passed. This Bylaw Amendment appears under Section 7 of Article III of the Constitution, printed below.

### CURRENT APPLICATION FORMS

Published in each issue, the Physiologist shall 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 returned to the sponsor to 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, 1970.

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. Graduate students in physiology who have completed their preliminary examinations for the doctoral degree provided they are residents of North America. No individual may remain in this category for more than five years.

#### 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.

This Form is Valid Only for 1979

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 \_\_\_\_\_ Birth Date: \_\_\_\_\_

Address \_\_\_\_\_ 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 (Predoctoral students indicate date preliminary examination was passed.)

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: \_\_\_\_\_ #2. Name: \_\_\_\_\_

Mailing Address: \_\_\_\_\_ Mailing Address: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

Telephone No. Zip Code 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.

**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.).

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1. Complete physiological papers, published or accepted for publication.
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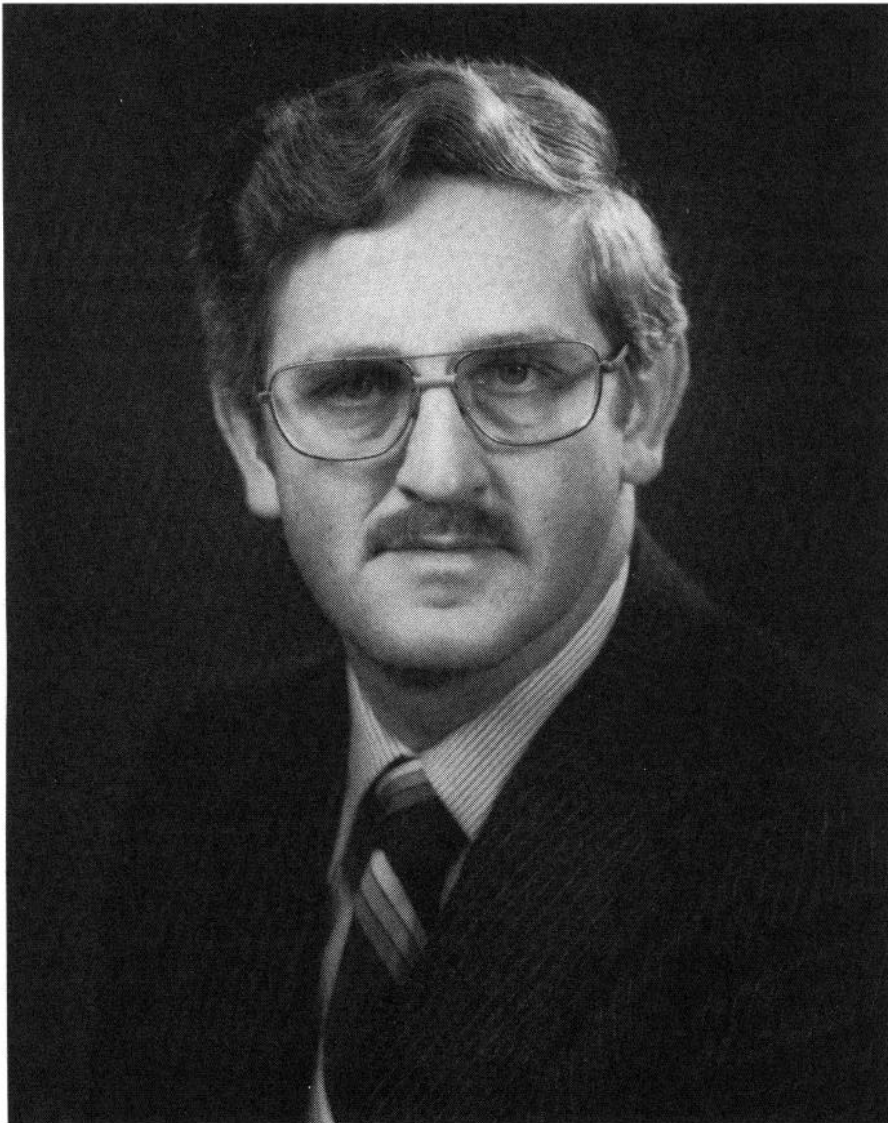
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### JOSEPH B. MARTIN

Dr. Martin, born in Alberta, Canada in 1938, has been a member of APS since 1974. He holds an M.D. degree from the University of Alberta and a Ph.D. from the University of Rochester. Since receiving the Ph.D., he has held positions of increasing responsibility at McGill University leaving that institution as Chairman of the Department of Neurology and Neurosurgery in September 1978 to become Chief of the Neurology Service at the Massachusetts General Hospital and Bullard Professor of Neurology at Harvard Medical School.

He has a family consisting of his wife, Rachel Ann, and four children.

Dr. Martin has received numerous honors of which this selection as Bowditch Lecturer is the latest. He is a member of some 13 scientific and professional societies, has served on several editorial boards, study sections and committees and is an author of approximately 100 scientific articles in well-reviewed journals and other publications.

# TWENTY THIRD ANNUAL BOWDITCH LECTURE

## Brain Mechanisms For Integration Of Growth Hormones Secretion

Joseph B. Martin, M.D., Ph.D.

It is a great honor to deliver the 23rd annual Bowditch lecture to the Fall meeting of the American Physiological Society. Although Professor Bowditch's primary research interest was vasomotor regulation, his published papers include one that is relevant to the topic under consideration.

In 1881, Bowditch addressed the section on Children's Diseases of the American Medical Association. His topic was the "Relation Between Growth and Disease." In his paper he noted that the size of adult Americans varied considerably in different states of the Union. Natives of Eastern states on migration to the West had children whose stature resembled that of the region to which they emigrated and they invariably seemed to grow larger. He speculated that climate, seasonal variations and the state of general health might contribute significantly to growth rates. Better statistics, however, were needed. Bowditch indicated that the Massachusetts State Board of Health, Lunacy and Charity was prepared to distribute cards to any physicians interested in measuring growth rates. In terms of acute illnesses, he noted that "a period of rapid growth is apt to follow certain fevers" and speculated that "it would be very interesting to inquire whether this accelerated growth after the disease is anything more than a compensation for the retardation during the disease and whether in this period of rapid growth the height and weight preserve their normal relation to each other."

This recognition that acute stress may inhibit growth is now a well-known clinical observation. Disordered growth may accompany either physical or emotional illness. Bowditch correctly pointed to the fact that acute physiological perturbations can have profound effects on neuroendocrine regulation.

The past decade has witnessed a marvelous explosion of insight into the mechanisms of hypothalamic-pituitary regulation. Some concepts have been clarified and others confounded. On the one hand, the discovery of three principal hypothalamic peptides, thyrotropin releasing hormone (TRH), gonadotrophin releasing hormone (GNRH) and growth hormone (GH) release inhibiting factor (GIF or somatostatin) by Guillemin and Schally and their respective colleagues, has provided great impetus to prove in detail biochemical and physiologic aspects of regulatory systems that control pituitary hormone secretion. At the same time, new discoveries have served to further complicate any simple analysis. TRH for example, is not specific in effect, but has potent releasing effects on prolactin as well as thyroid stimulating hormone (TSH). Somatostatin, in addition to its effects in inhibiting GH under a variety of circumstances, is also inhibitory to the secretion of TSH and a number of gut hormones, including glucagon, insulin, gastrin and secretin. Furthermore, radioimmunoassay and immunocytochemical evidence indicates that the peptides, although usually present in highest concentration in the hypothalamus, are also found in measurable quantities in other parts of the brain and spinal cord and in many instances also in the gut. Finally, the identity of other peptides such as substance P, neurotensin and the recently characterized opioid peptides has provided evidence that variety of unexpected substances may also participate in neuroendocrine control. For example, each of these peptides has been suggested to have stimulatory effects on GH secretion under certain circumstances (1,2).

The current view of the mechanism of hypothalamic-pituitary regulation is best understood by an analysis of the anatomic connections between these two structures. The principal blood supply to the anterior pituitary arises from portal vessels which drain the capillary plexus of the median eminence. The blood supply to this capillary zone is derived from the superior hypophyseal arteries which originate directly from the internal carotid. Small neurons in the basal hypothalamus are believed to be the origin of the hypothalamic hormones; axons of these cells terminate on capillaries in the median eminence and deposit their secretory products into the portal circulation. These final common pathway neuroendocrine cells in turn receive synaptic inputs from other brain regions which serve to mediate neuroendocrine reflexes in response to endogenous or exogenous signals.

One important aspect of pituitary hormone secretion, for the physiologist, is the documentation, now provided for all anterior pituitary hormones, that release from the gland *in vivo* does not occur in a steady-state fashion as doctrines of homeostasis implied a few years ago, but rather in an intermittent, episodic and irregular fashion. At first appearing rather random and chaotic, subsequent investigations have definitively shown that such secretion is, in fact, well-ordered and under precise regulation by the brain. Work in my own laboratory has focused on these processes with respect to GH secretion and the results of these experiments are the subject of this report.

GH is the principal regulator of body growth. Too much leads to giants and too little to dwarfs. The secretion of GH is precisely regulated by neural mechanisms, the final common path residing in the medial basal hypothalamus (Figure 1). Two hypothalamic factors are generally accepted to be required for this regulation: GH releasing factor (GRF) the structure of which is still unknown and as I will attempt to indicate must exist, and somatostatin (or GIF) which has been identified. The secretion of these two hormones is in turn regulated by influences from higher brain centers including limbic system structures such as hippocampus and amygdala and the brain stem. The latter is of particular importance because several monoaminergic inputs, which include norepinephrine and serotonin arise from cell nuclei located in the brain stem. These cells give rise to afferent connections to the hypothalamus which have important influences on GH secretion.

Within the hypothalamus, there are several regions which are important in GH control. Frohman and Bernardis showed in 1968 (3) that lesions in the hypothalamic ventromedial nuclei cause growth retardation in female rats accompanied by a fall in both plasma and pituitary GH levels. Subsequent studies in their laboratory and in ours documented that electrical stimulation of the ventromedial-arcuate region elicited prompt GH release in the anesthetized rat (4,5). Effective stimulation sites were confined strictly to this region of the hypothalamus. We also found, prior to the discovery of somatostatin, that stimulation of the medial preoptic area caused inhibition of GH release in anesthetized rats (6). It is now known that this region of the hypothalamus is enriched in cell bodies containing the inhibitory peptide somatostatin.

Electrical stimulation also permitted the identification of extrahypothalamic brain sites that were effective in either stimula-

tion or inhibition of GH release; stimulation of the hippocampus and of the basolateral amygdala resulted in GH release, whereas, stimulation of the corticomedial amygdala which is separated from the basolateral zone of this nuclear group by only a few mm, was inhibitory. It is now known that the corticomedial region of the amygdala has rich connections to the medial preoptic area and to the hypothalamic ventromedial nucleus. We concluded that these regions of the brain were important in mediation of neuroendocrine responses such as those observed during stress which has either potent excitatory or inhibitory effects on GH depending on the species involved.

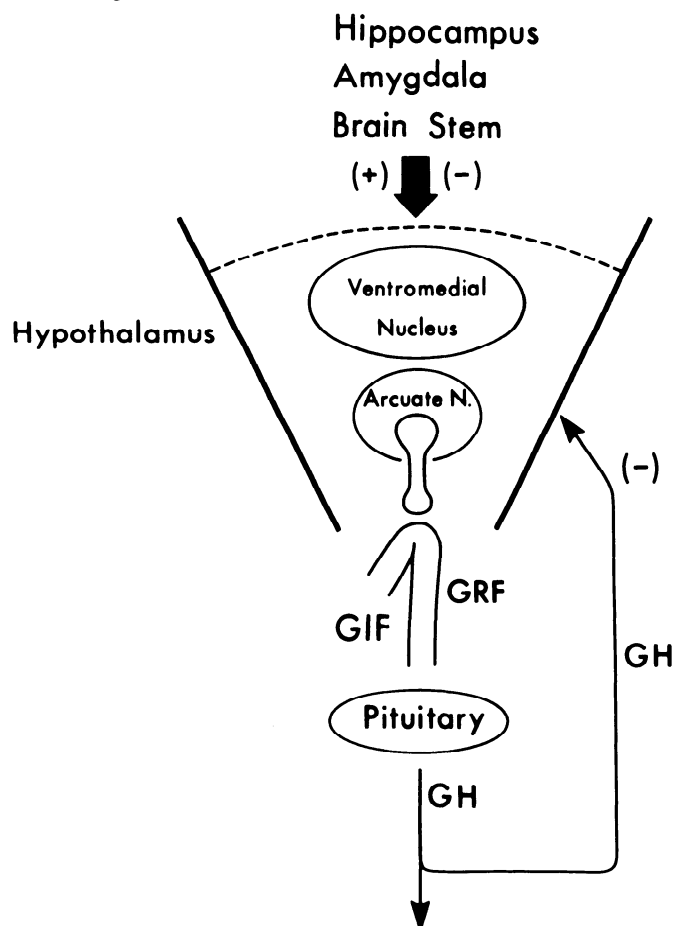


Fig. 1. Diagram of the GH regulatory system.

Abbreviations: GRF: GH releasing factor; GIF: GH release-inhibiting factor-somatostatin.

The problem with all of these experiments was the necessity to use general anesthesia to obtain reproducible results. This was due to the fact that random sampling of GH, particularly in the rat, gives extraordinarily variable results. Schalch and Reichlin (7) and Takahashi et al (8) had reported in the late 1960s that blood samples obtained rapidly from unanesthetized rats gave values that ranged from undetectable, or less than 1 ng/ml to levels that often exceeded 200 ng/ml. Although it was speculated that these effects might be due to uncontrolled stress or other variables, it seemed to us that another explanation might be exploited. Studies in man had shown that cortisol and ACTH are secreted entirely in bursts, and that the circadian variation of the pituitary-adrenal system could be accounted for by the summation of 6-9 individual surges of secretion (9). Could it be possible that similar mechanisms might explain the unusually wide variability in GH levels? Studies in man suggested such a possibility when it was shown that a large surge of GH accompanied early sleep and that repeated sampling throughout the day also frequently yielded

unexplained, intermittent, abrupt surges of GH release (10,11). These fluctuations could not be accounted for by metabolic influences, by exercise or by identifiable stress effects.

To study this question in the rat required development of non-stressful sampling techniques that would permit repeated blood removal with minimal effects on blood volume (12-14). To achieve this goal, silastic cannulae were inserted into the right atrium of the heart via the internal jugular vein and the external end was carried subcutaneously to the skull where it was attached to the head with dental cement. Polyethylene tubing was carried in a protective stainless steel coil spring to the exterior of the cage. A roller bearing at the top of the cage permitted total freedom of movement and samples could be removed every 15 minutes without any appreciable disturbance to the animal. To avoid hematocrit or blood volume changes, each sample of blood was centrifuged, the supernatant removed for immunoassay of hormones and red blood cells suspended in saline were returned to the animal at the time of the next sampling. Rats were permitted to recover fully from the surgical implantation prior to each experiment; this was found to be crucial for the documentation of normal hormone secretory patterns. Early experiments in animals prepared with such cannulae and permitted to recover for 7-10 days indicated that corticosterone secretion was normal with low-baseline and normal circadian variation.

The results of these experiments were dramatic. GH secretion in the rat was found to be entirely episodic (12). The profile of GH secretion was characterized by abrupt rises in plasma GH from basal undetectable levels to values that exceeded 200 ng/ml. The secretory bursts terminated abruptly, with circulating levels of the hormone declining at a time-course consistent with the known half-life of GH in the rat, i.e., about 5 minutes. The surges are commonly biphasic or in some cases triphasic.

Our subsequent interest turned to the mechanisms involved. What role does the hypothalamus have in the generation of these surges? Are both GRF and somatostatin involved? What factors can suppress secretion and what factors can enhance secretion?

Studies by Dr. Tannenbaum in my laboratory showed that the frequency and rhythm of the GH surges were not random but were rather precisely regulated in relation to external cues (13). Close scrutiny showed that the secretory bursts were entrained to the light-dark cycle. Secretion of GH terminated at the onset of the light period. Analysis of the 24-hour period showed seven distinct secretory peaks. Subsequent extensive experiments in hundreds of rats have confirmed this pattern. Dr. Tannenbaum labeled this an ultradian rhythm with a peak-to-peak interval that averaged just less than 3.5 hours.

The dependence of the rhythm on the light-dark cycle was further investigated by exposure of rats to either constant light or by blinding (12,13). In each instance the frequency of the surges was unaffected, i.e., the interval between individual surges remained about 3.5 hours but the timing was random or free-running. Subsequent return of rats to light-dark cycling resulted in entrainment of the rhythm and re-alignment of the secretory surges. In other words, the shift from light to dark appeared to act as a *Zeitgeber* to entrain the pulsatile rhythm to clock time.

What is the mechanism that underlies such a dramatic demonstration of episodic pituitary secretion? Does this reside in the pituitary itself or require neural drive? To analyze this question requires some understanding of hypothalamic anatomy and a focus on those regions that are implicated in GH regulation (Fig. 2). The pituitary (anterior and posterior components) is attached to the hypothalamus by a vascularized stalk which carries blood from the median eminence region to the anterior pituitary. The arcuate nucleus (ARC) is located in close proximity to the median

eminence of the basal hypothalamus and the ventromedial nucleus (HVM) is immediately superior to it. The anterior hypothalamic region is located between the optic chiasm (OC) and the HVM. The posterior edge of the chiasm forms the lower boundary of the suprachiasmatic nucleus (SC). The medial preoptic area (MPOA) is situated anterior and superior to the OC and the SC nucleus. Nerve fibers from the eye that enter the OC via the optic nerve (ON) also end in the SC nucleus. The bottom left portion of the figure shows a normal 6-hour GH secretory profile and the right prolactin. PRL levels in normal male rats are very low with occasional small blips of secretion evident. The simple hypothesis first tested was that the HVM-arcuate region of the hypothalamus (the only region which was effective in stimulating GH secretion in anesthetized rats,) might be an important key to the GH surges. Bilateral hypothalamic lesions were made using stereotactically placed platinum electrodes. Jugular cannulae were inserted. Large VM lesions totally abolished GH secretion and resulted in basal low levels in the blood, whereas, smaller lesions had proportionately less effect. Control animals demonstrated normal surges in GH. Thus destruction of the HVM. (Fig.3) caused a cessation of episodic GH secretion. The same lesions, by destruction of inhibitory hypothalamic influences for PRL resulted in a 5-10 fold rise in that hormone (Figure 3 lower right).

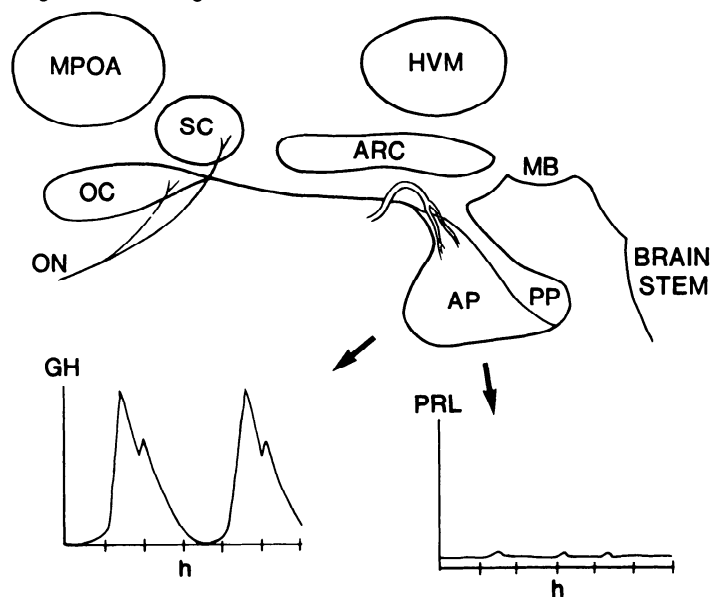


Fig. 2. Anatomy of hypothalamus as displayed in sagittal section. Six hour profiles of GH and PRL secretion are shown at the bottom left and right, respectively.

Abbreviations: AP: anterior pituitary; ARC: arcuate nucleus; HVM: ventromedial nucleus; MB: mammillary body; MPOA: medial preoptic area; OC: optic chiasm; ON: optic nerve; PP: posterior pituitary; SC: suprachiasmatic nucleus.

To further define the role of the medial basal hypothalamus in episodic GH secretion, rats were prepared with stereotactically produced hypothalamic islands (15). With the Halasz technique, which uses a bayonet-shaped wire lowered stereotactically into the hypothalamus and rotated in a circle, it is possible to produce an island of hypothalamic tissue separated from the overlying brain but, with preservation of anatomic and vascular connections to pituitary. The results were somewhat surprising. The surges of GH in such animals were very prominent and more frequent with levels between surges consistently failing to fall to low basal levels, (Fig. 4). PRL remained low indicating preservation of hypothalamic inhibition. Furthermore, stress failed to either suppress GH or to elevate PRL as would have occurred in intact rats. This observation provided further confirmation that the island

was complete and that neuro-endocrine reflexes had been interrupted. These findings were confirmed in a larger series of rats.

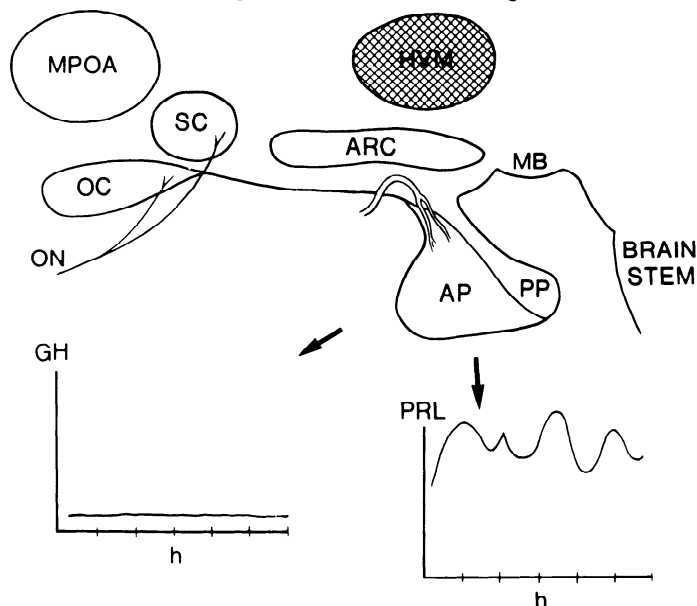


Fig. 3. Effect of lesions in HVM on secretion of GH and PRL.

