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EDITOR'S PAGE

PHYSIOLOGY TEACHERS NEEDED

The Central Office of APS receives many inquiries for names of physiologists who may be interested in teaching positions. Generally the inquiring parties are referred to the Federation Placement Service Office since The Physiologist is not designed to handle placement service activities. However we are calling attention to two very earnest appeals recently received mainly to emphasize the real need for more trained personnel in our discipline. The number of persons trained in physiology each year has not kept pace with the steadily increasing demand for trained personnel at all levels of experience.

The two cases in point at present are the University of California at Davis and the Christian Medical College in India. The former can be contacted by writing to Dr. F. W. Lorenz, Dept. of Animal Physiology; and the latter by writing to Dr. G. N. Constable at Ludhiana, Punjab, India.

The recent emphasis on training programs sponsored by NIH should eventually elevate this critical situation to some extent but professional physiologists must continue to recruit students at all levels of the educational ladder if we are to continue to have a discipline called physiology and have teachers to train students for the future.

One means of recruiting more young people for careers in physiology is becoming effective through the Education Committee's program of Visiting Scientists. Many of the smaller schools requesting visiting scientists have expressed the desire to have the scientist consult with students about graduate training. Several of the visiting scientists have been able to successfully plead the case for physiology in these informal talks and interviews, in some cases picking up good applicants for graduate study in their own departments.

The Visiting Scientist program is continuing this year with more emphasis on personal conferences with students and teachers as well as administrators and less emphasis on formal seminars and lectures. Both undergraduate schools and visiting scientists are finding the program highly rewarding. Schools are permitted to select a visiting scientist from a list of names and scientist interests. This method necessarily means that some scientists will not be called to make a visit while others will make several visits. We hope scientists will continue to make themselves available even though not called upon this year.

THE AMERICAN PHYSIOLOGICAL SOCIETY

Founded December 30, 1887; Incorporated June 2, 1923

OFFICERS, 1964-1965

President - John R. Pappenheimer, Harvard Medical School, Boston, Massachusetts
President-Elect - John M. Brookhart, University of Oregon School of Medicine, Portland, Oregon
Past President - Hermann Rahn, University of New York at Buffalo, Buffalo, New York
Council - H. Rahn(1965), J. R. Pappenheimer (1966), J. M. Brookhart (1967), R. E. Forster (1965), L. D. Carlson (1966), K. S. Cole (1967), J. D. Hardy (1968)
Executive Secretary-Treasurer - R. G. Daggs, 9650 Wisconsin Avenue, Washington, D.C. 20014

STANDING COMMITTEES

Publications - R. W. Berliner (1967), Chairman; C. N. Woolsey (1965), R. E. Forster (1966)
Finance - L. N. Katz (1968), Chairman; H. S. Mayerson (1966), S. M. Tenney (1967)
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Senior Physiologists - D. B. Dill (1965), Chairman; W. F. Hamilton (1965), E. F. Adolph (1966), P. Bard (1966)
International Physiology - M. B. Visscher (1965), H. S. Mayerson (1967), E. M. Landis (1969)

REPRESENTATIVES TO OTHER ORGANIZATIONS

American Association for the Advancement of Science - R. E. Smith (1967), R. G. Daggs
American Institute of Biological Sciences - J. R. Pappenheimer (1966)
American Documentation Institute - M. O. Lee (1967)
National Research Council - Division of Medical Sciences - R. W. Gerard (1967); Division of Biology and Agriculture - A. F. Sellers (1967)
Council on Medical Education and Hospitals, A.M.A. - J.R. Brobeck(1967)

APS Members of the U. S. National Committee for IUPS - M. B. Visscher (1965), H. S. Mayerson (1967), E. M. Landis (1969)
APS Members on the Federation Board - H. Rahn (1965), J. R. Pappenheimer (1966), J. M. Brookhart (1967)
Federation Advisory Committee - J. M. Brookhart (1967)
Federation Secretaries Committee - J. M. Brookhart (1965), R. G. Daggs
Federation Public Information Committee - A. C. Guyton (1967)

PUBLICATIONS

Publications Committee - R. W. Berliner (1967), Chairman; C. N. Woolsey (1965), R. E. Forster (1966)
Managing Editor - M. O. Lee
Executive Editor - Sara F. Leslie
Chief Editor of Journal of Neurophysiology - J. M. Brookhart
Editor of The Physiologist - R. G. Daggs
Associate Editor of Physiological Reviews - R. G. Daggs
Associate Editor of American Journal of Physiology and Journal of Applied Physiology - R. L. Zwemer

EDITORIAL BOARDS

American Journal of Physiology and Journal of Applied Physiology -
Section Editors - R. M. Berne, B. F. Hoffman (Circulation), Jere Mead (Respiration), Jack Orloff (Renal and Electrolyte Physiology), Franklin Hollander (Gastrointestinal Physiology), Jane A. Russell, R. K. Meyer (Endocrinology and Metabolism), L. D. Carlson (Environmental Physiology), Knut Schmidt-Nielsen (Comparative and General Physiology), E. V. Evarts (Neurophysiology).