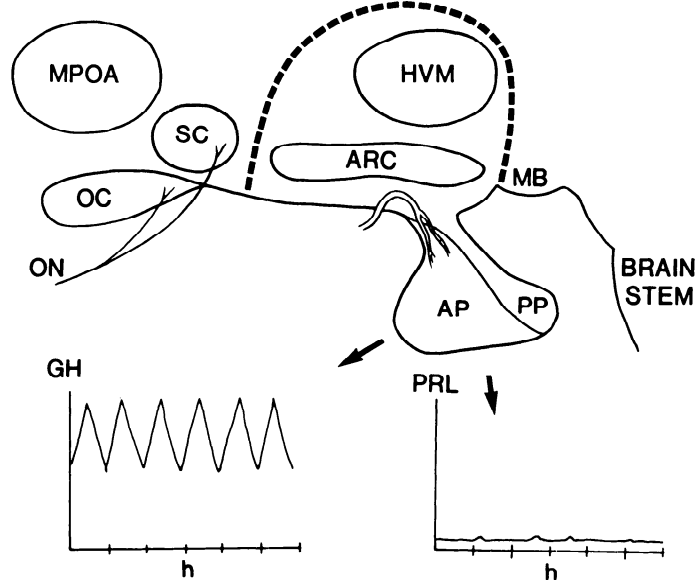


Fig. 4. Effect of hypothalamic disconnection (dotted line) on GH and PRL secretion.

Critchlow and coworkers (16) have reported similar findings. Rats with hypothalamic islands or with disconnection of anterior hypothalamic inputs had elevated GH levels when samples were obtained by guillotine and under certain circumstances such rats were found to grow more rapidly than controls and to attain greater body lengths (17).

These observations suggested two things: 1) that the HVM area is the region essential for pulsatile GH secretion and 2) that an influence outside this area serves to dampen or attenuate GH secretion.

The identification of somatostatin as a GH-inhibitory factor provided the means to directly assess the role of inhibitory hypothalamic mechanisms that might be operative through this peptide. Roger Guillemin and Ayerst Laboratories generously provided synthetic somatostatin for generation of antisera for use both in radioimmunoassays and for passive immunization studies. The rat is particularly sensitive to stress, minor disturbances, such as handling, producing significant suppression of GH secretion. We took advantage of antisera to somatostatin to determine whether release of the peptide might

account for the inhibition of GH during stress. Rats were required to swim in water at body temperature for 30 minutes. Such stress resulted in total suppression of GH secretion for up to 5-6 hours. That this stress-induced suppression of GH was due to somatostatin release was suggested by the effects of administration of specific antisera to somatostatin. The inhibitory effects of stress were rapidly reversed and episodic secretion of GH restored (18). Of particular interest in these studies was the finding that basal levels of GH remained low and that after administration of antisera the recovery of GH secretion occurred as bursts. Was somatostatin therefore secreted intermittently rather than continuously under such circumstances?

Studies from a number of laboratories using different antisera soon provided definitive evidence of the location of neurons that contain somatostatin in the hypothalamus. The cell bodies are located primarily in the periventricular region of the anterior hypothalamic-posterior preoptic region, (19) adjacent to the ependymal cells of the third ventricle.

What would happen to GH secretion if the somatostatin cell bodies were destroyed? To investigate this hypothesis, bilateral lesions were placed in the medial preoptic area. Such lesions resulted in more frequent surges of secretion with elevated baseline levels that only rarely or transiently fell to the normal basal levels of intact or control animals (20). The lesions caused a significant reduction in the interval between surges (Table 1); 9 control rats had an average interval of  $3.63 \pm .40$ h between surges compared to 6 rats with MPOA lesions with an interval of  $2.11 \pm .74$ h. The results were similar to those obtained in animals with total hypothalamic islands.

TABLE 1

EFFECT OF MEDIAL PREOPTIC LESIONS ON TIMING OF GH SURGES

|              | N | Interval between surges - h  |
|--------------|---|------------------------------|
| Control      | 9 | $3.63 \pm .40$               |
| MPOA Lesions | 6 | $2.11 \pm .74$<br>$P < .001$ |

To confirm that this effect was due to damage to the somatostatin system, a separate group of animals was lesioned and the median eminence assayed for somatostatin by specific radioimmunoassay (21).

Medial preoptic lesions resulted in a fall in concentration of somatostatin in the median eminence to approximately 20% of normal levels. Interestingly, such lesions had no effect on somatostatin levels in other brain areas such as amygdala or cerebral cortex. These observations, together with the findings of increased frequency and elevated basal levels of GH secretion in animals with preoptic lesions that destroyed somatostatinergic neurons, provide convincing evidence that this system is important in inhibition of the *physiologic* pattern of GH secretion (Figure 5).

Since lesions of the medial preoptic area impinge upon or partially destroy the SN it was important to determine the effects of selective lesions of this structure. A variety of experimental approaches have strongly implicated the SC nucleus in regulation of circadian and other neural rhythms. Rats with lesions of this nucleus show aberrations in activity cycles and in spontaneous running and demonstrate abnormalities of other rhythms including the circadian periodicity of the pituitary-adrenal system. There is controversy about the role of the suprachiasmatic nucleus in determination of circadian rhythmicity. Basically two

opposing viewpoints have emerged: (a) that the SN is the *origin* of endogenous brain rhythms versus (b) that it serves as a signal generator to *integrate* rhythms after appropriate analysis of external and internal cues.

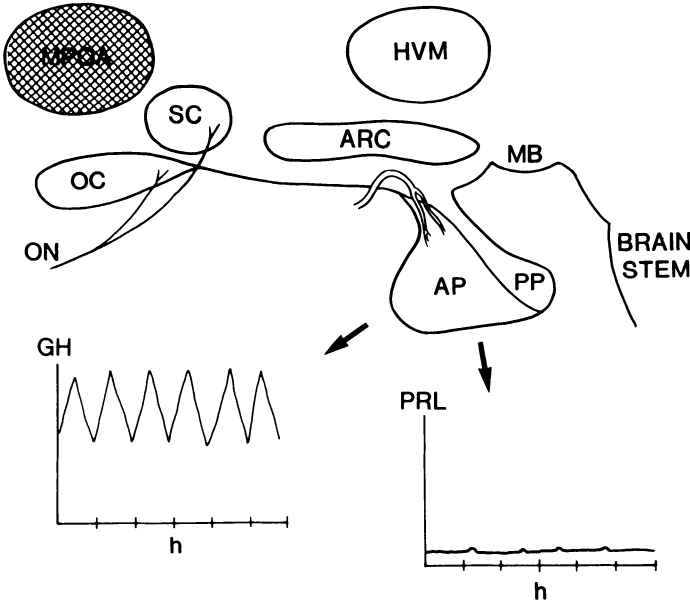


Fig. 5. Increased GH secretion after selective lesions of MPOA.

To investigate this point small, midline lesions were placed directly in the SC nucleus. The lesions had no effect on the fundamental rhythmic pattern of GH secretion but did abolish the normal entrainment of the GH surges to the light-dark cycle (22). The period of interval between individual surges was not different from control animals (Table 2.)

TABLE 2

EFFECT OF SUPRACHIASMATIC LESIONS ON INTERVAL BETWEEN GH SURGES

|            | N  | Interval between surges - h |
|------------|----|-----------------------------|
| Intact     | 20 | $3.17 \pm .36$              |
| Control    | 8  | $3.41 \pm .30$              |
| SC Lesions | 7  | $3.00 \pm .11$              |

As lesions and destruction to the hypothalamus could result in non-specific aberrations in the rhythms of hormone secretion, additional experiments were undertaken on normal animals to reinvestigate the effects of passive immunization with anti-somatostatin serum. If somatostatin has a role in determination of GH suppression during the trough periods between surges, it could be reasoned that antisera might alter normal secretory patterns. Antiserum produced elevation of the trough levels followed by a surge of GH secretion. The second trough was also elevated but less so than the first. Measurement of somatostatin binding capacity in blood samples removed from the rat at the two time intervals showed a decrease in antisera effect. When a group of animals was analyzed, it was apparent that the antiserum had no effect on mean peak levels of GH, but did significantly elevate GH during the trough periods. These results imply that SRIF is secreted intermittently and that its effects interact with a stimulatory *factor* (GRF) to produce the GH secretory pattern.

Recent studies published by Steiner and coworkers (23) have confirmed several of these findings in the primate. The chair-adapted baboon shows a very similar, regular pattern of GH secretion with surges occurring spontaneously at 3-4 hour intervals. Their data also suggest that light-dark entrainment of secretory bursts occur.

Active immunization of the baboon with somatostatin resulted in disintegration of the normal pattern of GH secretion. These workers also concluded that secretion of somatostatin is important for regulation of GH secretion.

A similar pattern of GH secretion is also characteristic of the human. Finkelstein and coworkers (24) showed that the pattern of GH secretion in adolescent males is entirely episodic. The prominent surge of secretion that occurs during the first two hours of sleep is probably no more than one instance of the general pulsatile surging pattern of GH releases which occurs at intervals throughout the 24h period.

How then does the hypothalamus integrate this rhythm? I would propose that the final profile of GH secretion, as determined by repeated sampling in the peripheral blood, is the result of integration of at least two separable regions of the hypothalamus (Figure 6). The HVM nucleus is the origin of a fast pulsatile pattern of stimulatory or excitatory influence, presumably mediated via an identified GRF. If unopposed, this region generates excessive GH secretion, as evidenced in the hypothalamic-deafferented animal. Superimposed upon this system is the influence of an anterior hypothalamic-preoptic somatostatinergic system which inhibits the GRF system in one or two ways. Direct release of somatostatin into the portal system to intermittently inhibit GH secretion is the most plausible explanation because of the results of the antisera experiments. Alternatively, direct neural connections to GRF neurons might relay the inhibitory influence with somatostatin serving as a neurotransmitter. The net result of the two integrated systems is the complex, multiphasic pattern of GH secretion observed in the peripheral blood (Figure 7). The function of the suprachiasmatic nucleus seems to be to regulate the timing of the pulses to an external cue, namely light-dark transition, but it does not function to determine the rhythm per se. This is consistent with other recent conceptualizations of the role of this structure in rhythms in general, i.e., as a coordinator rather than an originator of neural rhythms.

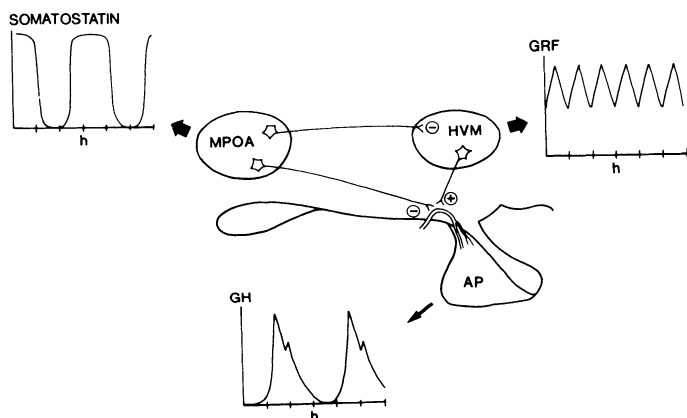


Fig. 6. Hypothesis on mechanism of integration of GH secretion by the hypothalamus. The HVM is the origin of a GRF driven periodic stimulation of GH. This secretory pattern is modulated by somatostatin release from nerve terminals, the cell bodies of which arise in MPOA. The GH secretory profile determined from systemic blood sampling is shown at the bottom.

There are several clinical observations that support this analysis. Lesions in the anterior hypothalamus in children can result in a hypersecretory GH syndrome with cachexia and depletion of body fat. Lesions of this region may also result in excessive GH release to pharmacologic stimuli.

In conclusion, two other issues need to be addressed; 1) what is the function of other neurotransmitters in the generation of the rhythm? and 2) what is the nature of the GRF implicated?

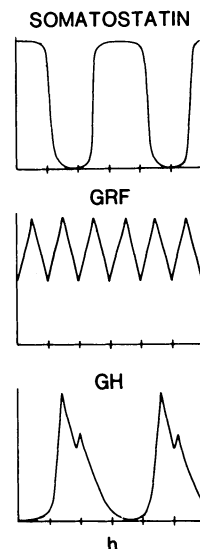


Fig. 7. Diagrammatic illustration of phased secretion of somatostatin, GRF and resulting effect on GH secretion.

There is a great deal of evidence to indicate that basal low levels of GH can be stimulated either in the anesthetized or unanesthetized state by administration of various precursors of dopamine, norepinephrine, and serotonin or by substances that directly stimulate amine receptors in brain. For example, L-dopa the precursor of both dopamine and norepinephrine is effective in stimulating GH secretion in monkey, dog and man (1). Apomorphine, a dopamine receptor agonist and clonidine and receptor agonist and clonidine an  $\alpha$ -adrenergic stimulating agent, are also effective in releasing GH in several species. It is possible using the pulsatile model to ask the opposite question. What effects do agents that deplete or block catecholamine function have on the episodic pattern of GH secretion?

In these experiments  $\alpha$ -methyl-p-tyrosine, an enzyme inhibitor that blocks the synthesis of both dopamine and norepinephrine in brain was administered. When the drug was given at 8:00 a.m., the effects were rapid and dramatic. Episodic GH secretion was entirely abolished (25). Levels of PRL increased due to the deficiency in hypothalamic dopamine, which is known to be a potent inhibitor of PRL secretion by an effect exerted directly at the pituitary level. The administration of apomorphine a dopamine receptor agonist had no effect in restoring GH secretion in catecholamine-depleted rat whereas, clonidine, an  $\alpha$ -adrenergic agent administered at a time of an expected pulse effectively restored the GH surges (25). Administration of  $\alpha$ -adrenergic receptors blocking agents also inhibited GH secretion in intact rats; whereas, dopamine blockers had minimal effects (26).

These results serve to emphasize that there are important interactions between neurotransmitter functions and the release of peptide substances in brain. However, the effects of neurotransmitter appear to be predominantly modulatory not mandatory, since hypothalamic isolation causes increased not decreased GH secretion. These observations have important implications in the pharmacologic manipulation of hormone secretion. Pharmacologic blockade only has transient effects and is not generally effective in long-term experiments.

What is the nature of GRF? Despite a great deal of effort in several laboratories to identify a specific substance that stimulates GH secretion, such attempts have so far been unsuccessful. I believe the experiments that I have described today comprise proof that a potent stimulatory factor is essential to account for the complicated GH secretory dynamics which appear to be a general phenomenon in mammalian species.

Several peptide substances have been demonstrated to cause GH secretion under various circumstances (Table 3). Several such as TRH, vasopressin and glucagon are used clinically to stimulate GH secretion. However, none of these substances have been shown to act directly on the pituitary *in vitro* to release GH and all are presumed to act at central brain levels. Of great interest in recent years have been the opioid or morphinomimetic peptides, met-enkephalin and B-endorphin. We reported several years ago that morphine is a potent stimulator of GH secretion in the rat (27). This response was not ablated by extensive hypothalamic lesions provided the median eminence was preserved. Since morphine had no effects directly on the pituitary *in vitro*, we postulated that its effects were mediated at the median eminence level. Several reports have now confirmed the presence of both endorphins and enkephalins in the median eminence. Autoradiographic studies using morphine antagonists have also shown prominent staining in the median eminence suggesting that opioid receptors are located here (28).

TABLE 3

PEPTIDES THAT STIMULATE GROWTH HORMONE SECRETION

- |                  |                          |
|------------------|--------------------------|
| 1. Vasopressin   | 7. Neurotensin           |
| 2. TRH           | 8. Enkephalin            |
| 3. LHRH          | 9. $\beta$ -Endorphin    |
| 4. $\alpha$ -MSH | 10. Bombesin             |
| 5. Glucagon      | 11. Cholera Enterotoxin  |
| 6. Substance P   | 12. Basic Myelin Protein |

As part of a general assessment of the role of various pharmacologically active substances in pulsatile GH secretion, we investigated the effects of naloxone, a specific morphine and opioid antagonist. There was no appreciable effect on either GH or prolactin secretion by doses of naloxone ranging from 0.1 to 20 mg/kg. The peaks of 6h secretion were unchanged and the trough suppression was not altered. A statistical analysis of GH secretion in which the area under each GH secretory profile was determined by planimetry, showed no significant difference.

These results are strongly indicative that the opioid peptides are not GRF nor that they mediate GRF release under physiological conditions. Furthermore, they suggest that the several reports which show that systemic or central administration of endorphins or enkephalins cause GH secretion may be spurious (29-31). One possible explanation is the fact that these agents are epileptogenic; administrations of doses required to induce GH secretion may elicit electrical discharges that activate GH release in much the same manner that electrical stimulation itself elicits GH release (5). It is probable that a specific GRF remains to be identified.

These studies have shown a surprisingly complex regulatory system for a hormone that is responsible for one of the most chronic of all endocrine functions, namely growth. The fundamental question of why hormones are secreted episodically has not been addressed, but is probably related to the intrinsic dependence of peripheral receptors on intermittent, pulsed exposure to hormone stimulation rather than continuous exposure which would result in down-regulation.

## ACKNOWLEDGEMENTS

The author wishes to thank Paul Brazeau, Gloria Tannenbaum, John Willoughby, Jacques Epelbaum, Dominique Durand, L. Cass Terry and Otto Rorstad who assisted in the conceptualization and execution of these experiments. Generous financial support was provided by the Medical Research Council of Canada.

## REFERENCES

- Martin, J.B., Reichlin, S. and Brown, G.M. *Clinical Neuroendocrinology* F.A. Davis Company, Philadelphia, 1977.
- Reichlin, S., Baldasserini, R. and Martin, J.B. *The Hypothalamus* Raven Press, New York, 1978.
- Frohman, L.A., and Bernardis, L.L. Growth Hormone and Insulin Levels in Weanling Rats with Ventromedial Hypothalamic Lesions. *Endocrinology* 82:1125-1132, 1968.
- Frohman, L.A., Bernardis, L.L. and Kant, K. Hypothalamic Stimulation of Growth Hormone Secretion. *Science* 162:580-582, 1968.
- Martin, J.B. Plasma Growth Hormone (GH) Response to Hypothalamic or Extra-Hypothalamic Electrical Stimulation. *Endocrinology* 91:107-115, 1972.
- Martin, J.B., Tannenbaum, G., Willoughby, J.O., Renaud, L.P., and Brazeau, P., Functions of the Central Nervous System in Regulation of Pituitary GH Secretion. In: *Hypothalamic Hormones; Chemistry, Physiology, Pharmacology, and Clinical Uses*, edited by M. Motta, P.G. Crosignani, and L. Martini, pp. 217-236, Academic Press, New York, 1975.
- Schalch, D.E. and Reichlin S. Plasma Growth Hormone Concentration in the Rat Determined by Radioimmunoassay: Influence of Sex, Pregnancy, Lactation, Anesthesia, Hypophysectomy and Extracellular Pituitary Transplants. *Endocrinology* 79:275-280, 1966.
- Takahashi, K., Daughaday, W.H. and Kipnis, D.M. Regulation of Immunoreactive Growth Hormone Secretion in Male Rats. *Endocrinology* 88:909-917, 1971.
- Weitzman, E.D., Fukushima, D., Nogeine, C., Rottwarg, H., Gallagher, T.F. and Hellman, L. Twenty-Four Hour Pattern of the Episodic Secretion of Cortisol in Normal Subjects. *J. Clin. Endocrinol. Metab.* 33:14-22, 1971.
- Takahashi, K., Kipnis, D.M. and Daughaday, W.H. Growth Hormone Secretion During Sleep. *J. Clin. Invest.* 47:2079-2090, 1968.
- Glick, S.M. and Goldsmith, S. The Physiology of Growth Hormone Secretion. In: *Growth Hormone*, edited by A. Pecile and E.E. Muller Amsterdam, Excerpta Medical Foundation. 2nd Congr. Ser. 158, 84-88, 1968.
- Martin, J.B., Renaud, L.P., and Brazeau, P. Pulsatile Growth Hormone Secretion: Suppression by Hypothalamic Ventromedial Lesions and by Long-Acting Somatostatin. *Science* 186:538-540, 1974.
- Tannenbaum, G.S., and Martin, J.B. Evidence for an Endogenous Ultradian Rhythm Governing Growth Hormone Secretion in the Rat. *Endocrinology* 98:540-548, 1976.
- Willoughby, J.O., Martin, J.B., Brazeau, P.B., and Renaud, L.P. Pulsatile Growth Hormone: Failure to Demonstrate a Correlation to Sleep Phases in the Rat. *Endocrinology* 98:593-598, 1976.
- Willoughby, J.O., Terry, L.C., Brazeau, P., and Martin, J.B. Pulsatile Growth Hormone, Prolactin and Thyrotropin Secretion in Rats with Hypothalamic Deafferentation. *Brain Research* 127:137-152, 1977.
- Mitchell, J.A., Smyrl, R., Hutchins, M., Schindler, W.J. and Critchlow, V. Plasma Growth Hormone Levels in Rats with Increased Naso-anal Lengths due to Hypothalamic Surgery. *Neuroendocrinology* 10:31-45, 1972.
- Mitchell, J.A., Hutchins, M., Schindler, W.J. and Critchlow, V. Increases in Plasma Growth Hormone Concentration and Naso-anal Lengths in Rats Following Isolation of the Medial Basal Hypothalamus. *Neuroendocrinology* 12:161-173, 1973.
- Terry, L.C., Willoughby, J.O., Brazeau, P., Martin, J.B., and Patel, Y. Antiserum to Somatostatin Prevents Stress-Induced Inhibition of Growth Hormone Secretion in the Rat. *Science* 192:565-567, 1976.
- Alpert, L.C., Brawer, J.R., Patel, Y.C., and Reichlin, S. Somatostatinergic Neurons in Anterior Hypothalamus: Immunohistochemical Localization. *Endocrinology* 98:255-258, 1976.
- Willoughby, J.O. and Martin, J.B. Pulsatile Growth Hormone Secretion: Inhibitory Role of Medial Preoptic Area. *Brain Research* 148:240-244, 1978.

21. Epelbaum, J., Brazeau, P., Tsang, D., Brawer, J., and Martin, J.B. Subcellular Distribution of Radioimmunoassayable Somatostatin in Rat Brain. *Brain Research* 126:309-323, 1977.
22. Willoughby, J.O. and Martin, J.B. The Supra-Chiasmatic Nucleus Synchronises Growth Hormone Secretory Rhythms with the Light: Dark Cycle. *Brain Research* 151:413-417, 1978.
23. Steiner, R.A., Stewart, J.K., Barber, J., Koerker, D., Goodner, C.J., Brown, A., Illner, P. and Gale, CC. Somatostatin: A Physiological Role in the Regulation of Growth Hormone. *Endocrinology* 102:1587-1594, 1978.
24. Finklestein, J.W., Roffwarg, H.P., Boyar, R.M., Kream, J., and Hellman, L. Aged-Related Changes in the Twenty-four Hour Spontaneous Secretion of Growth Hormone. *J. Clin. Endocrinol. and Metab.* 35:665-670, 1972.
25. Durand, D., Martin, J.B., and Brazeau, P. Evidence for a role of  $\alpha$ -adrenergic Mechanisms in Regulation of Episodic Growth Hormone Secretion in the Rat. *Endocrinology* 100:722-728, 1977.
26. Willoughby, J.O., Brazeau, P., Martin, J.B. Pulsatile Growth Hormone in Prolactin: effects of (+) Butaclamol, Adopamine Receptor Blocking Agent. *Endocrinology* 101:1298-1303, 1977.
27. Martin, J.B., Audet, J. and Saunders, A. Effect of Somatostatin and Hypothalamic Ventromedial Lesions on GH Release Induced by Morphine. *Endocrinology* 96:839-847, 1975.
28. Atweh, S.F. and Kuhar, M.J. Autoradiographic Localization of Opiate Receptors in Rat Brain. II. The Brain Stem. *Brain Research* 134:393-405, 1978.
29. Chihara, K., Arimura, A., Coy, D.H. and Schally, A.R. Studies on the Interaction of Endorphins, Substance P, and Endogenous Somatostatin in Growth Hormone and Prolactin Release in Rats. *Endocrinology* 102:281-290, 1978.
30. Bruni, J.F., Van Vugt, D., Marshall, S. and Meites, J. Effect of Naloxone, Morphine and Methionine Enkephalin on Serum Prolactin, Luteinizing Hormone. *Life Science* 21:461-466, 1977.
31. Shaar, C.J., Frederickson, R.C.A., Dininger, N.B. and Jackson, L. Enkephalin Analogues and Naloxone Modulate the Release of Growth Hormone and Prolactin-Evidence for Regulation by an Endogenous Opioid Peptide in Brain. *Life Science* 21:853-860, 1977.

## CAN DIET PREVENT DISEASE?

A scientific session entitled A Critique of the Nutritional Prevention of Disease is scheduled for Saturday evening, May 5, 1979 in the Sheraton Park Hotel, Washington, D.C., beginning at 7:30 PM in the Park Ballroom.

Admission is free to all interested persons. Participants in the symposium will include experts in each of the research areas of carbohydrates, fats, serum cholesterol, alcohol, salt, and obesity and calories. W. E. Connor, M.D., Department of Medicine, University of Oregon Health Science Center, and E. H. Ahrens, Jr., M.D., of Rockefeller University, will be cochairmen; Jules Hirsch, M.D., also of Rockefeller University, will summarize the talks.

The symposium is the result of a full year's major effort by the American Society for Clinical Nutrition to collect and evaluate existing evidence about the relationships between diet and health, and between diet and disease.

The original decision of the Society to organize and fund the project was the direct result of the publication "Dietary Goals for the United States," as written by the staff of the McGovern (now disbanded) Senate Select Committee on Nutrition and Human Needs. In publishing the revised edition of these Goals, Senator McGovern called for an interagency working group, headed by the Assistant Secretary for Health to evaluate the recommendations. Dr. Julius Richmond named a member of his Office of Health Policy to serve as liaison to the ASCN's committee selected to supervise the project. The resultant symposium, however, extends beyond the areas of the Goals.

The symposium will be published in the Society's official publication, The American Journal of Clinical Nutrition, sometime in 1979.

## AMERICAN SOCIETY FOR BIOMECHANICS

The Third Annual Conference of the American Society of Biomechanics will be held at The Pennsylvania State University, State College, PA on October 22 and 23, 1979.

Papers are requested in all areas of research involving the application of mechanics to biological problems.

Abstracts must be submitted prior to May 1, 1979. For more information, contact: Mr. Ron Avillon, Keller Bldg., Pennsylvania State University, University Park, PA 16802.

## INTERNATIONAL SYMPOSIUM ON THE ACTIONS OF TAURINE ON EXCITABLE TISSUES

The symposium which is to be held at the Sheraton-Valley Forge Hotel, King of Prussia, PA. on April 23 and 24, 1979, is being organized by Drs. S.I. Baskin (Medical College of Pennsylvania), J.J. Kocsis (Jefferson Medical College, Thomas Jefferson University) and S.W. Schaffer (Hahnemann Medical College), and is co-sponsored by The Physiological Society of Philadelphia and the three medical colleges listed above. Scientists from the United States and abroad will present their latest experimental findings in the following program sessions: Molecular And Cellular Effects Of Taurine, Effects Of Taurine On The Cardiovascular System, Effects Of Taurine On The Retina And Central Nervous System, Clinical Aspects Of Taurine. This symposium meets the criteria for 12 hours credit in category 1 for the physicians' recognition award of The American Medical Association.

For information contact Dr. S.I. Baskin, Department of Pharmacology, the Medical College of Pennsylvania, 3300 Henry Avenue, Philadelphia, PA 19129.

## SOME NOTES ON PREPARING A HISTORY OF A DEPARTMENT OF PHYSIOLOGY

Horace W. Davenport  
The University of Michigan

In anticipation of the celebration of the Centennial of the American Physiological Society in 1987 the Council is urging the preparation of a history of each Department of Physiology. Because I have plunged deep into the history of Physiology at Michigan, a history beginning with the appointment of a Professor of Physiology in 1850, the Centennial Committee has asked me to write a few notes which might help others in their work. Here I give some advice with examples drawn from my own experience.

The first requirement is a complete and accurate chronology: who and when. There is no physiological equivalent of the massive History of Biochemistry project whose headquarters are at the American Philosophical Society in Philadelphia, and the journals of the history of medicine or science have seldom carried pertinent articles. Nevertheless, the journals should be searched. There are usually several histories of a university, and there may be a history of the medical School. These are useful but not to be trusted, especially with dates. For example, one entry in Harrington's *History of Harvard Medical School* states twelve facts about a man I was interested in. Of these, five are definitely wrong, and four more are questionable. Emphasis may be wrong as well, for local piety makes things out to have been grander than they actually were.

Catalogs of the university and medical school, when they can be found, are helpful, but they are always a year out of date. Some, such as Harvard's in the 1890's, are minutely detailed, whereas others are vague. Minutes of Regents or Trustees are usually published, and they can probably be trusted with their bare facts. They tell who was appointed but not why. The reports of Presidents are unreliable. Faculty minutes are usually not published, and they may be hard to find. They, too, are incomplete, telling what happened but not why. Committee reports may be missing. I would like to have seen the one Victor Vaughan gave on the state of Physiology at Michigan in 1879, but it has not been saved. Old financial records of a University would be useful if they could be found.

Faculty members have often published historical articles in alumni magazines or in local medical journals. The latter were usually ephemeral, and their contents are not listed in standard bibliographies. Such articles are useful, but they are not to be trusted implicitly. The *Catalog of the Library of the New York Academy of Medicine* lists an enormous number of obscure items. Flexner's report of 1910 will contain a sketch of how things were in 1909. The University Archivist, if there is one, can be very helpful, and a well-cataloged Historical Collection is enormously valuable. Reference librarians are jewels, and they will do a lot of work to find something. Ours, however, have not been successful in getting inter-library loans.

Once the members of a Department have been identified, the facts of their careers, background, education, and appointments can be established. A surprising number of obscure persons have been commemorated in biographies and autobiographies hidden on the back shelves of the library, and library catalogs should be searched. Again, what they say must be read skeptically, and even autobiographical dates and assertions may be wrong. Gross and Kelly each edited a *Dictionary of Medical Biography* which

lists persons otherwise totally forgotten. Education can be traced through books on schools, colleges and universities. I have had occasion to look up, among many others, Rennselaer, Castleton Medical Academy, Geneva Medical School and P & S, and in each instance I have found at least one book. My predecessor, Henry Sewall, went to Wesleyan in 1871, and there is a book in our library describing Wesleyan's curriculum in the 1870's. Here, again, information can be found by searching the card catalog under every possible heading.

The standard reference books, *Who's Who in America*, *Who Was Who*, *American Men and Women of Science*, and the *Dictionary of Scientific Biography*, contain the basic facts, but they may be incomplete. Obituary notices, from the National Academy of Sciences, the Royal Society, the New York Times, the London Times, the J.A.M.A., have all helped me. The obituary notices may reveal personalities, as does Howell's of Meltzer, or they may be funny, as Lamson's of Abel. Local newspapers can be searched, and this may mean hours of going cross-eyed while unreeling photocopies of the *Washtenaw Whig* of the 1850's.

Research accomplishment can be traced through bibliographies, but it is only recently that bibliographies have become reasonably complete. Early papers may be hard to find. In addition to the catalog of the Library of the New York Academy of Medicine, I have used those of the Office of the Surgeon General, the Royal Society and the British Museum. I have tracked papers through references in other papers and in footnotes.

Sometimes it is difficult and sometimes easy to establish the place of Physiology in the curriculum. Detailed schedules may be given, as they are in the Harvard catalogs, or there may be only a list of subjects taught. In the early days, when the medical curriculum was merely a set of lectures, Physiology was skimmed, though someone may have been called Professor of Physiology as well as Professor of Materia Medica and Pathology. As the curriculum lengthened to three and then four years and became graded, the time devoted to physiology also increased. Here, one may be lucky as I was. Henry Sylvester Cheever was the first man to try to teach Physiology properly at Michigan. When he was dying in 1876 he wrote a 28-page letter to the President of the University describing how he had learned Physiology through Dalton, how he had taught it at Michigan and what Michigan needed if Physiology were to take its proper place in the curriculum. The letter was preserved in the President's files, and it is immediately followed by a letter from the Dean of our medical school reporting the results of a trip to Boston to spy out how Physiology was taught at Harvard in 1877.

The catalogs, Faculty Minutes and letters may describe the growth of Physiology as a laboratory science. Equipment is sometimes listed. At Michigan the Physiology Laboratory was voluntary for many years, and it alternated with Pharmacology. Who took it, including Jack Brookhart's father, and who taught it, including Carl Wiggers, is recorded in grade books which have been preserved.

Clothing the bones of the curriculum with the flesh of what actually was taught is difficult. I have not found any detailed lecture schedules, but I have found a few lecture notes. At Michigan,

Literary College students, "regular" medical students, homeopathic medical students and dental students were lectured for years by a faculty of one, but I don't know how it was done. Catalogs list recommended books, but we know the relation between such lists and what students really read. At Michigan from 1851 through 1877 each medical student wrote a thesis, and those on physiological topics reveal the state of physiological teaching of the time. The theses at Penn and Yale should be equally useful. Sometimes a student notebook is preserved. Examination files are revealing; the complete file begins at Michigan only with 1936, but I have found one examination of the 1870's. Beginning in the 1880's, a synopsis of the course was published through a local bookstore. Henry Sewall wrote three of these, and Lombard published laboratory manuals later. Victor Vaughan, who helped start physiological chemistry and bacteriology at Michigan, published enormous mimeographed volumes, and a student complained to the Dean about being required to purchase one.

Sometimes early equipment is saved. Lombard, who kept everything, including drafts of letters, preserved the invoices for equipment he bought in Germany in 1895 and the bills for kymographs purchased from the Harvard Apparatus Company in 1912. The cost was \$12, but it had been raised to \$13 by the time the kymographs were delivered. I sold the same kymographs back to the Company for \$15 in 1957. Lombard also saved a large collection of photographs of students working in the laboratory, and through them I learned that in the late 1890's students measured forearm blood flow with a plethysmograph. Sewall kept a detailed *Day Book* recording how he ran the laboratory course at Hopkins under Newell Martin.

At Michigan, beginning in the 1880's, and at Harvard a little earlier, students of many kinds have worked in the department. Some have formal appointments and can be traced in university records. Many, and these were often the most important, were volunteers. They may be identified only through memoirs or as co-authors of a paper. Once graduate degree programs were started, students can be identified through the records of the Graduate School. In the last four decades the multitudinous research and training grant applications contained names of students, collaborators and post-doctoral fellows. I have not saved ours, but copies must exist somewhere.

The best advice I can give is to plunge into the task. It is astonishing how much of the past one can recover. Persons who wring their hands over information storage in the computer age should learn how much information was stored with a quill pen. As I gathered material, I learned what to trust and what not. Each new fact brought with it a set of relations to other facts and frequently posed a question I did not know was there to be asked. As I became more familiar with the job I erected a great framework from which, metaphorically, streamed questions to be answered. Pondering these, often at 2 AM, I suddenly found an answer or, at least, where to look for an answer. For example, the first man to be Professor of Physiology at Michigan was abruptly fired by the Regents on May 4, 1854. The record is utterly silent on the reason except to hint that he was "obnoxious." Since it was clear that he was not obnoxious before 1854 and, in view of his highly successful subsequent career, not obnoxious after 1854, a glance at Nevins' *Ordeal of the Union* gave me the clue. I was quickly able to assemble the facts to substantiate my conclusion. That was a lot of fun, and I can recommend a similar search to anyone who has the energy and a sense of history. And don't be afraid to ask for help. Once you know enough to ask a well-phrased question, someone may be able and pleased to answer it.

[The foregoing article by Horace Davenport was prepared at the request of the APS Centennial Celebration Committee as an aid to potential authors of Departmental Histories. (O.E.R.)]

## AN HISTORICAL NOTE

Arthur B. Otis

Perhaps some other members of the American Physiological Society will be surprised, as I was recently, to learn that ours is not the first to bear this name. The first American Physiological Society was founded in Boston, MA on Feb. 11, 1837, when its constitution was signed by 124 men and 39 women. William Andrews Alcott, a medical practitioner and Sylvester Graham, a clergyman who invented the bread which bears his name, were the founding fathers. It was indeed, a health society rather than a scientific group. It enjoyed an active life of 3 years during which it sponsored a number of public lectures, maintained a library, ran a provision store, which sold a wide variety of health food including Graham flour, and took part in organizing two health conventions, one in Boston and one in New York. The society appears to have died in 1840.

Among the books in the library was Beaumont on the Gastric juice. Graham wrote a criticism of Beaumont's work with the implication that had he the opportunity to observe and investigate the stomach of Alexis St. Martin, a far greater contribution to physiology would emerge. The secretary of the Society went so far as to write Beaumont with regard to the possibility of engaging the services of St. Martin. Beaumont's reply was polite but not encouraging and there the matter apparently ended.

## REFERENCE

Hoff, Hebbel E. and John F. Fulton. The Centenary of the first American Physiological Society founded at Boston by William Alcott and Sylvester Graham. *Bulletin of the Institute of the History of Medicine*. 5:687-734, 1937.

**Efrén C. del Pozo** to Hal Davis:

At present, I have the honor to be named Emeritus Research Professor of the National University of Mexico, through my collaboration in the Institute of Biomedical Research at the same University. During the last 16 years I have worked as Secretary General of the Association of Latin American Universities, that with the proposal of affirming the character of latinamerican integration is denominated "Union de Universidades de América Latina", although this name has a very different meaning to that of the term "union" in the English language, as it has no relation with "laboral organization." We have a modern building and here we have our headquarters. My last scientific work deals with the pharmacology of Mexican plants and I am occupied on the publication of some fundamental works on this topic. With kind regards.

**Ann Minot** to Hal:

Thank you for the heartwarming birthday greeting from you and the Society. It gives me a feeling of still belonging to the group. My general health is very good. With fond greetings.

**Eugene Robillard** to Hy Mayerson:

I now perform administrative duties for the Professional Corporation of Physicians of Quebec. I have been away from teaching and research for a few years, but out of curiosity and personal interests, I continue to be interested by scientific literature. When I leave my administrative work, I intend to tackle a new activity as a challenge.

**Donald Proctor** to Hal:

At the moment I am active in three departments, Environmental Health Sciences, Otolaryngology, and Anesthesiology. My research continues. I leave soon for another study at the University of Aarhus in Denmark, effects of toluene on human volunteers, with my colleague Ib Anderson. Have just completed a book on the physiology of breathing, speech and song. Am working on a study of the history of breathing mechanics and currently am searching for information on John Mayow and Fritz Rohrer. I do not contemplate a move from Johns Hopkins where I have been since 1929.

**Ruth Pick** to Horace Davenport:

I am still working full-time in my old position as Chief of the Atherosclerosis Research Laboratory in the Cardiovascular Institute at Michael Reese Hospital and Medical Center. I began here under Dr. Louis N. Katz in 1949 right "off the boat" from Europe and I am still here. This is the only place I have worked on different rungs of the ladder since I came to this country. After July I hope to carry on on a half-time basis. As to words of wisdom only some old and trite ones: perseverance and patience are the main ingredients to carry out research. An optimistic outlook is of great help so as not to be easily subdued by disappointment. Without it one is bound to give up in frustration at the inevitable set-backs.

**Nathan R. Brewer** to Hy:

I am continuing activities as secretary of the Illinois Society for Medical Research, as a consultant in laboratory animal medicine, and as a contributor to "house organs." My contributions consist of items of comparative physiology as they relate to laboratory animals, especially those items of "practical" importance. I have also taken up chess, a hobby that is intended to keep my association neurons from lysing. It has the added effect of keeping me

humble. To keep in physical shape I do no jogging, but I do go through about 15 minutes of regular exercises every morning that includes 100 push-ups and other exercises.

**Allan Grafflin** to Hy:

I have completely retired from the practice of ophthalmology. I am not engaged in scientific or other type of writing. I am free to move to another area, and we might just do that, but not until our son Dennis has completed, at Harvard, his doctoral thesis on early Chinese history. We continue in good health as do our children.

**Esther M. Greisheimer** to Hal:

I am not doing any type of writing or scientific activities now. I have written about 150 papers and 9 editions of a textbook so I am "written out" as it were. Two capable young men are working on the tenth edition of my textbook. I taught 51 years. My only advice to the young is: Work hard as long as you can; Report your findings honestly; Use any talents God gave you.

**Hayden Nicholson** to Hy:

I am enjoying my retirement thoroughly. Both my wife, Marian, and I are in good health. Our major preoccupation seems to be gardening. In this climate (Illinois) there are several months when not much can be done in the garden, but we have a few orchids growing under fluorescent lights in the basement. We are doing some traveling, mainly to visit friends. I enjoy reading the letters from senior physiologists.

**O.M. Helff** to Dr. Adolph:

Yes, I am still interested in amphibian development, but for nearly 30 years now I have been working on extracts of larval amphibian tissues as they affect mammary tumors in mice. I have not been to New Hampshire for two years to make extracts, but after a winter in at Delray Beach, Florida, I hope to be able to go there and make extracts again. There I can collect suitable frog tadpoles.

**Virginia M. Fiske** to Edward:

I have continued with my pineal studies at Wellesley College. This September, however, has been particularly stimulating as I am currently a "Visiting Professor" at Wellesley, teaching a course in human physiology for non-majors which I helped to introduce some eight years ago. I also have an Honor's student working with me on an endocrine problem. The appointment is only for this year to cover work for someone on Sabbatical Leave, but I am thoroughly enjoying this commitment. My husband and I continue to enjoy gardening, an occasional trip, and our family of children and grandchildren. We are "rooted" to our old house in the country.

**H. Burr Steinbach** to Edward:

It is nearly 45 years since I had the pleasure of working in your laboratory and I still have a few things to do with frog skin, if I ever get around to getting in a lab again. A dozen or so years ago, I became involved in such remote operations as marine affairs and "food from the sea" problems. I've now retired five times from administrative jobs and stay here at Woods Hole as a consultant to the Marine Policy and Ocean Management Program of the Woods Hole Oceanographic Institution. All is well with the family. The kids are doing fine living in areas ranging from California to Switzerland. Woods Hole is a great place for retirement but

Susie likes Hawaii better so we get back there now and then. Still quite a bit of traveling also on various consulting assignments.

**Edward D. Freis** to Edward:

I am still full time Senior Medical Investigator at the Veterans Hospital, Washington, D.C. and still in charge of hypertension research. My major activities include cooperative studies involving antihypertensive agents, studies related to treatment, studies on the spontaneously hypertensive rat and hemodynamic effects of antihypertensive agents. In addition, I do some lecturing and consulting. My health remains excellent and my work capacity is undiminished.

I have several outside interests including competitive golf, music appreciation and paint collecting. I believe these outside interests plus an exercise program have kept me physically and mentally fit to carry on much as I have done in the past.

**Victor Guillemin, Jr.** to Edward:

Being born in 1896, I am four yours older than the 20th century. But it has not yet occurred to me that I am a "senior citizen." Officially, I am retired. But I still keep busy all day, every day. Among other matters, I read a lot and write a lot, working on a book I intend to publish. It is about a very big subject, namely, the future of the whole universe and, in particular, of our own little earth with everything upon it, both animate and inanimate. It is a subject that keeps expanding the more I think about it. The book is now about three-fourths finished but promises to keep me busy for at least another year.

My advice to others approaching retirement is to do some detailed planning on writing that book they have never seemed to find time for. It is great way to keep busy and to acquire new knowledge. For it has been truly said that, if you want to learn a subject thoroughly, write a book about it.

**William L. Doyle** to Edward:

I continue as Professor Emeritus of Anatomy at the University of Chicago and in providing instruction in Histology and Cell Biology. My principal research effort remains in collaborative projects with associates at the Mount Desert Island Biological Laboratory in Maine by providing some structural correlates to physiological studies on transport processes, particularly in chloride cells of fish gills and in the rectal salt gland of the dogfish. I also edit the Buletin of that laboratory.

**Harold C. Wiggers** to Horace Davenport:

I certainly enjoy the Senior Physiologist letters or news as published and it's surprising how many I know despite my deseration of physiology in 1953 to pursue some 23 years of Deaning at Albany and again after initial retirement at the new medical school at East Carolina University in Greenville. I retired again in September 1977. While visiting friends in Vero Beach, Florida, my wife found an appropriate size house and we moved here in December 1977. Vero Beach is a delightful small community with a good mix of young, middle age and senior people. I spend about half time caring for the yard, many flowers, and a small vegetable garden. I golf about four times a week and still get my share of drives in the 250-280 yard range, which shows its a game of timing, not brute strength. Leaves time to read some non-scientific, non-medical literature, especially historical, which I never had time for while active. I do manage to keep abreast of change and progress in medical education and physiology thru various media. Please indicate to Hy, Bruce, Hal, Ed, Sid and Ladd that I recall each with very fond memories. Congratulations to you on your remarkable achievements at the University of Michigan where my Dad got his M.D. and his start with Lombard.

**George Clark** to Horace:

I am continuing to enjoy "retirement." The VA Hospital supplies a small laboratory and some equipment. Luckily the research I do on staining methods is quite inexpensive, only time consuming. I spend 4-6 hours in my lab each day and will do some teaching next quarter. All in all I'm having fun with no deadlines that I don't make myself and virtually no paper pushing.