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Physiological Reviews - J. R. Brobeck (1966), Chairman; V. E. Amassian (1966), A. P. Fishman (1967), C. W. Gottschalk (1966), W. L. Nastuk (1966), J. E. Rose (1965), R. C. Swan (1966), J. V. Taggart (1966). Appointed from the Society of General Physiologists -

T. H. Bullock (1966), I. M. Klotz (1965). Appointed from the American Society of Biological Chemists - J. M. Buchanan (1967), A. E. Wilhelmi (1966). Appointed from the American Institute of Nutrition - Grace A. Goldsmith (1967). European Editorial Committee - Eric Neil, Chairman; N. Emmelin, R. B. Fischer, R. A. Gregory, Y. Laporte, G. Moruzzi.

Journal of Neurophysiology - T. H. Bullock, R. Granit, J. D. Green, Elwood Henneman, B. Katz, S. W. Kuffler, V. B. Mountcastle, W. D. Neff, J. E. Rose.

Handbook of Physiology, Editorial Committee - M. B. Visscher, Chairman; A. B. Hastings (1966), H. Rahn (1967), J. R. Pappenheimer (1965).

Physiology for Physicians - E. A. Stead, Jr., Chairman; J. H. Comroe, Jr., M. I. Grossman, I. M. London, I. H. Page, R. F. Pitts, Stewart Wolf, J. B. Wyngaarden.

PAST OFFICERS

Presidents - 1888 H. P. Bowditch, 1889-90 S. W. Mitchell, 1891-95 H. P. Bowditch, 1896-1904 R. H. Chittenden, 1905-10 W. H. Howell, 1911-13 S. J. Meltzer, 1914-16 W. B. Cannon, 1917-18 F. S. Lee, 1919-20 W. P. Lombard, 1921-22 J. J. MacLeod, 1923-25 A. J. Carlson, 1926-29 J. Erlanger, 1930-32 W. J. Meek, 1933-34 A. B. Luckhardt, 1935 C. W. Greene, 1936-37 F. C. Mann, 1938-39 W. E. Garrey, 1938 W. T. Porter Honorary President, 1940-41 A. C. Ivy, 1942-45 P. Bard, 1946-47 W. O. Fenn, 1948 M. B. Visscher, 1949 C. J. Wiggers, 1950 H. C. Bazett (April to July) D. B. Dill, 1951 R. W. Gerard, 1952 E. M. Landis, 1953 E. F. Adolph, 1954 H. E. Essex, 1955 W. F. Hamilton, 1956 A. C. Burton, 1957 L. N. Katz, 1958 Hallowell Davis, 1959 R. F. Pitts, 1960 J. H. Comroe, Jr., 1961 H. W. Davenport, 1962 H. S. Mayerson, 1963 Hermann Rahn.

Secretaries - 1888-92 H. N. Martin, 1893-94 W. P. Lombard, 1895-1903 F. S. Lee, 1904 W. T. Porter, 1905-07 L. B. Mendel, 1908-09 R. Hunt, 1910-14 A. J. Carlson, 1915-23 C. W. Greene, 1924-29 W. J. Meek, 1930 A. C. Redfield, 1931-32 A. B. Luckhardt, 1933-35 F. C. Mann, 1936-39 A. C. Ivy, 1940-41 P. Bard, 1942 C. J. Wiggers, 1943-46 W. O. Fenn, 1947 M. B. Visscher.

Treasurers - 1888-92 H. N. Martin, 1893-94 W. P. Lombard, 1895-1903 F. S. Lee, 1904 W. T. Porter, 1905-12 W. B. Cannon, 1913-23 J. Erlanger, 1924-26 C. K. Drinker, 1927-36 A. Forbes, 1937-40 W. O. Fenn, 1941 C. J. Wiggers, 1942-46 Hallowell Davis, 1947 D. B. Dill.

Executive Secretary-Treasurer - 1948-56 M. O. Lee, 1956 - R. G. Daggs.