**Charles D. Howell** to Bruce:

I retired from teaching at the University of Redlands in June 1976, but was kept on the active faculty until 1977, teaching physiology, anatomy, and embryology. During the last few years of teaching I added a natural history course to my schedule. I saw little chance of carrying on physiological work after retirement, so I chose to gradually transform a hobby of mine into a specialty. That hobby was the study of evolution in nature. I had taught evolution with genetics, embryology and physiology in mind, but now I wanted to see it at the species level. I chose to do this with insects, and began with serious study of them during my last sabbatical in 1970. I took up work on *Dasytidae*, a long neglected family of beetles and have been studying their speciation ever since.

In 1977, I was offered the title of Curator of Entomology and Invertebrate Zoology at the San Bernardino County Museum, here in Redlands. I accepted and that is the seat of my research. I also set up Museum displays, organize their insect collection, train Docents, teach school children from local schools, serving as a Biological Consultant and answering innumerable questions from the public every day. I am enjoying an active retirement, but do miss the college student contacts.

**Jonathan E. Rhoads** to Bruce:

I am still practicing surgery, teaching surgery, and editing the journal *Cancer*. I have been able to attend some APS meetings. I continue some writing, mainly of an educational or biographical nature. I am not actively doing any bench research.

**Robert W. Dougherty** to Horace:

I took an early retirement from New York State Veterinary College at Cornell University in 1961 to accept a position on the staff of the National Animal Disease Center, Ames, Iowa. I retired from NADC in 1974.

Since 1974 I have had a one year Visiting Professorship at North Carolina State University, one year at Tuskegee Institute, and this Fall I am a Visiting Professor in the Department of Veterinary Science, University of Wisconsin. During this past four years I have been working on a book, "Experimental Surgery on Farm Animals." This has been illustrated by Marion Newson, the well known medical illustrator. The book is nearing completion and should be in the publishers hands soon. Letters from Senior Members of the Society are very interesting. Hearing about the activities of others in our age group is an excellent stimulus.

**Hans Selye** to Hy:

I have traveled throughout Canada, the United States, and Europe for lectures and television programs, and in order to organize stress centers and institutes. Soon I will undertake a similar trip to Asia, Japan, North Korea, and Taiwan. As long as I remain healthy, I am definitely not planning to retire from scientific life in my adopted country. I was married on October 5, 1978 to Louise Drevet.

**Florent E. Franke** to Hal:

On May 7, 1978 my wife and I celebrated our golden wedding anniversary. About 200 persons attended a reception, over half of them relatives.

I wrote a 21-page history of the St. Louis University Department of Physiology which I read to the Graduate Students of the Department in 1966. There were two periods when St. Louis U. had a Medical School, 1842-1855, and 1903 up to the present time.

On June 6th I celebrated my 83rd birthday. We had a family dinner for thirty. I often wished I knew more about living conditions when my parents and grandparents were young. I wrote an account of my experiences, particularly in the boyhood days. Unknown to me, my daughter typed it and presented it to the St. Louis Division of Missouri University. It was accepted by the Urban and Industrial Manuscripts Collection and given an Accession Number. This is one way that one can preserve recollections of events, often of a personal or humorous nature. I keep busy with things that interest me, such as reading, sports on TV and radio, family and church.

**Eleanor Mason** to Edward:

It was a pleasure to receive the eightieth birthday greetings from the Committee. Thank you for the accompanying note expressing interest in my letter to Bruce Dill (Physiologist, Vol. 21, No.2, P.25). It was fun writing that letter, reviving those memories. I was interested that in the same issue there were notes from Ancel Keys and Otto Edholm. It was Dr. Edholm who, in London, encouraged me to assemble and write up my remaining unpublished data for my paper on responses to changes of climate.

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### John W. Remington 1914-1978

John W. Remington, Emeritus Professor of Physiology at the Medical College of Georgia in Augusta, Georgia died suddenly October 31, 1978. He had recently moved to Deland, Florida and was busily establishing a retirement home where he and Mrs. Remington could not only enjoy the climate but carry on his interests in wood and stone carvings as well as painting.

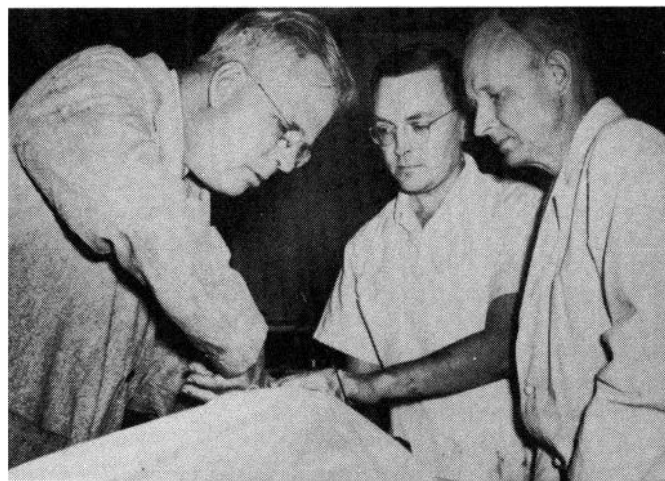
Dr. Remington was born in Fargo, North Dakota and at an early age moved to Charleston, South Carolina when his father, R. E. Remington a prominent biochemist interested in thyroid function, moved to the medical college in that city. Dr. Remington received his B.S. degree from the College of Charleston in 1935. He collaborated with his father at this stage in his career, on thyroid research that resulted in his first three full length publications.

When Dr. Robert Gaunt moved from the College of Charleston to the New York University Department of Biology, Dr. Remington went with him as a graduate student in his laboratory. Dr. Remington obtained his M.S. in 1937 and his Ph.D. degree in 1939 from that institution. He was Dr. Gaunt's first graduate student and was distinctive from most graduate students then and now in that his dissertation was originally conceived and carried out independently by him. During the period of his graduate education he also was a Teaching Fellow in Biology. His research during this period was the beginning of his interests in the effects of the

adrenal and pituitary glands on water and electrolyte metabolism

Dr. Remington then joined the laboratory of Dr. W. W. Swingle in the Department of Biology at Princeton University. He was associated with this group for four years as Reaserach Associate. During this period of time he continued his interest in the effects of adrenal cortical hormones on water and electrolyte metabolism and initiated his studies on the problems associated with the collapse of the circulation subsequent to adrenalectomy. The roles of the adrenal cortex and the nervous system in shock were also explored by this group. This work was carried out with many individuals associated with Dr. Swingle during that period. These include W. Doyne Collings, Harry W. Hays, William M. Parkins, Victor A. Drill, Richard R. Overman and William Kleinberg. The classical review paper published in *Physiological Reviews* (1944) by Swingle and Remington on "The Role of the Adrenal Cortex in Physiological Processes" culminated this period of Dr. Remington's research career.

In 1943, Dr. Remington joined the faculty of the Department of Physiology of the Medical College of Georgia as assistant professor. He remained at this institution for thirty years until his retirement in 1972. The Department of Physiology at Georgia in those days was composed of William F. Hamilton and Philip Dow. Dr. Remington joined this distinguished pair of cardiovascular physiologists and became a very significant contributor to the cardiovascular literature. During this time at the Medical College of Georgia he continued his work in the area of shock, and in collaboration with Dr. Hamilton defined the role of vasoconstriction as a precipitating factor in the development of shock from hemorrhage and trauma. Dr. Remington also in collaboration with Hamilton and Dow carried out many studies on the measurement and regulation of stroke volume and cardiac output and other related hemodynamic problems. This work resulted in a method for calculating cardiac output from the aortic pressure pulse contour. When Robert S. Alexander joined the Department of Physiology in 1953 there was an immediate collaboration in the area of blood vessel physiology particularly in the properties of vascular smooth muscle and tissue distensibility.



The Department of Physiology, Medical College of Georgia ca. 1950. Left to right-William F. Hamilton, Chairman, John W. Remington, and Philip Dow.

This collaboration lasted until Alexander became Chairman of Physiology at Albany Medical College. During this period Dr. Remington edited a symposium monograph on "Tissue Elasticity". In 1955 it was my good fortune to join the department and to become associated with him for a period of thirteen years.

This included collaboration on several papers concerning blood volume measurement and regulation of vascular capacity. Dr. Remington was associated with others at the Medical College of Georgia during this period including Raymond Ahlquist, Russell Huggins, Walter Brown, F.K. Brown, J.E. Meisner, D.L. Davis and L.J. O'Brien. Dr. Remington was also a member of the group from the Medical College of Georgia that worked with Andre Cournand that laid the foundation for cardiac output methods in man.

Dr. Remington also spent time at the Mayo Clinic with Earl Wood and a sabbatical year in Munich, Germany in the laboratory of E. Wetterer. The association with Wetterer resulted in his work on the input impedance of the aorta.

Dr. Remington became a member of the American Physiological Society in 1942. He served as a member of the Membership Committee (1950-53) and on the joint Board of Editors of the American Journal of Physiology and the Journal of Applied Physiology from 1958 to 1964. Dr. Remington was also a member and later Chairman of the Steering Committee of the Circulation Group. Dr. Remington was also active in formation of the Basic Science Council of the American Heart Association.

John Remington was a dedicated educator. He was an important force on the Curriculum and Medical Education committees at the Medical College of Georgia. These groups guided the medical school through progressive stages of evaluation and reform of the medical curriculum.

Dr. Remington's outside interests and activities included music, painting and sculpting. He was a past president of the Augusta Music Club, and a member of the Augusta Choral Society. He was chief reviewer on music and arts for the *Augusta Chronicle* and founder of the Medical Arts series sponsored by the Medical College of Georgia. He was also a member of the Rotary Club.

Dr. Remington is survived by his wife Marceline Remington and two daughters, Ms. Porter Remington of Atlanta, Georgia and Mrs. Martha Sharnitzky of Georgetown, South Carolina.

Dr. Remington was a dedicated scientist and teacher. His contributions to physiology have been numerous and of the highest caliber. He will be missed by those of us who were fortunate enough to know him as a colleague and teacher. He will also be missed by those of us who knew him as a true friend.

Carleton H. Baker, Ph.D.  
Professor and Chairman  
Department of Physiology  
College of Medicine  
University of South Florida  
Tampa, Florida

I wish to acknowledge the assistance of the following in the preparation of this remembrance:

Dr. Robert Gaunt, Clearwater, Fla.

Dr. Philip Dow, Medical College of Georgia, Augusta, Ga.

Dr. Robert Little, Medical College of Georgia, Augusta, Ga.

## ROBERT EMRIE SMITH

1913-1979

Dr. Robert Emrie Smith, Professor Emeritus of Animal Physiology at the University of California, Davis, died after a prolonged illness on January 1, 1979 in Palo Alto. He is survived by his wife, Kerttu of Palo Alto and his brother, Winchell of Hayward.

Dr. Smith was born in 1913 and matriculated at the University of California, Berkeley, receiving his Bachelor's (1934) and his Master's degree (1938) in Zoology and his Ph.D. in Physiology (1948). Upon the outbreak of World War II, he left his graduate studies and joined the U.S. Navy (1942) where he served as an environmental physiologist and radiobiologist at the Naval Medical Research Institute. Although he returned to Berkeley to complete his Ph.D. when the war ended, he remained associated with the Naval Medical Research Institute until 1948 when he moved to the National Institutes of Health.

In 1951, Dr. Smith left his position as Chief of the Section on Metabolic and Degenerative Diseases (National Institute of Arthritis and Metabolic Diseases) and joined the new medical school at UCLA as a charter member of the Faculty of Medicine. There he served as a teacher and researcher until late in his career (1966) when he moved to the University of California at Davis as Chairman of the Department of Physiological Sciences. At the time of his retirement in 1972, Dr. Smith had become internationally known for his research on the physiological mechanisms allowing mammals to survive in cold environments. In particular, it is to Dr. Smith that we owe the initial demonstration that a primary function of the brown adipose tissue is that of heat generation.

Dr. Smith's contributions to physiology include the promulgation of forums from which scientific ideas can be exchanged. As an example of the latter, his organization of the International Symposium on Cold Acclimation (1959) in Buenos Aires, Argentina, a satellite to the XXI International Congress of Physiological Sciences, marked the first of a series of five such conferences (taking place over the next 12 years) in which he played a major role as an organizer, a scientific contributor, and an editor of the conference proceedings. The first conference was so successful in bringing together international investigators with common interests that it served as a model for the future symposia on temperature regulation, bioenergetics, thermogenesis and depressed metabolism as well as for the numerous satellite meetings that now accompany International Physiological Congresses.

The family would prefer memorials be made to the Physiology Graduate Group, and sent to the Department of Animal Physiology, University of California, Davis, California 95616.

## U.S. and U.S.S.R. ACADEMIES RENEW SCIENTIFIC EXCHANGE AGREEMENTS

WASHINGTON--The U.S. National Academy of Sciences and the Academy of Sciences of the U.S.S.R. signed a two-year agreement February 7 extending scientific exchanges conducted by the two academies since 1959.

The exchange agreement was signed by Philip Handler, U.S. Academy president, and Yu. A. Ovchinnikov, U.S.S.R. Academy vice president. The protocol was signed by Thomas F. Malone, U.S. Academy foreign secretary, and G.K. Skryabin, chief scientific secretary of the U.S.S.R. Academy.

Both academies have agreed on the "desirability" of using the new agreement to place greater emphasis on cooperative activities, such as joint symposia, on important scientific problems.

The 1979-80 agreement reaffirms the exchange of U.S. and Soviet scientists for up to 100 annual person-months in each country. Also, the final agreement provides for 12 one-person-month-lecture and familiarization visits annually to each country. The remaining 88 person-months allowed each country annually may be used in scheduling up to 18 research visits from three to 12 person-months each. A person-month is one month spent by one scientist in a host country.

The U.S.-U.S.S.R. agreement differs from similar U.S. Academy exchange agreements with East European Academies in Bulgaria, Czechoslovakia, the German Democratic Republic, Hungary, Poland, Romania, and Yugoslavia in the number of exchanges and the emphasis on jointly sponsored activities. Exchanges exceeding 55 person-months annually and cooperative activities have not been included in agreements with Eastern European academies.

Exchange agreements of the U.S. National Academy of Sciences are supported by contracts with the National Science Foundation. Participating universities and research institutions voluntarily provide facilities and staff time for the exchanges.

(Copies of the full exchange agreement are available from the Office of Information, National Academy of Sciences, 2101 Constitution Ave. N.W., Washington, D.C. 20418)

# # # #

## FOUNDATIONS' FUND FELLOWSHIPS FOR SABBATICAL RESEARCH IN PSYCHIATRY AND ITS BASIC SCIENCES

The Foundations' Fund for Research in Psychiatry announces a limited program of support for scholars on sabbatical leave in order to further their research and contribute to the knowledge of psychiatric diagnosis, treatment, and prevention. The sabbatical must be spent away from the home institution at an internationally recognized institution.

Applications are open to distinguished and creative investigators with demonstrated research contributions in the field who hold full-time positions in professional schools and graduate departments of universities or equivalent institutes of research. Applicants must be U.S. or Canadian citizens or permanent residents of the U.S. or Canada.

The deadline for receipt of applications is May 1 of the year preceding the proposed sabbatical.

Information may be obtained from:

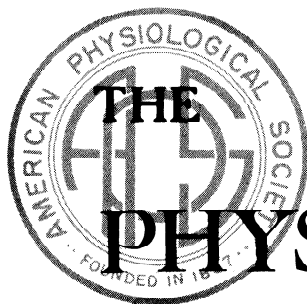
Foundations' Fund for Research in Psychiatry  
100 York Street  
New Haven, Connecticut 06511

## INTERNATIONAL SYMPOSIUM ON DRUGS AND THE LIVER

The Medical Section of the Canadian Pharmaceutical Manufacturers' Association is organizing a two-day International Symposium entitled "Drugs and the Liver" to be held in Toronto, Canada, on May 29th and May 30th, 1979. The meeting will provide a valuable insight into the most recent advances of the drug/liver and liver/drug interaction. Details may be had from Colin Granger, M.D., Medical Director of Dow Pharmaceuticals, Dow Chemical of Canada, Limited, 380 Elgin Mills Road, East, Richmond Hill, Ontario, Canada L4C 5H2.

## IUPS NEWSLETTER

Volume 7, Number 1, dated May, 1978 was received for distribution in January 1979. Since the quantity received was inadequate for general distribution, copies will be mailed to those who request them from APS Headquarters.



Editor: Orr E. Reynolds, Education Office, APS  
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# THE PHYSIOLOGY TEACHER

## A DIGITAL COMPUTER SIMULATION OF CARDIOVASCULAR AND RENAL PHYSIOLOGY

Charles S. Tidball  
Department of Physiology  
The George Washington University Medical Center  
Washington, DC

[The following papers by Tidball and by Stewart, complete the set of articles on "An Expression of the State of the Art with Regard to Physiological Simulation" started in the previous issue of *The Physiology Teacher* section of *The Physiologist* (21(6): 35-44, 1978. In the forthcoming issue Professor Charles Tidball, Guest Editor of the series will present a summation and epilogue. We plan, also to include a Glossary of terms relevant to these papers. (M.C.S.)]

The other three articles\* in this series have described physiological simulations which can be performed on a microprocessor, a minicomputer, and an analog computer. The simulated areas included, respectively, portions of cellular, cardiovascular, and respiratory physiology. In this article, interaction with a more ambitious simulation dealing with both cardiovascular and renal physiology at the same time, will be described. It was developed on a medium scale computer and is intended for larger machines which are generally accessed under time-sharing operating systems enabling many users to interact with various programs and data bases simultaneously. Unlike the other items in the series, cost information on current equipment or new equipment is not presented because it is assumed that physiological simulation alone would be an insufficient basis for acquiring such an advance computer resource. Nevertheless, technical information has been included in the Appendix to enable the reader, or a computer knowledgeable colleague, to determine if locally available equipment will be able to support physiological simulation at this level of sophistication. In the absence of an adequate institutional computer resource, it is also possible to utilize commercial service bureaus or educational networks. However neither of these approaches are likely to be economical in the long run, therefore they should probably be restricted to trial use or other relatively short-term applications such as a workshop or a conference.

\*Randall, J. R. Teaching by Simulation with Personal Computer. *The Physiology Teacher*, *The Physiologist*, 21(6): 37-40, 1978.  
Katz, S., R. G. Holligsworth, J. G. Blackburn, and H. T. Carter. Computer Simulation in the Physiology Student Laboratory. *The Physiology Teacher*, *The Physiologist*, 21(6): 41-44, 1978.  
Stewart, P. A. The Analog (Computer) as a Physiology Teaching Adjunct. *The Physiology Teacher*, *The Physiologist*, 22(1) 00-00, 1979.

The physiological MACPEE (1) is one of a family of digital computer simulations developed by C. J. Dickinson and colleagues as the result of collaborative efforts extending continuously since 1970, between McMaster University Medical School in Hamilton, Ontario, Canada; University College Hospital Medical School, London, England; and (more recently) St. Bartholomew's Hospital Medical College, London, England.

The first program developed by this group was a computer model of the heart and peripheral circulation called MACMAN (2, 3). This program is a relatively simple simulation of cardiovascular physiology, not unlike the one described by Katz *et al* in a preceding paper (4); it has been in use for sufficient time that it no longer requires frequent revision. Under the name Cardiac Simulation, it is available from a computer at The Massachusetts General Hospital (5) which is connected to a national network thus obviating long distance telephone charges. The latter can be accessed through the auspices of the Health Education Network, Inc., a user-directed, not-for-profit corporation supporting inexpensive distribution of interactive, computer-driven, educational materials in the health sciences (6).

The second member of the MAC family of physiological models is a simulation of pulmonary physiology called MACPUF (7). This is a somewhat more complex model which has also been available long enough to be in a stable configuration. The physiology underlying the assumptions used to develop the equations is well documented in a recent monograph by Dickinson (8). The latter contains a complete listing of the program which is written in the computer language FORTRAN.

### Rationale for Selection

There are advantages in describing one or the other of the original models, however there are also some reasons which favor the selection of MACPEE. First that simulation incorporates the essential features of MACMAN plus a good deal more:

1. kidneys capable of excreting water, urea, sodium, and potassium;
2. a gastro-intestinal tract which absorbs water, protein, sodium, and potassium;

3. a thirst mechanism governing water control in accordance with the body needs; and
4. an endocrine system with individual control of the secretion rates of vasopressin (ADH), aldosterone and angiotensin.

Thus MACPEE represents an ambitious attempt to undertake physiological simulation under circumstances involving interplay among a number of different organ systems.

Second, the stimulation is still under active development. As the authors state:

Whereas we believe that MACPUF is in most essentials physiologically and clinically accurate, we recognize that this is not (yet) the case with MACPEE. In particular, quantification of stress relaxation of veins, circulation and interstitial space compliance, auto-regulatory behavior of systemic circulation, renal blood flow, and GFR, and renin-angiotensin-aldosterone interactions are not well enough understood to allow an entirely accurate simulation. We hope that users' comments and criticisms will help us to improve the model (9).

Third, the model has been available for more than five years and has had considerable student and professional feedback. And fourth, the model incorporates significant flexibilities in format presentation which are not usually found in simpler simulations. For all these reasons, MACPEE seemed a likely candidate to round out the state-of-the-art of physiological simulation which we are trying to present in these two issues of *The Physiology Teacher*. Because description of only one simulation program is intended in this article, readers interested in other models and a programming aid developed by this group are referred to the Appendix for additional details.

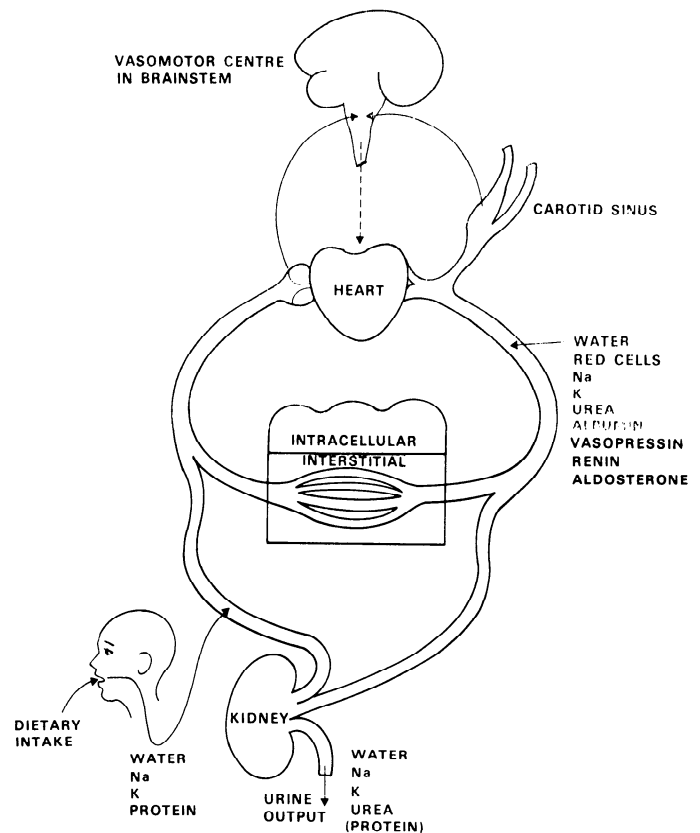
## DESCRIPTION OF MACPEE

### A General View of the Model

The description of MACPEE contained herein is based on version 78.2 dated July 28, 1978 as noted in the first line of the program. In Figure 1, taken from the MACPEE User Manual (10), is shown a diagram with the essential elements of the model. The model contains 25 changeable parameters (see Table 1) and 95 computed variables (see Table 2). For convenience these are called "factors" by the program and are referred to by unique numbers in the range from 1 to 120. Perusal of these tables is the best way to appreciate the scope of the model. The presentation of variables in Table 2 is by physiological system. It is also interesting to note a few variables, such as 'Urine output in previous iteration interval'; these are not physiological values in the customary sense but represent intermediate quantities necessary for successful operation of the computer model. Similarly, a number of arbitrary indices, such as 'Average sympathetic nervous activity' are also defined to permit the model to have a broader latitude of operation.

### Format of Computer Output

MACPEE does not require a unique terminal since it does not utilize any special graphic capabilities. The output can be displayed either on a cathode ray tube device using conventional video technology, or the alphabetic and numeric characters can be printed by any hard-copy terminal which is compatible with the computer system. In either case, typing skills are not needed since responses to MACPEE consist entirely of numbers.



1. Diagrammatic representation of the MACPEE physiological model with particular reference to input/output considerations and available regulatory features.

Table 1

## LIST OF CHANGEABLE PARAMETERS (FACTORS) IN MACPEE\*

| Factor # | Title                             | Units         | Approximate Normal Value |
|----------|-----------------------------------|---------------|--------------------------|
| 1        | Dietary sodium intake             | mM/day        | 140                      |
| 2        | Dietary protein intake            | g/day         | 90                       |
| 3        | Potassium gain or loss            | mM/day        | 0                        |
| 4        | Cardiac contractility             | % of normal   | 100                      |
| 5        | Whole body arterial resistance    | % of normal   | 100                      |
| 6        | Renal arterial resistance         | mm Hg         | 0                        |
| 7        | Whole body venous resistance      | % of normal   | 100                      |
| 8        | Renal glomerular function         | % of normal   | 100                      |
| 9        | Renal tubular sodium reabsorption | % of normal   | 100                      |
| 10       | Vasopressin function              | % of normal   | 100                      |
| 11       | Renal protein loss                | g/day         | 0.1                      |
| 12       | Aldosterone function              | % of normal   | 100                      |
| 13       | Intrathoracic pressure            | mm Hg         | -2                       |
| 14       | Cardiac filling pressure          | mm Hg         | 8                        |
| 15       | Total body exchangeable sodium    | mM            | 3,000                    |
| 16       | Total body exchangeable potassium | mM            | 3,500                    |
| 17       | Total body urea                   | mg            | 1,500                    |
| 18       | Total body albumin                | g             | 120                      |
| 19       | Total body red cell mass          | ml            | 2,300                    |
| 20       | Lean tissue mass**                | Kg            | 30                       |
| 21       | Total body water                  | l             | 38                       |
| 22       | Venous system capacitance***      | ml/mm Hg (14) | 170                      |
| 23       | Baroreceptor sensitivity          | mm Hg         | 0                        |
| 24       | Allowable maximum fluid intake    | ml/day        | 10,000                   |
| 25       | Extra fluid intake                | ml/6 hours    | 0                        |

\* The first 8 of these factors and their current values are printed in abbreviated form in the standard MACPEE output (see Figure 2).

\*\* The body weight is the sum of factors 20 and 21.

\*\*\* The volume which this capacitance determines is added to the obligatory volume of 3000 ml that is necessary to fill the circulatory system at atmospheric pressure.

TABLE 2

## PARTIAL LIST OF COMPUTED VARIABLES IN MACPEE\*

| General Area  | Name (Units)                                           |
|---------------|--------------------------------------------------------|
| Hemodynamics  | Cardiac Output (liters/min)                            |
|               | Effective Cardiac Contractility (liters/min per mm Hg) |
|               | Effective Filling Pressure)                            |
|               | Heart Rate (beats/min)                                 |
|               | Systemic Arterial Blood Pressure (mm Hg)               |
|               | Average Capillary Pressure (mm Hg)                     |
|               | Average Tissue Pressure (mm Hg)                        |
|               | Cardiac Filling Pressure (mm Hg)                       |
|               | Effective Venous Capacitance (ml/mm Hg)                |
|               | Systemic Arterial Resistance (mm Hg/(L/min))           |
| Fluid Intake  | Systemic Venous Resistance (mm Hg/(L/min))             |
|               | (ml/day)                                               |
| Kidneys       | Intake in Previous Iteration Interval (ml)             |
|               | Renal Blood Flow (ml/min)                              |
|               | Glomerular Filtration Rate (ml/min)                    |
|               | Glomerular Filtration Pressure (mm Hg)                 |
|               | Pre-glomerular Vascular Resistance (ml/min per mm Hg)  |
| Urine         | Pressure Difference)                                   |
|               | Renal Interstitial Fluid Pressure (mm Hg)              |
|               | Output/Day (ml)                                        |
|               | Output in Previous Iteration Interval (ml)             |
|               | Sodium Output/Day (mM)                                 |
|               | Sodium Output in Previous Iteration Interval (mM)      |
|               | Potassium Output/Day (mM)                              |
|               | Potassium Output in Previous Iteration Interval (mM)   |
| Blood         | Urea Output/Day (mM)                                   |
|               | Urea Output in Previous Iteration (mM)                 |
|               | Albumin Output/Day (g)                                 |
|               | Volume (ml)                                            |
|               | Hemoglobin Concentration (g/100 ml)                    |
|               | Hematocrit (%)                                         |
|               | Plasma Volume (ml)                                     |
|               | Plasma Osmolality (mOsm/kg)                            |
|               | Plasma Sodium Concentration (mM/L)                     |
|               | Plasma Potassium Concentration (mM/L)                  |
| Cells         | Plasma Urea Concentration (mM/L)                       |
|               | Blood Albumin Concentration (g/100 ml)                 |
|               | Intracellular Water (ml)                               |
|               | Intracellular Sodium Concentration (mM/L)              |
|               | Total Intracellular Sodium (mM)                        |
|               | Intracellular Potassium Concentration (mM/L)           |
|               | Total Intracellular Potassium (mM)                     |
|               | Interstitial Fluid Volume (ml)                         |
| Whole Body    | Total Extracellular Fluid (ml)                         |
|               | Weight (kg)                                            |
| Hormones      | Autoregulation (Arbitrary Index)                       |
|               | Renin (Plasma Renin Activity)                          |
|               | Vasopressin (Arbitrary Index)                          |
| Miscellaneous | Aldosterone (nanag/100 ml)                             |
|               | Average Sympathetic Nervous Activity (Arbitrary Index) |

As can be seen in Figure 2, the material delivered by the computer occurs in several portions. Initially there are some queries relating to: a) obtaining a brief description of the program (not requested in the run shown) and to b) selecting the units to be used (grams and milligrams were requested). Then there is a chart which indicates the time in days and hours. For each time entry there are corresponding data for cardiac rate (pulse) as well as diastolic and systolic blood pressure. These values are ordinarily presented at six hour intervals. The user can, however select other time spans. This is followed by a tabulation of laboratory data for the simulated patient based on the preceding 24 hour period, and by a listing of the first eight of the changeable parameters with their current values. (The latter feature is deleted automatically after several data presentations on the same subject.) Occasionally, simulated comments from the patient or the nursing staff are appended to the bottom of the output. Finally,

--MACPEE--VERSION 78.2--28 JULY 1978--  
TO PROCEED TYP 1 THEN PRESS 'RETURN' KEY,  
TO GET BRIEF DESCRIPTION TYPE 2 AND THEN 'RET'  
?

1

IF ANYTHING GOES WRONG NOTE WHAT YOU DID AND INFORM YOUR TUTOR. A PRIZE OF \$1 WILL BE GIVEN TO ANYONE CONVINCINGLY SHOWING IMPOSSIBLE BEHAVIOUR OF THE MODEL IN A POSSIBLE CLINICAL SITUATION. ANY TIME YOU CAN'T UNDERSTAND SOME QUESTION OR INSTRUCTION TYPE 'Q' (QUERY) AND PRESS THE 'ESCAPE' KEY

OK, WE'RE OFF . . .

TO USE G. AND MG. TYPE 1, FOR S.I. UNITS TYPE 2

?

1

SYMBOLS XXXXX= SYST. + DIAST. B.P. \*\*\*= HEART RATE  
TIME 0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300  
DAY HRS. . . . .  
0. 600. XX\*XXXXX

FINAL VALUES RECORDED (SINCE 6 A.M.) WERE...

FLUID INTAKE= 1796. ML URINE UREA= 24.5 G  
URINE OUTPUT= 1351. SODIUM= 136. MMOL  
POTASSIUM= 66.  
PLASMA(NA)= 142.(K)= 4.1MMOL/L UREA= 23.6 MG/DL  
(DIV.BY 2 FOR BUN)  
PCV= 48. PERCENT

HAEMOGLOBIN= 15.7 G/DL  
PLASMA ALB.= 4.1 G/DL 24 HR UR.PROT.= 0.1 G  
BODY WEIGHT = 70.4 KG  
B.P. 99/59 (MEAN= 73.) R.ATRIAL PRESS.= 2. MM HG  
HEART RATE= 69.

1.DIET NA= 140. 2.PROT.= 80. 3.+/- K= 0.  
4.CARD.FUNCT.= 100.:  
5.ART.R.= 100. 6.R.ART.P.D.= 0.MM 7.VEN.R.= 100.  
8.GLOM.FUNC.= 100.:

DO YOU WANT TO..1.CHANGE, 2.CONTINUE, 3.RESTART,  
4.INSPECT, 5.STOP

?

2

TIME 0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300  
DAY HRS. . . . .  
0.1200. \*XXXXXXXXXX  
0.1800. \*XXXXXXXXXX  
0.2400. X\*XXXXXXX  
1. 600. X\*XXXXXXX

FINAL VALUES RECORDED (SINCE 6 A.M.) WERE...

FLUID INTAKE= 1792. ML URINE UREA= 23.5 G  
URINE OUTPUT= 1158. SODIUM= 100. MMOL  
POTASSIUM= 66.  
PLASMA(NA)= 142.(K)= 4.1 MMOL/L UREA= 25.7 MG/DL  
(DIV.By 2 FOR BUN)  
HAEMOGLOBIN= 15.5 G/DL PCV= 47. PERCENT  
PLASMA ALB.= 4.0 G/DL 24 HR UR.PROT.= 0.1 G  
BODY WEIGHT= 70.6 KG  
B.P. 105/63 (MEAN= 78.) R.ATRIAL PRESS.= 2. MM HG  
HEART RATE= 68.

2. Typical run of MACPEE indicating blood pressure/pulse chart, laboratory data, and settings for the first 8 factors on the factor list. Underlined values represent user input.

there is the request from the computer to indicate what action is desired next. This is a standard message which occurs at the end of each major action by the program, therefore its various options have been detailed in Table 3.

Table 3

EXPLANATION OF OPTIONS IN STANDARD MESSAGE

| Option # | Name     | Action                                                                                          |
|----------|----------|-------------------------------------------------------------------------------------------------|
| 1        | CHANGE   | permits the user to alter any of the 25 changeable parameters listed in Table 1.                |
| 2        | CONTINUE | causes the computer to provide an additional 24 hours worth of subject data.                    |
| 3        | RESTART  | cancels the current subject and causes the computer to begin the presentation of a new subject. |
| 4        | INSPECT  | causes the computer to print a complete table of computed results.                              |
| 5        | STOP     | returns the user to the monitor level of the computer system being used.                        |

Options for Making Interventions

In Figure 3, a sequence is depicted in which the CHANGE option was utilized to reset the value of Factor 8 (Renal Glomerular Function) from 100% of normal to 20% of normal. Then the CONTINUE option was requested twice, in a single command (2/2), to obtain two consecutive 24 hour presentations which detail the consequences of that particular alteration in renal glomerular function. Note that the urine volume decreases for the first 24 hour period but then returns toward normal, as one would expect, if the fluid intake continues at approximately 1800ml/day. By contrast, the plasma urea concentration approximately doubles over the first 24 hour period and continues to increase on the second day but at a slower rate of rise. Although the original decrease in renal glomerular function imposed on the simulated patient is a more abrupt change than one would expect under ordinary clinical circumstances, the alterations in function produced by the model represent reasonable approximations of what would occur in a human patient under such conditions.

It should also be pointed out that other possibilities exist with regard to the CHANGE option. As shown in Figure 3, requesting a change calls up a new query in which CHANGE VALUES is only the first among a number of choices. The FLUID (+/-) choice enables one to determine the intake of parenteral and oral fluids. Not only is it possible to select any of eleven standard fluids which are customarily infused intravenously, but one can also instruct the nursing staff either to restrict or to encourage a specified extent of oral fluids. The fluid therapy "orders" can be modified or cancelled after each iteration of the model. The remaining choices offered in the CHANGE option are described in the following section.

DO YOU WANT TO..1.CHANGE, 2.CONTINUE, 3.RESTART,  
4.INSPECT, 5.STOP  
?  
1  
1.CHANGE VOLUES, 2.FLUIDS( + /-), 3.STORE/BKTRK,  
4.RUN CHANGE, 5.PRESETS  
?  
1  
TYPE NUMBER OF FACTORS (1-25) TO CHANGE  
?  
8  
FACTOR 8 (CURRENT VALUE = 100.0), SPECIFY NEW VALUE  
?  
20  
FACTOR 8 = 20.0 (PREVIOUSLY = 100.0)  
DO YOU WANT TO..1.CHANGE, 2.CONTINUE, 3.RESTART,  
4.INSPECT, 5. STOP  
?  
2/2  
TIME 0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300  
DAYS HRS. . . . .  
0.1200. \*XXXXXXXXXX  
0.1800. \*XXXXXXXXXX  
1.2400. \*XXXXXXXXXX  
1. 600. \*XXXXXXXXXX  
FINAL VALUES RECORDED (SINCE 6 A.M.) WERE...  
FLUID INTAKE= 1734. ML URINE UREA= 8.4 G  
URINE OUTPUT= 607. SODIUM= 85.MMOL  
POTASSIUM= 16.  
PLASMA(NA) = 141.(K) = 4.6MMOL/L UREA= 60.3 MG/DL  
(DIV.BY 2 FOR BUN)  
HAEMOGLOBIN= 15.2 G/DL PCV= 46. PERCENT  
PLASMA ALB.= 3.9 G/DL 24 HR UR.PROT. = 0.0G  
BODY WEIGHT= 71.1 KG  
B.P. 106/63 (MEAN=78.) R.ATRIAL PRESS. = 2. MM HG  
HEART RATE= 67.  
TIME 0 20 40 60 80 100 120 140 160 180 200 220 240 260 280 300  
DAY HRS. . . . .  
1.1200. \*XXXXXXXXXX  
1.1800. \*XXXXXXXXXX  
2.2400. \*XXXXXXXXXX  
2. 600. \*XXXXXXXXXX  
FINAL VALUES RECORDED (SINCE 6. A.M.) WERE...  
FLUID INTAKE= 1672.ML URINE UREA= 17.3 G  
URINE OUTPUT= 1223. SODIUM= 135.MMOL  
POTASSIUM= 60.  
PLASMA(NA) = 141.(K) = 4.8 MMOL/L UREA= 76.2  
MG/DL  
(DIV. BY 2 FOR BUN)  
HAEMOGLOBIN= 15.1 G/DL PCV= 46. PERCENT.  
PLASMA ALB. = 3.9 G/DL 24 HR UR.PROT. = 0.0G  
BODY WEIGHT= 71.1 KG  
B.P. 106/63 (MEAN= 78.) R.ATRIAL PRESS. = 2. MM HG  
HEART RATE= 66.

3. Run of MACPEE in which CHANGE option is utilized to decrease Factor #8, Renal Glomerular Function, from 100% of normal to 20% of normal. The simulated patient is then followed for two 24 hour periods.

DO YOU WANT TO..1.CHANGE, 2.CONTINUE, 3.RESTART, 4.INSPECT, 5.STOP

?

4

|                | WATER                      |       | SODIUM     |            | POTASSIUM   |      | UREA                  | OSM     | ALBUM.   |
|----------------|----------------------------|-------|------------|------------|-------------|------|-----------------------|---------|----------|
|                | ML.                        | MMOL  | MMOL/L     | MMOL       | MMOL/L      | G    | MG/DL                 | MOSM/LG | G/DL     |
| WHOLE BODY     | 42185.                     | 2689. |            | 3140.      | (TOT.EXCH.) |      |                       |         |          |
| UNSPECIFIED    | 10233.                     | 538.  |            | 201.       |             |      |                       |         |          |
| CELLS          | 18006.                     | 168.  | 9.         | 2881.      | 160.        | 11.) | 26.                   | 278.    |          |
| E.C.F.         | 13946.                     | 1988. | 142.       | 58.        | 4.1         | )    |                       |         |          |
| INT.FLUID      | 11439.                     |       | 142.       |            | 4.1         |      | 26.                   | 278.    | 0.8      |
| BLOOD          | 4725.                      |       |            |            |             |      |                       |         |          |
| PLASMA         | 2500.                      |       | 142.       |            | 4.1         |      | 26.                   | 278.    | 101. 4.0 |
| RED CELLS      | 2218.                      |       |            |            |             |      | 26.                   |         |          |
| CUM.INTAKE     | 1792.                      | 140   |            | 63.        | (           | 24.) |                       |         |          |
| CUM.URINE      | 1158.                      | 100.  | 86.        | 66.        | 57.         | 23.  | 2028.                 | 644.    | 0.1      |
| (SINCE 6 A.M.) | (FOR BUN DIVIDE UREA BY 2) |       |            |            |             |      |                       |         |          |
|                | ART. VEN. CAP.             |       | GLOM. INT. | RENAL INT. | FL.         |      |                       |         |          |
| PRESSURES      | 105/63                     | 2.    | 13.        | 50.        | 13.         | -6.  | HB = 15.5 G PCV = 47. |         |          |
| MM HG          | ( 77.6)                    |       |            |            |             |      |                       |         |          |
| FLOWS - L      | 4.8                        |       |            | 129.       | (GFR)       | 874. | HEART RATE = 68./MIN  |         |          |
| OR ML/MIN      |                            |       |            |            |             |      |                       |         |          |
| RESISTANCES    | 13.8                       | 2.4   |            | 31.        | (PRE)       | 87.  | BODY WEIGHT = 70.6 KG |         |          |
| MMHG/L/MIN     |                            |       |            | 55.        | (POST)      |      |                       |         |          |

4. Example of INSPECT option format. This feature displays most of the variables used by MACPEE.

Now let us return to the remainder of the options in the standard message as shown in Table 3. RESTART and STOP seem reasonably obvious. In Figure 4 are depicted the results of requesting the INSPECT option. As is indicated in the MACPEE User Manual, "Nearly everything you could possibly want to know is displayed". This option can be selected each time the computer requests what action is desired next.

#### Advanced Capabilities of MACPEE

It is beyond the scope of this presentation to provide details of the ways in which MACPEE can be altered for special categories of users. However, because program flexibility is often unavailable in physiological simulations, some of these capabilities deserve recognition. For example, it is possible to store the present status of a particular subject and have the computer return to that status upon request. This is accomplished by using the STORE/BKTRK choice in the second query which comes up after requesting the CHANGE option. It is also possible to change the display by suppressing portions of the standard output or by deleting the graph and/or the laboratory data. Similarly, the number of hours for the next run and the number of minutes in the iteration interval may be altered. These features operate from the RUN CHANGE choice. Finally, there are additional flexibilities which would be of value to those who might like to use the model for research purposes.

#### MAXIMIZING THE STUDENT EXPERIENCE

It should be emphasized that a computer-driven physiological simulation differs from a reading assignment, a traditional audio-visual presentation, or even a module utilizing computer assisted instruction. It cannot be successful if "thrown" at the student

without adequate preparation. At this institution we have, for more than five years, incorporated a required computer session as part of our laboratory teaching to first year medical and graduate students (11). These experiences have a limited set of learning objectives in part because of the lack of prior exposure to computational devices as well as differences in motivation to become involved at the computer terminal.

In essence, in order to gain maximum utility from a computerized physiological model, it is necessary to acquire three somewhat different sets of skills. The first of these sets is to develop sufficient familiarity with computer systems so that learning the following relatively simple but critical maneuvers does not inhibit further involvement with Computer Systems: a) connecting the terminal to the appropriate computer mainframe, b) satisfying the computer's "login" requirements, c) creating the necessary computer language environment, d) causing a copy of desired program to be transferred from mass storage to a user memory partition, e) beginning execution of the program, f) discontinuing interaction with the program, and g) making a legal disconnect from the system. For many educational computers a number of the skills enumerated above may be accomplished automatically by the computer. However such "convenience" at one stage of the student's exposure exacts a price when that student moves on to another computer system. It may not be quite as cordial to the user and, inevitably, has an entirely different set of conventions for these critical maneuvers.

The second set of skills involves understanding what is meant by a simulation. In our experience this has represented at least as difficult a challenge as mastering the first set of skills. Unfortunately, in spite of the fact that some of our students have previous exposure to computer technology, the concept of simulation is rarely taught. In order to introduce simulation principles, we found it highly successful in our laboratory sessions to use a simple simulation of a rocket ship attempting a soft landing

on the moon. The problem posed to the student was not merely making a safe landing once, but discovering the key factors which make it possible to land safely every time. Under the conditions of the particular simulation we use, it is very difficult to land the craft successfully by trial and error; however when the principles are understood, it becomes trivial to land the craft perfectly at every attempt. This experience was perceived by the students as a legitimate exercise in developing problem solving skills using a simulation as a facilitator. It improved the performance in the more substantive portion of the laboratory exercise.

Finally, the third set of skills requires the integration of physiological principles into a human, or patient oriented, frame of reference. We generally teach physiology by organ system and perforce take up processes one at a time. The task of integrating these into a functioning whole is often left to the student with little or no guidance as to how this process is to be accomplished. A physiological simulation program is an ideal medium to support this important integrative activity. The MACPEE User Manual contains ten practice problems which have considerable clinical relevance, but even these must be placed in the local instructional context before the students will make the desired associations. However, it must be acknowledged, integration does *not* take place in the absence of adequate instructor support: there is no substitute for the involved presence of faculty members while the students interact at the terminal with the physiological simulation models.