CONSTITUTION AND BYLAWS

Adopted at the 1964 Spring Meeting

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

(Amended April 1961)

ARTICLE I. Membership

Section 1. The Society shall consist of members, honorary members, associate members, and sustaining associates.

Section 2. Members. Any person who has conducted and published meritorious original research in physiology and/or biophysics and who is a resident of North America shall be eligible for membership in the Society.

Section 3. 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 4. Associate Members. Advanced graduate students in physiology at a predoctoral level, teachers of physiology, and investigators who have not yet had the opportunity or time to satisfy the requirements for full membership shall be eligible for associate membership in the Society provided they are residents of North America.

Section 5. Sustaining Associates. Individuals and organizations who have an interest in the advancement of biological or biophysical investigation, may be invited by the President, with the approval of Council, to become sustaining associates.

ARTICLE II. Officers

Section 1. The management of the Society shall be vested in a Council consisting of the President, the President-Elect, the Past-President for the previous year, and four other members. The terms of the President and of the President-Elect shall be one year. The terms of the four additional Councilors 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 person may 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 1st.

Section 2. Nomination and election of a President-Elect and Councilor(s) shall be by ballot at the Spring meeting of the Society. They shall assume office on July 1 following their election.

Section 3. The President-Elect shall serve as Vice-President and Secretary. Should he have to function as President prematurely, the Council shall select from among its own members a Secretary.

Section 4. 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.

Section 5. The Council may fill any interim vacancies in its membership or vacancies on any Board or Committee of the Society, unless otherwise provided.

ARTICLE III. Dues

Section 1. The annual assessment on members and on associate members shall be determined by the Council and shall be due in advance on July 1.

Section 2. A 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 Spring meeting by special vote of the Council. It shall be the duty of the Secretary to notify the delinquent of his right to request reinstatement.

Section 3. A member who has retired from employment because of illness or age may, upon application to the Council, be relieved from the payment of the annual member assessment.

ARTICLE IV. Meetings

Section 1. A meeting of the Society for transacting business, electing officers and members, presenting communications, and related activities, shall be held in the Spring of each year, with other member Societies of the Federation of American Societies for Experimental Biology, except that under exceptional circumstances the Council may cancel such a meeting.

Section 2. A Fall meeting of the Society shall be held at a time and place determined by the Council, for presenting communications and for transacting business except the election of officers.

Section 3. Special meetings of the Society or of the Council may be held at such times and places as the Council may determine.

Section 4. Regional meetings of the Society, for the purpose of presenting scientific communications, may be authorized by the Council.

ARTICLE V. Publications

Section 1. The official organs of the Society shall be the American Journal of Physiology, the Journal of Applied Physiology, Physiological Reviews and such other publications as the Society may own.

Section 2. A Publications Committee composed of three members of the Society appointed by the Council shall be responsible for the management of all of the publications of the Society; the Managing Editor, Executive Secretary and President of the Society shall be members ex-officio, without vote. The Committee shall have the power to appoint a Managing Editor and editorial boards for the Society's publications. The term of each member of 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. The Committee shall present an annual report on publications and policies to the Council for approval and an annual budget to the Finance Committee for its approval.

ARTICLE VI. Committees and Representatives

Section 1. The Council may appoint such special and standing committees as it deems necessary or that are voted by the Society.

The Council may name members of the Society as representatives to other organizations whenever it deems such action desirable.

Section 2. A Finance Committee, composed of three members of the Society appointed by the Council, shall receive budget proposals annually from the Committees, the Council and the Executive Secretary of the Society and shall determine the annual budget, reserve funds and investments of the Society, subject to approval by the Council.

The capital fund of the present Board of Publication Trustees (defined as the investments and unencumbered funds of that Board as of April 1, 1961) shall be a reserve fund for publications and may be used by the Publications Committee to finance new or established publications without authorization of the Finance Committee (though subject to approval by Council). The Finance Committee shall not approve the expenditure of any of this capital fund for nonpublication 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 the value of it). Annual income from the investment of the fund may be used for any of the activities of the Society including publications.

The term of each member of the Finance Committee shall be three years; a member may not serve more than two consecutive terms. The Managing Editor, the President and the Executive Secretary shall be ex-officio members, without vote. The Council shall designate the Chairman of the Committee who shall be an ex-officio member of the Council, without vote.