## EVALUATION OF MACPEE

The model is almost infinitely versatile; and being a true simulation, it can accommodate any sequence of alterations which the user desires to request. Unfortunately, as discussed elsewhere (2), the model does not warn the user when it embarks on ranges of values which are no longer reasonable. That, however, is easier to point out than to correct; many variables are involved and the many pathological conditions which can be simulated cause a great variety of alterations in each variable. Nevertheless, to enhance the utility of this model for teaching purposes, it would be desirable to incorporate some built-in warnings to indicate when the model is entering areas where the results may not be entirely plausible.

A second criticism is the lack of a description detailing the overall design of the model from the physiological point of view. Documentation, when it does become available, should include assumptions that had to be made as well as values that had to be assigned arbitrarily, in order to render the model functional. It is recognized that this sort of documentation is available for MACPUF (8), and it may be that MACPEE is not yet sufficiently mature to permit developing and publishing the overall design of the model. Nevertheless a documented model can be incorporated into a teaching program with greater ease and confidence.

Finally, many features not only in the practice of science and medicine but also in all aspects of this complex 20th century existence, are relying more and more on computer technology for essential support. Thus it is desirable to have a variety of computer-based learning experiences available to the student and the practitioner who feel a need for the better understanding of physiology which a computerized model can convey. MACPEE is an excellent vehicle for this purpose and is recommended to all institutions wishing to expand their capabilities in the area of physiological simulation.

## APPENDIX

### The MAC Family of Physiological Models

|          |                                                                                                                      |
|----------|----------------------------------------------------------------------------------------------------------------------|
| MACMAN:  | Computer Model of Heart and Peripheral Circulation*                                                                  |
| MACPUF:  | Computer Model of Lungs and Blood Gas Exchange*                                                                      |
| MACPEE:  | Computer Model of Kidneys and Body Fluids*                                                                           |
| MACDOPE: | A Computer-based Model for Training in Pharmacokinetics and Techniques of Prescribing*                               |
| MACBABE: | Computer Model of Lungs and Blood Gas Exchange, relevant to Newborn and Premature Infants                            |
| MACDIVE: | Computer Model of Blood/Gas Exchange, Gas Transport and Storage, applicable to Decompression and Compressed Air Work |
| MACAID:  | McMaster Computer-aided Instructional Driver                                                                         |

\* Introductory lecture demonstrating the model is available in three different videotape formats at price ranging from \$100-160. For more information contact:

Mrs. Sheila D. Tibbats  
Co-ordinator, Learning Resources, Room 1 G 8  
McMaster University Medical Centre  
1200 Main Street West,  
Hamilton, Ontario, CANADA L8S 4J9

### Technical Information for Running a MAC Model.

MACPEE (and the other MAC physiological models) are coded in the computer language FORTRAN. Care has been taken to avoid, as far as possible, machine dependent features so that the program can be adapted to other computers with a minimum of inconvenience. At McMaster University the model is implemented on a Hewlett-Packard 3000 computer but the author accesses the programs from a Digital Equipment Corporation PDP-10 computer located at the National Institutes of Health in nearby Bethesda, MD. Virtually any computer which has an *Interactive* FORTRAN capability and at least 56 thousand bytes of memory should be able to run the program. The program is available from McMaster University or from St. Bartholomew's Hospital at a nominal fee of \$250. An additional charge of \$100 is made for the listing of the code. Updates are distributed at \$50 each. Various tape formats can be requested.

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1. Dickinson, C. J. and E. P. Shephard. A digital computer model of the systemic circulation and kidneys, for studying renal and circulatory interactions involving electrolytes and body fluid compartments (MACPEE). *J. Physiol. (Lond.)* 216:11P-12P, 1971
2. Dickinson, C. J., D. Ingram, and E. P. Shephard. A digital computer model for teaching the principles of systemic haemodynamics (MACMAN). *J. Physiol. (Lond.)* 216:9P-10P, 1971.
3. Katz, S., R. G. Hollingsworth, J. G. Blackburn, and H. T. Carter. Computer Simulation in the Physiology Student Laboratory. *Physiology Teacher, Physiologist* 21(6):41-44, 1978.
4. Dickinson, C. J., C. E. Goldsmith, and D. L. Sackett. MACMAN: A digital computer model for teaching some basic principles of hemodynamics. *J. Clin. Comp.* 2(4):42-50, 1973.
5. Farquhar, B. B., E. P. Hoffer, and G. O. Barnett. Patient simulations clinical education. In: *Information Technology in Health Science Educated*, Edited by E. C. Deland, Plenum, New York, 1978, pp 397-422.
6. Tidball, C. S., Health Education Network. In: *Information Technology in Health Science Education*, Edited by E. C. Deland, Plenum, New York, 1978, pp 195-209
7. Dickinson, C. J. A digital computer model to reach and study gas transport and exchange between lungs, blood, and tissue (MAC-PUF). *J. Physiol. (Lond.)* 224:7P-9P, 1972.
8. Dickinson, C. J. *A computer model of human respiration*. University Park Press, Baltimore, 1977, 256 pp.
9. *The MAC family of physiological models* Appendix I, Page 9. (Descriptive brochure obtained from McMaster University Medical Centre) January, 1978, 13 pp.
10. *MACPEE: Computer simulation of systemic circulation and body fluids*. (User Manual obtained from McMaster University Medical Centre) April, 1978, 34 pp.
11. Tidball, C. S. Teaching Computer Literacy and Physiological Simulation. *Physiol. Teacher* 5(3):5-10, 1976.
12. Standing, R. A. and C. S. Tidball. Physiological simulation: an assessment of its advantages as well as its limitations. *Physiol. Teacher* 6(4):6-10, 1977.

## THE ANALOG (COMPUTER) AS A PHYSIOLOGY ADJUNCT

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### I. INTRODUCTION

The analog computer is a much maligned, sadly neglected and yet a very helpful tool in physiology teaching and research laboratories. It should never have been called a *computer* - partly because what it does is so different from what digital computers do, and partly because then, perhaps, physiologists and students who are "math-negatives" or "computer negatives," or both, would not be so likely to ignore it. In the hopes of minimizing emotional reactions, we shall refer to it as just an *analog*, an analog *computer*, from here on.

Historically, one of the classical analogs in physiology for many years has been the Wiggers' Model of the systemic circulation. While this analog took many local forms, they all had in common some sort of pulsatile pump, fed from a fluid reservoir of adjustable height, (the veins) pumping water through a valve into a low compliance large diameter tube (the arteries) from which the fluid flowed through an adjustable resistance (the arterioles and capillaries) back into the venous reservoir. Some of the hydraulic, and even physiologic, properties of the cardiovascular system can be demonstrated very well on this hydraulic analog, and properly used it can be very effective as a teaching device. This analog forms the conceptual basis for the cardiovascular model already described by Katz *et al* in their contribution to this series of papers.

Another very simple, qualitative analog for demonstrating the relationships between alveolar, pleural and external air pressures, thorax structures, and air flows in the respiratory system is often pictured in text books, and sometimes demonstrated in physiology lectures. It consists of a Bell jar representing the thorax, with two balloons inside, representing the lungs. The balloons are connected to the atmosphere via rigid tubes representing the bronchi and the trachea. A sheet of rubber,

stretched across the bottom of the Bell jar represents the diaphragm. Pulling down on the rubber sheet results in air entering the balloons; pushing up on the sheet causes air to leave. The analogy to normal quiet, diaphragmatic breathing is clear and direct.

Such physical models, while readily accepted as analogs, would probably not be designated as "computers" by the physiologists and their students who find them useful. The reason seems to be that they are *not* normally set up with measuring instruments to give quantitative data. Moreover they are usually not built with careful attention to quantitative matching between values of model variables (volumes, compliances, flow resistances), and values of the same quantities in the "real" physiological system. The tremendous advantage which the electrical analog has is that it is *so easy* to achieve that quantitative match merely by turning a few dials. No long hours in the machine shop, or searching for tubing with just the right elastic character *and* wall thickness *and* bore. All your hands have to do is twiddle knobs, flip switches, and plug in wires. The main work, as it should, involves the head! In order to know how to twiddle those knobs, you must have a very clear *quantitative* description of the system, because what you do when you "patch" - i.e. connect up - an analog, is create an electric circuit whose components are interconnected so as to obey *exactly the same quantitative relationships* as you claim are obeyed by the components of the physiological system you want to understand.

In the case of the mechanics of the respiratory system, for example, we could have capacitors representing compliances, electric resistors representing airflow resistances, voltages representing pressures, and currents representing air flows. Since we know the numerical values of all these entities in the normal real

respiratory system, we can set our analog circuit values to those same numbers, and simply monitor its behavior with voltmeters and ammeters. Furthermore, since electrical plotting devices like oscilloscopes and pen recorders are rather common around a physiology department, we can hook them up to our analog and watch or record "behavior," just as we would do to ourselves or our experimental animals in a "wet lab" situation.

One may ask, on the other hand, if it's just the same as the person or animal, why use the analog? There are several answers and they appeal to different interests. First, with the analog it's very easy, and completely safe, to ask, and answer quantitatively, *any* meaningful question you wish to pose about how the real system would respond to any imagined changes in any desired variables. You can do any experiment you like on the analog; it can't hurt the analog, and, if the results indicate non-variable conditions, the experiment is immediately reversible just by re-setting the potentiometer knobs.

A closely related advantage is that you can measure any variable in the analog system without disturbing the system. You don't have to worry about the notorious reactivity and fragility of real living systems. No anesthetic deaths, for example. Even more interesting, many of those variables may be not accessible in the real system.

The inexorability and uncontrollability of *time* in real systems is also subject to easy modification in the analog. Time can be stopped, slowed down, speeded up, as you wish. The system behavior can be examined on different time scales, and this can be done repeatedly.

One more use for the analog is really in the realm of experiment, although it is more likely to be described as "mere" curve-fitting. If you know that the real system has a particular quantitative behavior, and there is one parameter in the system whose value you do not know - perhaps because it is inaccessible *in vivo* - then you can turn the knob which represents that parameter on the analog until the quantitative behavior of the analog accurately matches that of the real system. The knob setting then provides a reasonable estimate of the value which you would have measured for that inaccessible parameter if you could have!

Another psychological advantage to the analog is that it can never come up with long, completely meaningless, strings of digits as if they were significant. It will tell you a pressure is 42 mmHg, not 42.032842936284 mmHg, for example. In general, its overall precision is about the same as real measurements on real systems, from 1 to 5%. It never tempts you to think you know a number to one part in a million billion just because your computer program uses double precision!

What about disadvantages? Criticisms of analog simulation mainly seem to be either criticisms of the foibles of the simulator (person), such as not including enough variables, for example, or invidious comparisons of the analog, as a device, with the digital computer, a very different device which can be programmed to *calculate* similar simulations. A good, fast, digital computer program *can* produce the same results that an analog can in most situations, including run a plotter, but it does it differently; and it's *much* more difficult to understand how it is getting those results. What distinguishes an analog from a digital computer is that the analog is a physical (usually electrical) model of the biological system being analogized; it therefore simulates the physiological system by *behaving* like it, not by *calculating* the behavior as the digital computer does. The physical directness of the analog can make it much more meaningful and effective as a learning device than a set of equations, even though "in principle" they are the same.

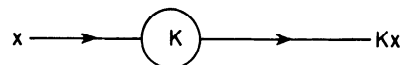
One serious disadvantage of analog (computers) in comparison with digital computers is that analogs are more often "hardware limited." This means that if you want to analyze a bigger system, you need more components - amplifiers, pots, etc. In a digital computer simulation, you simply have to write a longer, possibly more complicated, program, but it will usually still run on the same machine; it will just take longer. This limitation on analogs is a real one, especially in research applications, but is seldom incapacitating in a teaching-learning situation. If you run out of hardware, chances are your model is too complicated to be a useful learning device. Successful analogizing involves abstracting and simplifying, and these are also essential components of successful teaching.

## II WHAT IS AN ANALOG (COMPUTER)?

In current use, an analog computer is a conveniently arranged set of electronic circuits, plus a "patch panel" which enables the operator to interconnect them, so that the quantitative relationships between them are just the same as those specified for the "real" system being analyzed. At the simplest useful level, the basic circuits provided are generally the following:

### 1. Potentiometer.

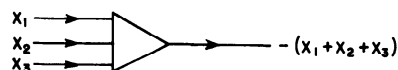
(universally designated "pot".) This is a simple rotary voltage divider, usually requiring 10 or 15 turns to go from zero to full output, with a remarkably accurate mechanical scale attached to the knob. A pot produces an output voltage  $K$  times the input voltage, where  $K$  is the fraction of its total travel its knob is set to, and is therefore not greater than 1.0. The symbol for a pot is:



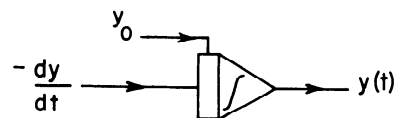
### 2. Operation amplifiers. (known as "op amps" or just "amps".)

An op amp is a high gain DC amplifier connected, usually on the patch panel, into a feedback circuit which results in the desirable properties of very low output impedance, high input impedance, and overall circuit gain determined only by the ratio of feedback to input resistors. Op amps usually produce an output of opposite sign to the input, so they are also called "inverters" or "sign changers". An op amp will accept more than one input, and produce an output equal to (minus) their algebraic sum, so it can also be called a "summer" or "adder".

The symbol used for a connected op amp is:



3. *Integrator.* This is an op amp with a capacitor instead of a resistor in the feedback circuit. Its output voltage is the negative time integral of the input voltage. It must also be supplied with an "initial condition", the value of the output when time = 0. Its symbol in analog diagrams is:

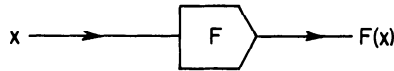


4. *Multipliers (dividers).* These circuits take advantage of the algebraic fact that  $(a+b)^2 = a^2 + 2ab + b^2$  and  $(a-b)^2 = a^2 - 2ab + b^2$  so that  $(a+b)^2 - (a-b)^2 = 4ab$ , as well as the electronic fact that it is not difficult to make a circuit which produces the

square of its input. By changing the input and output connections, the same circuit can also be made into a divider. Usual symbols are:



5. *Function generators.* These are surprisingly simple circuit boxes, with large numbers of screwdriver controls, which permit adjustment of both the magnitude and slope of the output voltage as a function of input voltage. They can be set up to approximate very well a large variety of empirical curves. (for example, the hemoglobin-O<sub>2</sub> dissociation curve.) They are usually symbolized by:



To use these five types of circuits, you connect them together by plugging in wires on the patchboard in such a way that the operations they will carry out match precisely the operations indicated by the equations which describe the system you wish to study.

How each of these "black boxes" does what it does is not difficult to understand at the level of the usual freshman physics course, and is generally well explained in books on analog computing, or handbooks provided by manufacturers. What matters most is that such devices do exist, and carry out, remarkably reliably, the indicated operations.

Before wiring a real problem on a patchboard, it is always helpful, and usually essential, to re-write the equations for the problem in the language of the above circuit symbols, thereby converting the equations into an "analog diagram". Such a diagram is not only a guide to the actual wiring of the patchboard, it is also a very informative way of displaying many aspects of the information content of the equations, as well as the properties of the system.

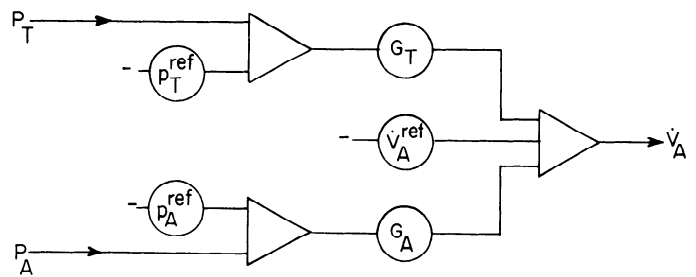
### III A SIMPLE (ALGEBRAIC) EXAMPLE: THE RESPIRATORY CONTROL FUNCTION

Chemical control of alveolar ventilation has been a favorite topic for mathematical modelling, and we shall discuss a simple model for the whole system in the next section. In most such models, for conditions not too far from physiologically normal values, the basic control can be satisfactorily represented by a linear controller with different sensitivities to CO<sub>2</sub> partial pressures in body tissues (or venous blood) and in alveolar gas (or arterial blood). The simplest equation to represent such a control function is:

$$\dot{V}_A = G_T \cdot (P_T - P_T^{\text{ref}}) + G_A \cdot (P_A - P_A^{\text{ref}}) + \dot{V}_A^{\text{ref}} \quad (1)$$

Where  $G_T$  and  $G_A$  are "gains" or "sensitivities",  $P_T^{\text{ref}}$ ,  $P_A^{\text{ref}}$ , and  $\dot{V}_A^{\text{ref}}$  are "set points" or reference values,  $\dot{V}_A$  = alveolar minute ventilation,  $P$  = CO<sub>2</sub> partial pressure, "T" means "tissues" and "A" means "alveoli."

If voltages representing  $P_T$  and  $P_A$  can be assumed to be available, then the analog representation of this equation is simply:



The five parameters in equation (1) are represented by 5 pots, which must be set to appropriate values in order to achieve the desired match with experimental behavior. Reasonable values for the author turn out to be:

$$\dot{V}_A = 2.0 (P_T - 46) + 0.20 (P_A - 40) + 7.0 \quad (2)$$

Going from this equation and the above diagram to actually connecting up (patching) the analog requires one more step, because the analog can only deal with voltages up to a fixed limit, 10 volts or 100 volts, depending on the manufacturer. Equation (2) must therefore be re-written with new ("scaled") variables, proportional to the real ones, so that all numerical values are within acceptable limits. Finding suitable conversions, or scaling factors, is easily done systematically by defining analog variables as follows:

$$p \text{ (volts)} = K_p \times P \text{ (mmHg)}$$

$$\dot{V}_A \text{ (volts)} = K_V \times \dot{V}_A \text{ (Liters/Min)}$$

Equation (2) then becomes:

$$\frac{\dot{V}_A}{K_V} = 2.0 \left( \frac{P_T}{K_p} - 46 \right) + 0.20 \left( \frac{P_A}{K_p} - 40 \right) + 7.0$$

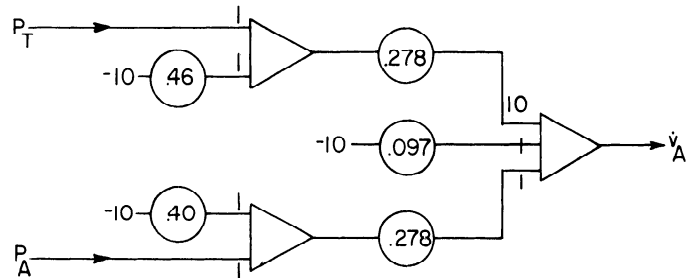
or

$$\dot{V}_A = \frac{K_V}{K_p} \times 2.0 \times (P_T - 46) + \frac{K_V}{K_p} \times 0.20 \times (P_A - 40) + 7.0 \times K_V \quad (3)$$

Choosing  $K_V = 0.139$ ,  $K_p = 0.1$ , this becomes:

$$\dot{V}_A = 2.78 (P_T - 4.6) + 0.278 (P_A - 4.0) + 0.97 \quad (4)$$

The coefficients larger than 1.0 are taken care of by amplifying the pot outputs by 10 rather than 1, which is easily done by patching an op amp input with an input resistor 1/10th as large. The final scaled analog diagram now looks like this:



This analog circuit will produce a voltage,  $v_A$ , proportional to  $\dot{V}_A$ , which is determined by  $P_T$  and  $P_A$  in exactly the way that equation (2) says  $\dot{V}_A$  is determined by  $P_T$  and  $P_A$ . If  $P_T$  or  $P_A$  increases,  $v_A$  will increase, and vice versa. If  $P_T = 4.6$ , and  $P_A = 4.0$ , then  $\dot{V}_A = 0.97$ , corresponding to the physiological values of  $\dot{V}_A = 7.0 \text{ L/Min}$  when  $P_T = 46 \text{ mmHg}$  and  $P_A = 40 \text{ mmHg}$  in this subject.

#### IV A MORE COMPLEX EXAMPLE: CO<sub>2</sub> CONTROL IN THE RESPIRATORY SYSTEM

This example requires non-linear differential equations, and is therefore somewhat more sophisticated than the previous, strictly algebraic example, but the approach and principles are the same. We assume that the reader is familiar with the physiological details, and consider here mainly the process of getting the system on to the analog.

The physiological model is at the level of Grodins' "Respiratory Chemostat", and lumps the many complexities of the respiratory and control systems into 3 compartments plus a control equation. The 3 compartments are the alveolar volume,  $V_A$ , the circulating blood, flowing at a constant rate,  $\dot{Q}$  and the tissues volume  $V_T$ . Control is represented by the linear relationship presented in the previous section. Capillaries are assumed 100% effective, so that alveolar and arterial partial pressures are the same, as are venous and tissue partial pressures; i.e.  $P_a = P_A$  and  $P_v = P_T$ . The CO<sub>2</sub> dissociation curves for the various compartments are approximated, near physiological values, by straight line segments, so that for compartment x we have  $[CO_2]_x = S_x \cdot P_x + K_x$  where S and K are constants to be evaluated from the known dissociation curves.

Application of conservation of mass for CO<sub>2</sub> to the tissue and alveolar compartments, after a little rearranging and algebra, then gives these two differential equations:

$$\frac{dP_T}{dt} = \underbrace{\frac{S_a \cdot \dot{Q}}{S_v V_T}}_{K_{T_1}} \cdot P_A - \underbrace{\frac{P_A \cdot \dot{Q}}{V_T}}_{K_{T_2}} \cdot P_T + \underbrace{\frac{METAB}{S_v \cdot V_T}}_{K_{T_3}} \quad (5)$$

$$\frac{dP_A}{dt} = \underbrace{BP \cdot S_v \cdot \frac{\dot{Q}}{V_A}}_{K_{A_1}} \cdot P_T - \underbrace{BP \cdot S_a \cdot \frac{\dot{Q}}{V_A}}_{K_{A_2}} \cdot P_A - \frac{\dot{V}_A}{V_A} \cdot (P_A - P_I) \quad (6)$$

METAB is the rate of CO<sub>2</sub> production by the tissues, BP = ambient barometric pressure, and  $P_I$  the partial CO<sub>2</sub> pressure in inspired air.

The control equation is equation (1) as presented in the previous section. Combining constants as indicated, translation of equations (5), (6), and (1) into analog symbols then gives us this diagram: (See bottom page)

The scaling problem also exists here, in time as well as in the magnitude of the variables expressed as voltages. For analysis of the system it is very convenient to express all values in terms of minutes, but have them run on the analog as seconds. An hour's response by the body can then be followed in just a minute on the analog. On the other hand, direct comparison with actual body behavior requires scaling seconds as seconds, but this is easily done by re-setting all the pots appropriately.

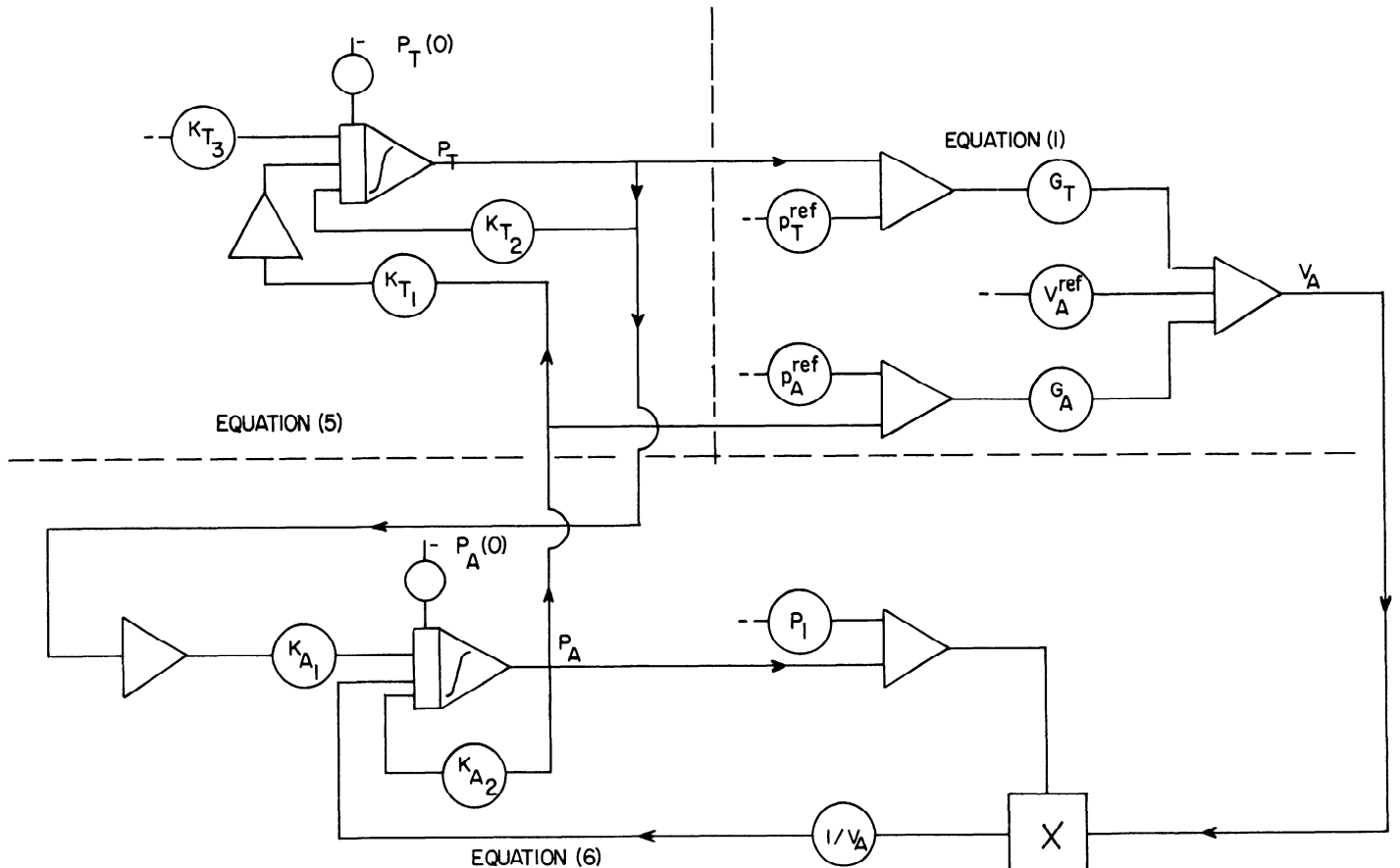
The actual scaled equations, suitable for setting numerical values onto the pots and running in the 1-second-represents-1-minute mode, using body parameters for the writer, and using the same scaling factors as before, are as follows:

$$P_A = 3.80 p_T - 3.53 p_A + v_A (p_I - p_A)$$

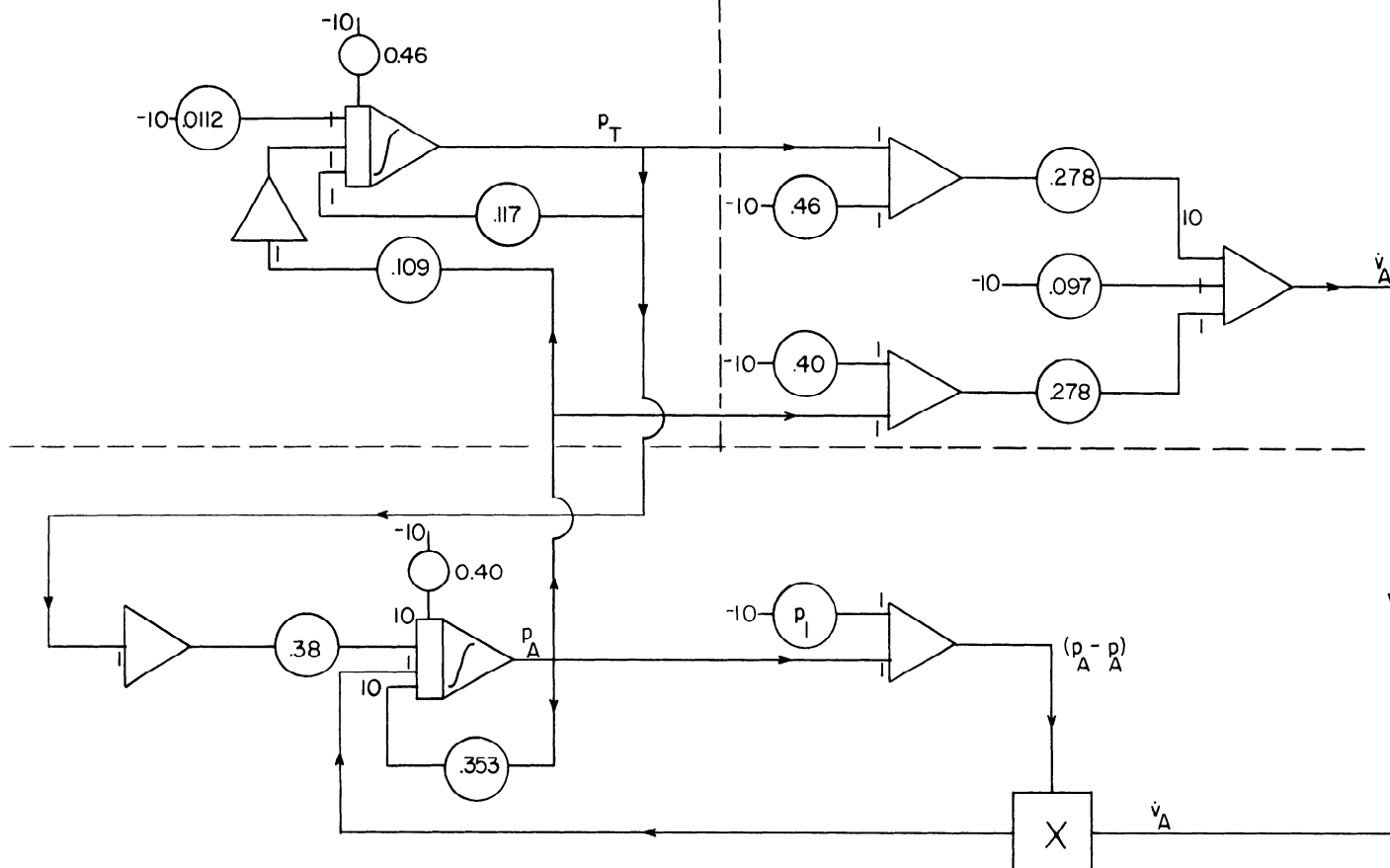
$$p_T = 0.109 p_A - 0.117 p_T + 0.112 \quad (7)$$

$$v_A = 2.78 (P_T - 4.6) + 0.278 (p_A - 4.0) + 0.970$$

The scaled analog diagram for this system therefore is: →



Physiologists who would like to explore analog possibilities, but do not have lavish instructional budgets, should know that many electrical engineering departments are well equipped in this area, and their equipment is often readily available for learning, prac-



Our experience with the Electronic Associates Inc. (EAI) analog machines has been good. Their current and much improved equivalent to the TR-20 is called "MINIAC", and sells for about \$10,000 with comparable hardware to our TR-20's. EAI will respond to telephone inquiries if more detailed information is needed. (Electronic Associates, Inc., 185 Monmouth Pkwy, West Long Beach, NJ 07764. (210) 229-1100)

1. Defares, J.G. Principles of feedback control and their application to the respiratory control system. *Handbook of Physiology*, Sect.3. Vol.1, Chapt. 26, 1964.
2. Milhorn, H.T. *The Application of Control Theory to Physiological Systems*. Chapt. 15. Saunders, Philadelphia, 1966.
3. Grodins, F.S. *Control Theory and Biological Systems*. Chapt. 7. Columbia Univ. Press, New York, 1963.
4. Stice, J.E. and B.S. Swanson. *Electronic Analog Computer Primer*. (Paperback) Blaisdell, New York, 1965.
5. Wass, C.A.A. and K.C. Garner. *Introduction to Electronic Analogue Computers*. Pergamon Press, New York, 1965.
6. *Handbook of Analog Computation*. EAI, Princeton, NJ 1965

## A BOOK LIST FOR THE TEACHING OF MEDICAL SCHOOL PHYSIOLOGY

In February 1978, Dr. Eugene Renkin of the Department of Human Physiology at the Medical School of the University of California, Davis, addressed the following question to 127 departments of physiology in medical and veterinary schools in the United States and Canada. "Would you please let me know what physiology textbooks your Department recommends to medical students and what textbooks your students actually use for your course?"

The report submitted by him to the Education Committee of the American Physiological Society was stimulating and revealed the need for more elaborate and detailed study of the entire question of textbook and teaching aids for physiologists.

His report contained an appendix which the Editor believes warrants publication now, and need not await the results of a more extensive survey. That appendix is this Book List and is based on the Textbooks, Comprehensive and Specialty, assigned, recommended, or suggested by one or more departments for use by their students. (M.C.S.)

### Comprehensive Textbooks

- Brobeck, J.R. *Best and Taylor's Physiological Basis of Medical Practice*, 9th edition 1973, Williams & Wilkins, Baltimore. (This text is also available as nine separate paperback volumes.)
- Ganong, W.F. *Review of Medical Physiology*, 8th edition 1977, Lange, Los Altos.
- Guyton, A.C. *Textbook of Medical Physiology*, 5th edition 1976, Saunders, Philadelphia.
- Guyton, A.C. *Basic Human Physiology*, 2nd edition 1977, Saunders, Philadelphia.
- Guyton, A.C. *Function of the Human Body*, 4th edition 1974, Saunders, Philadelphia.
- Mountcastle, V.B. *Medical Physiology*, 13th edition 1974 (2 vols.), Mosby, St. Louis.
- Ruch, T.C. and Patton, H.D. *Physiology and Biophysics*, 20th edition (3 vols. of which only the 2nd and 3rd have been published) 1973-1974, Saunders, Philadelphia.
- Selkurt, E.E. *Physiology*, 4th edition 1976, Little, Brown & Co., Boston.
- Selkurt, E.E. *Basic Physiology for the Health Sciences*, 1975, Little, Brown & Co., Boston.
- Shepard, R.S. *Human Physiology*, 1971, J.B. Lippincott Co., Philadelphia.
- Shepard, R.S. *Human Physiology Examination Review*, 1975, Arco Medical Review Series, New York (not a text, but a comprehensive compilation of examination questions).
- Swenson, M.J. *Duke's Physiology of Domestic Animals*, 9th edition 1975, Comstock.
- Vander, A.J., Sherman, J.H. and Luciano, D.S. *Human Physiology*, 2nd edition 1975, McGraw Hill, New York.

*Year Book Series* (Six volumes available in soft cover. See in the list of specialty texts; Eyzaguirre and Fidone, Little, Comroe, Pitts, Davenport, Tepperman).

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*Addendum.* The following text was published too late for use during 1977-1978:

Ross, G. *Essentials of Human Physiology*, 1978, Yearbook Medical Publishers, Chicago.

### Specialty Texts

1. *General Physiology*  
 Davson, H.H. *A Textbook of General Physiology*, 4th edition 1970, Little, Brown & Co., Boston.  
 Schwartz, I.L. *General Physiological Processes*, (Vol. 1 of the Best and Taylor series), 1973, Williams & Wilkins, Baltimore.
2. *Excitable Cells, Nerve-muscle*  
 Aidley, D.J. *Physiology of Excitable Cells*, 1971, Cambridge University Press, New York.  
 Junge, D. *Nerve and Muscle Excitation*, 1976, Sinauer, Sunderland, MA.  
 Katz, B. *Nerve, Muscle and Synapse*, 1966, McGraw Hill, New York.  
 Kuffler, S.W. and Nichols, J.G. *From Neuron to Brain*, 1976, Sinauer, Sunderland, MA.  
 Schmidt, R.F. *Fundamentals of Neurophysiology*, 2nd edition 1975, Springer-Verlag, New York.
3. *Central Neurophysiology*  
 Bhagat, B.D., et. al. *Fundamentals of Visceral Innervation*, 1977, Thomas, Springfield.  
 Clark, R.G. *Manter and Gatz's Essentials of Clinical Neuroanatomy and Neurophysiology*, 5th edition 1975, F.A. Davis, Philadelphia.  
 Cooper and Beal. *Neurological Case Studies, Spinal Cord, Brain Stem* (microfiche), 1976, Educational Media Inc., Dallas.  
 Cooper and Beal. *Neurological Case Studies, Brain Stem, Cerebellum, Cerebrum* (microfiche), 1976, Education Media Inc., Dallas.  
 Curtis, B.A., Jacobson, S. & Marcus, E.M. *Medical Neurobiology*, 1973, Mosby, St. Louis.  
 Daube, J.R., Sandok, B.A., Reagan, T.J. and Westmoreland, B.F. *Integrated Neuro-Sciences: systems and levels*, 1978, Little, Brown & Co., Boston.  
 Eccles, J.C. *Physiology of Nerve Cells*, 1957, Johns Hopkins Press, Baltimore.  
 Eccles, J.C. *The Physiology of Synapses*, 1964, Springer-Verlag, New York.  
 Eccles, J.C. *The Understanding of the Brain*, 1973, McGraw Hill, New York.  
 Eyzaguirre, C. and Fidone, S.J. *Physiology of the Nervous System*, 1975, Year Book Medical Publishers, Chicago.

- Guyton, A.C. *Organ System Physiology: Structure and Function of the Nervous System*, 2nd edition 1976, Saunders, Philadelphia.
- Melzak, R. *The Puzzle of Pain: Revolution in Theory and Treatment*, 1973, Basic, New York.
- Noback, C. and Demarest, R. *The Nervous System: Introduction, Review*, 1977, McGraw Hill, New York.
- Patton, H.D., Sundsten, J.W., Crill, W.E. and Swanson, P.D. *Introduction to Basic Neurology*, 1976, Saunders, Philadelphia.
- Robertson, D.M. and Dinsdale, H.B. *The Nervous System, Structure and Function in Disease*, 1972, Williams & Wilkins, Baltimore.
- Willis, W.C. and Grossman, R.G. *Medical Neurobiology*, 2nd edition 1977, Mosby, St. Louis.
4. *Cardiovascular*
- Berne, R.M. and Levy, M.N. *Cardiovascular Physiology*, 3rd edition 1977, Mosby, St. Louis.
- Braunwald, E., Ross, J. and Sonnenblick, E.H. *Mechanisms of Contraction of the Normal and Failing Heart*, 2nd edition 1976, Little, Brown & Co., Boston.
- Burch, G.E. and Winsor, T. *A Primer of Electrocardiography*, 6th edition 1972, Lea and Febiger, Philadelphia.
- Burton, A.C. *Physiology and Biophysics of the Circulation*, 2nd edition 1972, Year Book Medical Publisher, Chicago.
- Folkow, B. and Neil, E. *Circulation*, 1971, Oxford University Press, New York.
- Guyton, A.C. *Cardiovascular Physiology I and II*, 1974, MTP International Review of Science, Butterworth (University Park Press), Baltimore.
- Henry, J.P. and Meehan, J.P. *The Circulation*, 1971, Year Book Medical Publishers, Chicago.
- Katz, A.M. *Physiology of the Heart*, 1977, Raven Press, New York.
- Levine, H.J. *Clinical Cardiovascular Physiology*, 1976, Grune & Stratton, New York.
- Little, R.C. *Physiology of the Heart and Circulation*, 1977, Year Book Medical Publishers, Chicago.
- Noble, D. *The Initiation of the Heartbeat*, 1975, Oxford Univ. Press, New York.
- Rushmer, R.F. *Cardiovascular Dynamics*, 4th edition 1976, Saunders, Philadelphia.
- Rushmer, R.F. *Organ Physiology: Structure and Function of the Cardiovascular System*, 2nd edition 1976, Saunders, Philadelphia.
- Stein, E. *The Electrocardiogram*, 1976, Saunders, Philadelphia.
5. *Respiration*
- Bouhuys, A. *Breathing, Environment and Lung Disease*, 1975, Grune & Stratton, New York.
- Cherniak, R.M., Cherniak, L. and Naimark, A. *Respiration in Health and Disease*, 1972, Saunders, Philadelphia.
- Comroe, J.H. *Physiology of Respiration*, 2nd edition 1974, Year Book Medical Publishers, Chicago.
- Comroe, J.H., Forster, R.E., Du Bois A., Briscoe, W.A. and Carlsen E. *The Lung-Clinical Physiology & Pulmonary Function Tests*, 2nd edition 1962, Year Book Medical Publishers, Chicago.
- Dejours, P. *Principles of Comparative Respiratory Physiology*, 1975, American Elsevier, New York.
- Fraser, R.G. and Peter-Paré, J.A. *Organ Physiology: Structure and Function of the Lung*, 2nd edition, 1977, Saunders, Philadelphia.
- Jones, J.D. *Comparative Physiology of Respiration*, 1972, Crane-Russak, New York.
- Kao, F. *An Introduction to Respiratory Physiology*, 1973, Elsevier, New York.
- Lippold, O.C. *Human Respiration*, a programmed course, 1968, W.H. Freeman, San Francisco.
- Murray, J.F. *The Normal Lung-The Basis for Diagnosis and Treatment of Pulmonary Disease*, 1976, Saunders, Philadelphia.
- Slonim, N.B. and Hamilton, L.F. *Respiratory Physiology*, 3rd edition 1976, Mosby, St. Louis.
- West, J.B. *Ventilation, Blood Flow and Gas Exchange*, 1970, F.A. Davis, Philadelphia.
- West, J.B. *Respiratory Physiology, The Essentials*, 1974, Williams & Wilkins, Baltimore.
- West, J.B. *Respiratory Pathophysiology*, 1977, Williams & Wilkins, Baltimore.
6. *Acid-Base*
- Davenport, H.W. *The ABC of Acid-Base Chemistry*, 6th edition 1974, University of Chicago.
- Masoro, E.J. and Siegel, P.D. *Acid-Base Regulation: Its Physiology, Pathophysiology and the Interpretation of Blood Gas Analysis*, 1978, Saunders, Philadelphia.
- Rose, B.D. *Clinical Physiology of Acid-Base and Electrolyte Disorders*, 1977, McGraw Hill, New York.
7. *Kidney, Fluid-Electrolyte*
- Bauman, J.W., Jr. and Chinard, F.P. *Renal Function: Physiological and Medical Aspects*, 1975, Mosby, St. Louis.
- Brenner, B.M. and Rector, F.C. *The Kidney* (2 vols.) 1976, Saunders, Philadelphia.
- Deetjen, P., Boylan, J.W. and Kramer, K. *Physiology of the Kidney and of Water Balance*, 1975, Springer-Verlag, New York.
- De Wardener, H.E. *The Kidney-An Outline of Normal and Abnormal Structure and Function*, 4th edition 1973, Churchill and Livingstone, London.
- Hamburger, J., Richet, G., Grinfeld, J.A. and Walsh, A. *Organ Physiology; Structure and Function of the Kidney*, 1971, Saunders, Philadelphia.
- Knox, F. *Renal Pathophysiology*, 1978, Harper, & Row, New York.
- Koushanpour, E. *Renal Physiology*, 1976, Saunders, Philadelphia.
- Maude, D.L. *Kidney Physiology and Kidney Disease-An Introduction to Nephrology*, 1977, Lippincott, Philadelphia.
- Leaf, A. and Cotran, R. *Renal Pathophysiology*, 1976, Oxford Univ. Press, New York.
- Netter, F.H. Ciba Collection Vol. 6: *Kidneys, Ureters and Urinary Bladder*.
- Pitts, R.F. *Physiology of the Kidney and Body Fluids*, 3rd edition 1974, Year Book Medical Publishers, Chicago.
- Schrier, R.W. *Renal and Electrolyte Disorders*, 1976, Little, Brown & Co., Boston.

- Shoemaker, W.C., and Walker, W.F. *Fluid-Electrolyte Therapy in Acute Illness*, 1970, Year Book Medical Publishers, Chicago.
- Sullivan, L. *Physiology of the Kidneys*, 1975, Lea & Febiger, Philadelphia.
- Valtin, H. *Renal Function: Mechanisms Preserving Fluid and Solute Balance in Health*, 1973, Little, Brown & Co., Boston.
- Vander, A.J. *Renal Physiology*, 1975, McGraw Hill, New York.
- Wesson, L.G. *Physiology of the Human Kidney*, 1969, Grune & Stratton, New York.

## 8. *Gastrointestinal*

- Brooks, F.P. *Control of Gastrointestinal Function*, 1970, Mac Millan, New York.
- Davenport, H.W. *A Digest of Digestion*, 1975, Year Book Medical Publishers, Chicago.
- Davenport, H.W. *Physiology of the Digestive Tract*, 4th edition 1977, Year Book Medical Publishers, Chicago.
- Greenberger, N.J. and Winship, D.H. *Gastrointestinal Disorders, A Pathophysiologic Approach*, 1976, Year Book Medical Publishers, Chicago.
- Hightower, N.C. and Janowitz, H.D. *Digestion* (Vol. 2 of Best & Taylor paperback series) 1973, Williams & Wilkins, Baltimore.
- Jacobson, E. *Gastrointestinal Physiology*, 1974, University Park Press, Baltimore.
- Johnson, L.R. *Gastrointestinal Physiology*, 1977, Mosby, St. Louis.
- Texter, E.C. *Physiology of the Gastrointestinal Tract*, 1968, Mosby, St. Louis.