ARTICLE VII. Standing Rules

1. Election to Membership. Two members of the Society must join in proposing a person for membership, in writing and with a statement of his qualifications. The Council may, from the persons so proposed, nominate candidates for election to membership. Nominations shall be presented at Spring and Fall meetings; a two-thirds majority vote of the members present and voting at the next following Fall or Spring meeting shall be necessary for election.

If a Spring or Fall meeting of the Society is not held, the procedures of nomination and/or election of new members may be effected by mail.

The names of the candidates nominated by the Council for membership and statements of their qualifications signed by their proposers shall be available for inspection by members during the Society meetings at which their election is considered.

2. Election to Honorary Membership. The proposal of an honorary member shall be made by two members of the Society to the Council in writing. The Council may, from the candidates so proposed, make nominations to the Society at a Spring meeting. A two-thirds majority vote of the members present shall be necessary for election.

Honorary members shall have the privilege of attending business sessions of the Society but shall have no vote. They shall pay no membership dues.

3. Election to Associate Membership. Associate members shall be proposed, nominated and elected in the same manner as full members.

Associate members shall have the privilege of attending business sessions of the Society but shall have no vote. Associate members may be nominated for full membership.

4. Presentation of Papers. At a Spring meeting of the Society, held in conjunction with the Federation meetings, a member, retired member, or honorary member must be one of the authors of each scientific paper submitted to the Society for presentation. Also a person's name may appear only once. An associate member or a non-member may present orally one scientific paper only if a full member is a co-author. At a Fall meeting, a member, retired member, honorary member, or associate member may present orally not more than one paper.

Upon invitation by the Council, a member may contribute papers to specially designated sessions of the Society without forfeit of his privilege of presenting a regular scientific communication.

5. There shall be a Committee on Membership appointed by and advisory to the Council.

6. There shall be a Program Advisory Committee appointed by the Council.

ARTICLE VIII. General

Section 1. Amendments. These Bylaws, except Article VII, may be amended at any Spring meeting of the Society by a three-fourths majority vote of the members present.

The Standing Rules of Article VII may be amended by a majority vote of the members present at either a Spring or Fall meeting of the Society.

Section 2. Quorum. At all business meetings of the Society fifty members shall constitute a quorum.

Section 3. Parliamentary Authority. The rules contained in Roberts Rules of Order 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.

APS MEMBERSHIP STATUS

OCTOBER 1964

Regular members	2320
Associate members	180
Retired members	133
Honorary members	17
Total membership	2650

SUSTAINING ASSOCIATES

Abbott Laboratories
Ayerst Laboratories
Beckman Instruments, Inc.
Burroughs Wellcome and Co.
CIBA Pharmaceutical Products, Inc.
Ethicon, Inc.
Gilford Instrument Laboratories, Inc.
Gilson Medical Electronics
Grass Instrument Co.
Harvard Apparatus Co.
Hoffman-La Roche, Inc.
Lakeside Laboratories
Eli Lilly and Co.
Merck Sharp and Dohme Research Laboratories
The Norwich Pharmacal Co.
Chas. Pfizer and Co., Inc.
Phipps and Bird, Inc.
Riker Laboratories, Inc.
A. H. Robins Co., Inc.
Sherman Laboratories
Smith Kline and French Laboratories
The Squibb Institute for Medical Research
Tektronix, Inc.
The Upjohn Co.
Warner-Lambert Research Institute
Wyeth Laboratories

DECEASED MEMBERS

The following deaths were reported since the 1964 Spring meeting.

R. H. Beutner (R) - April 15, 1964
Paul M. Harmon (R) - July 16, 1964
E. A. Hewitt (R) - December 29, 1963
Henry A. Imus - May 18, 1964
Yale J. Katz - December 6, 1963
Simon A. Komarov - March 29, 1964
George Misrahy - March 7, 1964
W. J. Osterhout (R) - April 9, 1964
Charles M. Pomerat - June 17, 1964
Julian Tobias - April 12, 1964
Charles I. Wright (R) - April 16, 1964

NEWLY ELECTED MEMBERS

The following, nominated by the Council, were elected to membership in the American Physiological Society at the Fall meeting, 1964.