## 9. *Endocrinology*

- Cryer, P.E. *Diagnostic Endocrinology*, 1976, Oxford University Press, New York.
- Morgan, M. *Endocrine Control Systems* Vol. 7 of Best & Taylor paperback series), 1973, Williams & Wilkins, Baltimore.
- Tepperman, J. *Metabolic and Endocrine Physiology*, 3rd edition 1973, Year Book Medical Publishers, Chicago.
- Williams, R.H. *Textbook of Endocrinology*, 5th edition 1974, Saunders, Philadelphia.

## 10. *Miscellaneous*

- Alexander, R.S. *Case Studies in Medical Physiology*, 1977, Little, Brown & Co., Boston.
- Frohlich, E.D. *Pathophysiology: Altered Regulation Mechanisms in Disease*, 2nd edition 1976, Lippincott, Philadelphia.
- Goodman, L.S. and Gilman, A. *Pharmacological Basis of Therapeutics*, 5th edition 1975, Mac Millan, New York.
- Kuebler, R.R. *Statistics; A Beginning*, 1976, Wiley, New York.
- Robbins S.L. *Pathological Basis of Disease*, 1974, Saunders, Philadelphia.
- Roddie, I.C. and Wallace, W.F.M. *The Physiology of Disease*, 1975, Year Book Medical Publishers, Chicago.
- Sparks, H. *Case Book of Physiology*, 1973, Year Book Medical Publishers, Chicago.

"I like the idea of the crossword puzzle, as you published in the October issue. You inspired me to polish a neurophysiology puzzle that I had been using for several years in a course that I teach. Such puzzles make an interesting addition to the journal, and it would be nice to build up a collection of them I hope you consider this one favorably."

W. R. Klemm  
Texas A & M University

(See page 52. M.C.S.)

## BOOK REVIEWS

*Fundamentals Of Neurophysiology*, edited by Robert F. Schmidt, with contributions by Josef Dudel, Wilfrid Janig, Robert F. Schmidt, and Manfred Zimmermann, second, revised and enlarged edition, Springer-Verlag, New York, Heidelberg, Berlin, 1978. 339 pp. \$14.80.

This is not the first attempt to outline all the essentials of neurophysiology in a short and easily readable text, but may well be the one coming closest to its goal. It bears the stamp of competence and authority one may expect from its authors, without being cumbersome and heavy, as one may fear from its continental roots.

Certainly the second edition is an improvement over the first. In part the improvement has been achieved by the simultaneous publication of a companion volume on Sensory Physiology which allowed the deletion of one chapter, and thus the addition of new material. It may in fact have been more realistic to designate "Fundamentals of Neurophysiology" and "Fundamentals of Sensory Physiology" as volumes one and two of the same work. There are some exceptions. For example, fig. 2-16 was much clearer in the first edition than in the second. On the original, it was obvious that potassium conductance ( $g_K$ ) is in the "resting state" of nerve membranes higher than sodium conductance ( $g_{Na}$ ). In the new edition, as in the similar illustrations in almost all textbooks,  $g_K$  is made to appear equal to  $g_{Na}$  at "rest," which is the kind of inconsistency in small detail which so readily baffles students. By and large the illustrations are however lucid, vivid, and serve their purpose well at least in a "first reader" in this complex and difficult subject.

This brings us to the crucial question: to what class of students is this text most suited? For medical students the balance of topics may not be ideal. While 174 pages are devoted to nerve, muscle, synapses, and simple reflex functions the brain, cerebellum, and brainstem get only 133 pages. This results in undesirable compression of some topics. For example, the discussion of the ascending reticular activating system is squeezed into two short paragraphs. While the author quite properly criticizes the "reticular theory" of the regulation of the sleep-wake cycle, a more detailed presentation of the known experimental and clinical observations relating to this part of the brain stem would nevertheless seem important in a medical course. This sort of curtailment seems to stem from the attempt to keep the total number of pages not much more than 300.

For graduate students concentrating on the study of the nervous system the text seems too simplified. For them the color-

coded smoothed drawings illustrating the volume are not an adequate substitute for reproductions of original recordings. They would also need more advanced treatment in the text, and better referencing of original papers.

This leaves advanced undergraduate classes in neurobiology, and graduate students in other biological areas who require only a simple general overview of the function of the nervous system as the proper audience of this book.

Apparently this book began as a self-teaching text, and as a vestige of its origins there are multiple choice questions at the end of each chapter. There also is a short list of suggested further readings, and an index.

The text reads smoothly. One barely notices, that it is a translation from a foreign language.

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*Laboratory Investigations in Human Physiology.* George K. Russell Macmillan Publishing Co., Inc. New York. 1978, 342pp. illus. \$6.95

Russell gives us a one-semester laboratory manual for undergraduate physiology consisting of 27 exercises. He mentions that the wide range of representative experiments can be used with most lecture texts for general, mammalian, and human physiology courses. Basic physiology experiments use students as experimental subjects rather than laboratory animals. As far as I could determine, no laboratory animals were used as test models. The author strongly opposes inflicting unnecessary suffering on animals. He feels, as many people do, that animal experiments "harden the hearts" of undergraduates even though he realizes its importance in medical and biological research. However, laboratory instructors must assume full responsibility for safety procedures and for determining the health status of students which could be exacerbated by stress experiments. Films, videotapes and models replace the non-invasive techniques in teaching basic physiological principles. The manual provides addresses for buying specialized equipment and it suggests that some of the items can be obtained from local hospitals, medical centers and private physicians. Limited equipment could be remedied by conducting several exercises simultaneously. After each section of study has been completed, the students rotate to the next experiment.

Seven sections include: the blood, the heart, respiration, nerve-sensory processes, digestion, cellular-subcellular processes, renal function and regulatory processes. Clear cut objectives, practical theory, "easy to follow" procedures and elegant "how to" illustrations give students fine tools for study. Certainly, a picture is worth a 1000 words. Study questions go beyond the laboratory experiment and pertinent references supplement the course text. Results and Conclusions "tear out" sheets provide the student report. This forms a basis for writing future manuscripts, grants and proposals. Active personal writing and expert editing combined with broad laboratory experience makes this a manual students will enjoy.

I feel that many basic physiologic principles demand the use of laboratory animal preparations for specific study. For example,

capillary circulation, nerve-muscle experiments and numerous other fundamental concepts can only be obtained by these data. Despite some student attitude toward animal studies, common sense tells us that electrodes can not be inserted into human muscles or blood vessels when these data can be obtained from lower animals. Also, in my opinion that informed consent, "risk" and student health status should never be placed in the young instructor's hand. It seems to me that the "Human Rights and Experimentation Group" has clear cut guidelines in this regard whereby the "risk" for the student for each study must be pre-judged by qualified individuals. The young instructor is not qualified to make these decisions. The labs offer physical diagnosis, pulmonary function tests, EKG and ECG readings and many other practical studies. However, instructors may find it difficult obtaining used equipment from hospitals and physicians. In my opinion, this "bedside approach" to physiology favors the manual's application to human physiology with limited use in general and mammalian physiology. Most advances in physiology come from students who search for objective truth and who fight to understand without necessarily attaining the practical ends. Practical achievements come from basic fundamental concepts that serve the increased clinical competence.

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## COURSE IN DESIGN AND ANALYSIS OF SCIENTIFIC EXPERIMENTS

Massachusetts Institute of Technology will offer a one-week course in Design and Analysis of Scientific Experiments, June 25-June 30, 1979. Applications will be made to the physical, chemical, biological, medical, engineering and industrial sciences, and to experimentation in psychology and economics. The course will be taught by Professors Harold Freeman and Paul Berger. Further particulars may be obtained by writing to the Director of the Summer Session, Room E19-356, MIT, Cambridge, MA 02139.

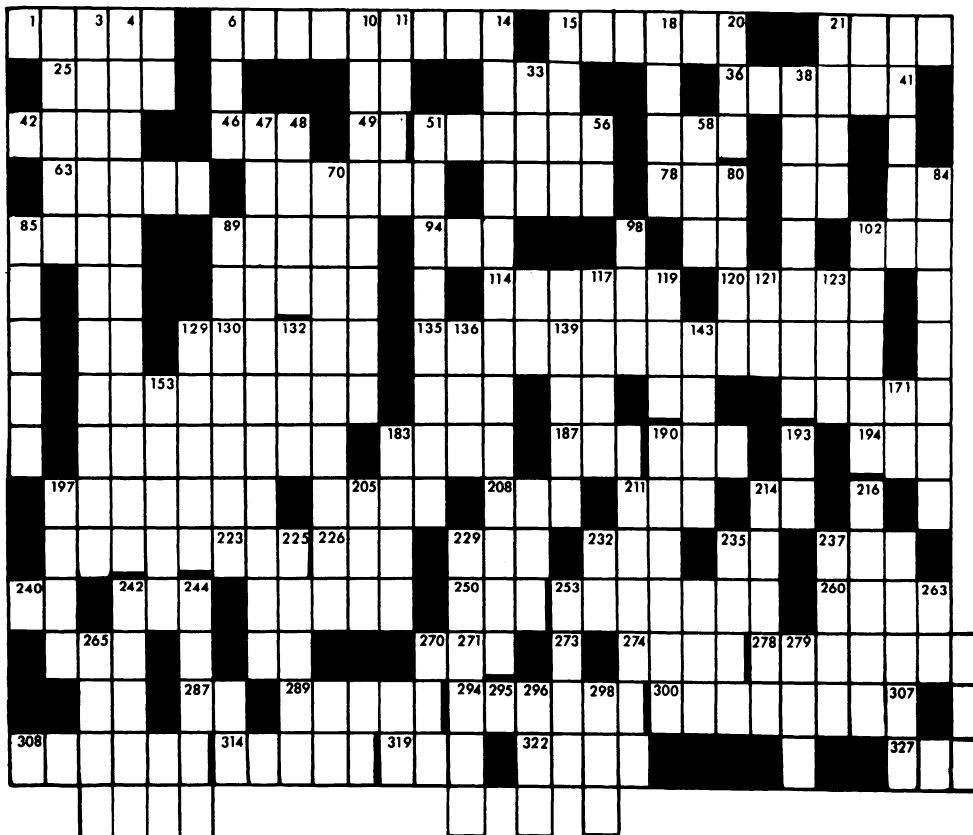
# NEUROPHYSIOLOGY CROSSWORD PUZZLE

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This puzzle has been used as a final examination on two occasions. However, the uproar of protests after the first occasion led to it being only a supplemental part of the examination on the second occasion. The puzzle has 99 answers, graded at 1 point each.

Although many students complained vigorously about the unfairness of using such a "surprise" and "tricky" approach, the better students generally did better on the crossword than did other students. That proves little, of course, because good students are good because they usually do perform better, no matter what. In any case, the puzzle was a refreshing change for the teacher and an intriguing challenge to the more adventuresome students.



## Across

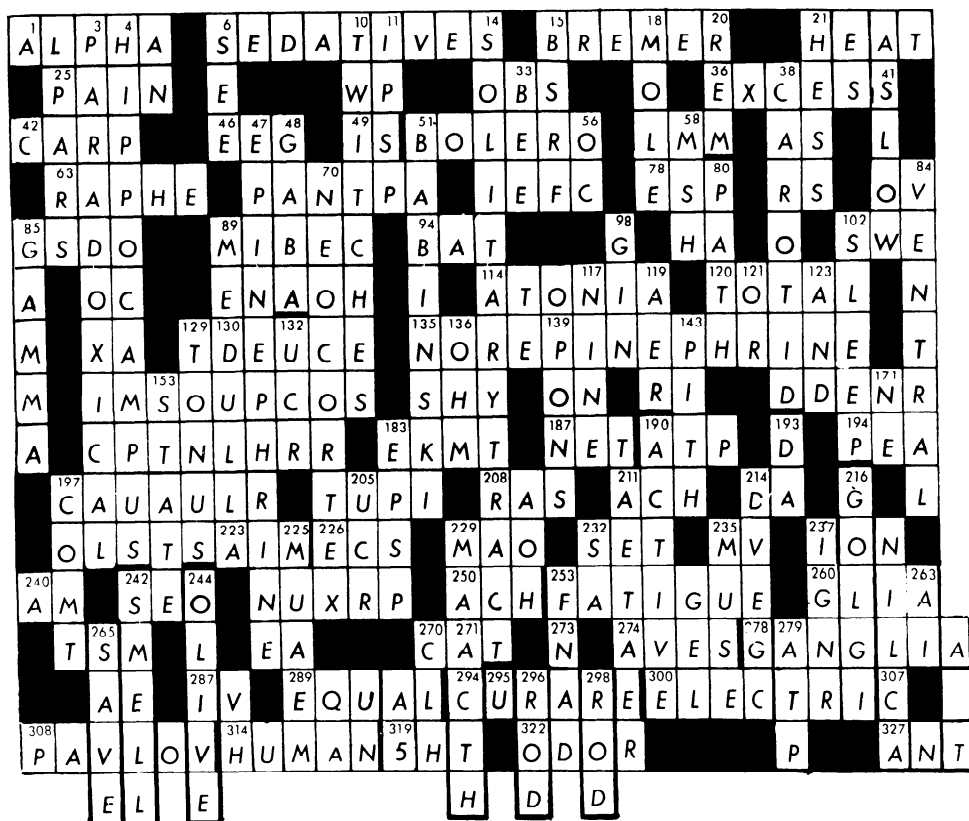
1. EEG rhythm
6. class of drugs that deactivates EEG
15. man who located an arousal system by brain transections
21. initial \_\_\_\_\_, due to ion flow
25. sensation dealt with by gate-control theory
36. potassium concentration inside of cell is in \_\_\_\_\_ of that outside
42. animal that never sleeps
46. brain waves
49. verb form of "to be"
51. Spanish dance in  $\frac{3}{4}$  time
63. sleep "center"
78. apparent sensations without a known physiological basis
94. animal with "radar"
114. cardinal sign of dream sleep
120. sum of
130. a pair
135. transmitter in postganglionic sympathetic fibers
187. nerve \_\_\_\_\_ organization in coelenterates
190. energy source for neurons
194. a plant
208. brain stem activating system, abbreviation
211. abbreviation for transmitter in autonomic ganglia
214. abbreviation for transmitter that is norepinephrine precursor
223. objective
226. disrupts memory consolidation
229. enzyme that destroys norepinephrine
232. learning \_\_\_\_\_
235. order of magnitude for size of nerve impulses, abbreviation
237. charged particle
240. time of day when human glucocorticoid blood levels are high
250. abbreviation for transmitter in neuromuscular junction
253. phenomenon more evident in synapses than in axons
260. most common cells in brain
270. animal that sleeps a lot that has been used in sleep studies
274. group of animals that show all signs of dream sleep, but only for short times
278. structures containing junctions of sympathetic nerves
287. Roman numeral for the trochlear nerve
289. ratio of influx/outflux at equilibrium potential
294. blocks neuromuscular junction nicotinic receptors
300. one form in which information is transferred and processed in nervous system
308. discoverer of the conditioned reflex
314. species with the most developed cerebral hemispheres
319. another name for serotonin
322. sensation closely linked to limbic system
327. animal in the invertebrate group with the most advanced nervous system organization, outside of vertebrates.

327 across has several other correct answers; bee (or any other 3-letter insect)

## Down

3. dream sleep
4. area needed for memory consolidation

6. function of onmatidia
10. muscle activity during dream sleep
11. inhibitory action on a neuron
14. sleep "center"
15. abbreviation for part of brain mediating arousal
18. primitive mammal showing dream sleep
20. another term for dream sleep
21. man who first produced sleep by brain stimulation
25. \_\_\_\_\_ medialis
33. animal that navigates by plane of polarized light
38. major arterial supply for brain
41. \_\_\_\_\_ -wave sleep
47. released during stress
48. inhibitory transmitter
51. reflex of humans present in pathological states
56. abbreviation for cross-over point of cranial nerves concerned with vision
58. pituitary hormone affecting skin color
70. brain area most developed in primates
80. connection route between brain areas
84. thalamic nucleus that relays specific sensory information to cortex
85. motor fibers to muscle spindle
89. site of cardiovascular and respiratory reflex systems
98. liquid that can cause EEG-behavioral dissociation
102. needed by all higher animals
117. glossopharyngeal nerve, cranial nerve number \_\_\_\_\_
119. abbreviation for evoked response that is computer averaged
121. a gating organization of neurons in a parallel circuit
123. a gating organization of neurons in an in-series circuit
129. electro- \_\_\_\_\_
132. a response that occurs without learning, abbreviation
136. unit of measure of brain resistance to electric current flow
139. part of brain containing a nucleus which relays auditory input
143. the center of
153. memory can be \_\_\_\_\_ -dependent
171. abbreviation for chemical depleted by reserpine
183. an excitatory electric process in the synapse
190. type of ionic transport needed to maintain resting membrane potential
193. abbreviation for transmitter release by substantia nigra neurons
197. destructive enzyme for norepinephrine abbreviation
205. response which occurs in absence of learning
216. name of stain that marks all parts of a given neuron
225. abbreviation for impulse activity from a population of neurons
235. to ponder
242. sensation that is brought directly into septal area
244. brain stem relay center for hearing
265. to hoard is to \_\_\_\_\_
271. compound secreted in response to a hypothalamic releasing factor
273. compound that accepts hydrogen in glutamate metabolism
274. same as 119 down.
279. energy source.
296. visual receptor
238. same as 296 down



# COUNCIL OF ACADEMIC SOCIETIES BRIEF

ASSOCIATION OF AMERICAN MEDICAL COLLEGES  
(202) 466-5100

• 1 DUPONT CIRCLE NW  
WINTER, 1979

• WASHINGTON DC  
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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.

PRESIDENT CARTER REVEALS BUDGET REQUEST FOR FY 1980. On January 22, President Carter sent his \$531.6 billion FY 1980 budget request to the Congress. The unveiling of the President's budget for FY 1980 ends a period of speculation and debate which began two months ago when the Office of Management and Budget (OMB) proposed severe cuts for both FY 1979 and FY 1980. OMB proposed, for example, a rescission (an effort by the Administration to cut or eliminate programs already funded by the Congress) of about 10% of the current National Institutes of Health (NIH) budget and recommended that the NIH be funded at this reduced level for FY 1980. Other programs, such as capitation, exceptional need scholarships, and financial distress grants, would have been cut drastically in this fiscal year and eliminated entirely in FY 1980 if the initial OMB proposal had been accepted.

After the OMB submitted its proposal, each department was given the opportunity to defend its current budget and to make recommendations on the 1980 budget. Apparently, DHEW Secretary Califano made a particularly vigorous appeal, arguing that the cuts recommended for NIH were inconsistent with the Administration's stance in support of biomedical research. As a result of Califano's appeal and of strong protestations from Senator Kennedy and other staunch supporters of health programs, many of the proposed cutbacks were restored.

Although the budget picture is not as bleak as had been feared, Mr. Carter will be asking Congress to approve three rescissions which directly affect the academic medical community. The first rescission would cut medical school capitation by 50% this year; the second would reduce the NIH budget by \$37 million--money intended for construction of a child health research facility; and the third would decrease health professions student loans by \$10 million.

Capitation. For FY 1980 the President is requesting no funding for medical school capitation. Secretary Califano told the press recently that capitation encouraged the production of specialists and subspecialists and was therefore being eliminated. He expressed the Administration's opinion that while there may soon be an oversupply of physician manpower, the problem of specialty maldistribution remains. In order to address this problem, the Administration is increasing the budget by \$28 million to support primary care and family medicine training and residency programs.

NIH. The 1980 budget request for the National Institutes of Health, excluding money for buildings and facilities, shows very slight increases over fiscal 1979. This "no-growth" budget will not allow NIH to keep pace with inflation and will, in fact, mean a 7-10% reduction in programs.

Loans and NHSC scholarship program. Also for fiscal 1980, Mr. Carter would eliminate all health professions student loans and increase the budget for the National Health Service Corps Scholarship program by only \$5 million--not nearly enough to meet the need.

(continued)

ADAMHA. The Alcohol, Drug Abuse and Mental Health Administration's budget for 1980 reflects a \$91 million increase over the previous year. Of the \$1.2 billion requested, \$99 million will support a new program of grants to improve mental health service delivery. Approximately \$160 million is requested for mental health research and \$134 million for a new initiative to reduce alcoholism and related problems, particularly among women and youth.

Other new initiatives. In addition to the alcoholism program, the budget seeks two additional initiatives--an increase of \$137 million for preventive health programs and \$194 million for programs to reform the health system. The latter would aim to attract doctors to medically underserved areas, encourage medical students to enter family practice, help communities to eliminate unnecessary hospital beds, and accelerate the creation of health maintenance organizations.

The President's budget, which has been strongly criticized by many as boosting national defense at the expense of health and other "people" programs, is now in the hands of the Congress. Traditionally, the Congress could be depended on to augment the President's recommended budget levels in the health area. But with a new Congress, purported to be more fiscally conservative and intent on reducing the federal deficit, it is difficult to predict the final outcome of the budgetary process.

TECHNICAL STANDARDS FOR MEDICAL SCHOOL ADMISSION. In the Rehabilitation Act of 1973, as amended, Section 504 specifies that "no otherwise qualified handicapped individual...shall, solely by reason of his handicap be excluded from participation in, be denied benefits of, or be subject to discrimination under any program or activity receiving federal financial assistance." DHEW issued regulations implementing this legislation in May 1977. The regulations are detailed and inclusive and could result in medical schools being challenged to admit individuals who have physical or mental handicaps inconsistent with their developing the skills usually expected of all physicians. The regulations provide for the application of nonacademic technical standards in assessing an individual's suitability for admission.

An AAMC panel, appointed last spring, has developed a guide that can be adapted for use by medical schools in framing their institutional policy on nonacademic technical standards for admission.

NEW REGULATIONS AFFECTING CLINICAL RESEARCH ARE ISSUED. The Food and Drug Administration (FDA) has moved to regulate institutional review boards (IRBs) for the protection of human subjects of research. The proposed regulations would add requirements for scientific review and monitoring to the ethical review now required by the DHEW. A storm of protest has arisen, forcing the FDA to extend comment on the regulations by six months to June, 1979. Most observers feel that the FDA should simply adopt existing DHEW regulations.

The DHEW moved suddenly in late November to require that all human subject consent forms be changed to notify prospective subjects as to the availability of compensation for injuries received in the course of experiments. Serious legal objections have been raised to this action. How this new requirement can be implemented, since no compensation insurance is likely to be available, is among questions that remain unanswered.