FULL MEMBERS

ADAMS, Thomas: Asst. Prof. Res. Physiol., Univ. Oklahoma Med. Sch.
AKERS, Thomas K.: Asst. Prof. Pharmacol., Stritch Med. Sch., Loyola
ANGELONE, Luis: Assoc. Prof. Physiol., Washington Univ. Dent. Sch.
ARMALY, Mansour F.: Assoc. Prof. Ophthalmol., State Univ. Iowa
ASCANIO, Guido: Asst. Prof. Physiol., Temple Univ. Med. Sch.
BENTIVOGLIO, Lamberto G.: Cardiac Cath., Albert Einstein Med. Ctr.
BICKFORD, Arthur F.: Assoc. Staff, Cardiovascular Res. Inst., Univ. California
BIRD, John W. C.: Asst. Prof. Physiol., Rutgers Univ.
BORLE, Andre B.: Asst. Prof. Physiol., Univ. of Pittsburgh
BOUHUYS, Arend: Asst. Prof. Physiol. & Med., Emory Univ.
BRAY, George A.: Asst. Physician, New England Center Hosp.
BREDECK, Henry E.: Assoc. Prof. Physiol., Colorado State Univ.
BUNNELL, Ivan L.: Assoc. Prof. Med., State Univ. New York, Buffalo
CARDUS, David: Asst. Prof. Physiol. & Rehab., Baylor Univ.
CASSIN, Sidney: Asst. Prof. Physiol., Univ. of Florida
CELANDER, David R.: Prof., Chmn. Biochem., Coll. Osteopathic Med.
CHIDSEY, Charles A.: Sr. Investigator, Cardiology Br., NHI
CLAPP, James R.: Assoc. Med., Duke Univ. Med. Ctr.
COLLINS, William F., Jr.: Prof. Neurol. Surg., Med. Coll. Virginia
COOPER, Bernard A.: Asst. Prof. Med. & Clin. Med., McGill Univ.
DALY, Walter J.: Asst. Prof. Med., Indiana Univ. Sch. Med.
DANFORTH, William F.: Prof. Physiol., Illinois Inst. Technology
DaVANZO, John P.: Lect. Pharmacol., Med. Coll. of Virginia
DAVIS, Robert P.: Asst. Prof. Med., Albert Einstein Coll. Med.
DAVIDSON, Julian M.: Asst. Prof. Physiol., Stanford Univ.
DOWNIE, Harry G.: Prof., Head Physiol. Sci., Ontario Vet. Coll.
DUTTON, Robert E.: Instr., Environ-Med., Johns Hopkins Univ.
EBLE, John N.: Sr. Res. Pharmacologist, Pitman-Moore Co., Indianapolis
EMERSON, Geraldine M.: Instr. Biochem., Univ. of Alabama Med. Ctr.
ESSIG, Alvin: Instr. Med., Harvard Med. Sch.
FLAMBOE, Eugene E.: Assoc. Prof. Physiol., Colorado State Univ.
FRAYSER, Katherine R.: Asst. Prof. Med., Physiol., Indiana Univ.
GAENSLER, Edward A.: Res. Prof. Surg., Boston Univ. Sch. Med.
GILLENWATER, Jay Y.: Res. Fell. Renal & CV, Bockus Res. Inst.
GINSBURG, Jack M.: Asst. Prof. Physiol., Univ. of Rochester
GOLD, Ernest M.: Assoc. Prof. Med., UCLA
GOLDSMITH, Dale P. J.: Instr. Physiol., Univ. of Rochester
GORDON, Helmut A.: Prof. Pharmacol., Univ. of Kentucky Med. Coll.
GORSKI, Jack: Asst. Prof. Physiol., Univ. of Illinois
GRAY, Seymour J.: Assoc. Clin. Prof. Med., Harvard Med. Sch.
GROLLMAN, Arthur P.: Assoc. in Med., Molecular Biol., Albert Einstein Coll. Med.
GROSS, Nathan B.: Prof. Physiol., Psychol., Univ. of Michigan
GUNTHEROTH, Warren G.: Assoc. Prof. Pediat., Univ. of Washington

HAFT, David E.: Assoc. Prof. Med., New York Med. Coll.
HERD, James A.: Instr. Physiol., Harvard Med. Sch.
HILLS, Arthur G.: Prof. Med., Chmn. Sect. Metabol., Univ. of Miami
IBER, Frank L.: Asst. Prof. Med., Johns Hopkins Univ. Sch. Med.
ISAACSON, Allen: Asst. Mem., Physiol. Div., Inst. Muscle Disease
JOHNSON, Donald C.: Asst. Prof. Gynecol. & Obstet., Kansas Univ.
JOHNSON, Edward A.: Assoc. Prof. Physiol., Duke Univ. Med. Ctr.
JONES, Richard D.: Assoc. in Res., St. Luke's Hosp., Cleveland
KALDOR, George J.: Res. Assoc., Phys. Chem., Isaac Albert Res. Inst.
KAPPAS, Attallah: Assoc. Prof. Med., Univ. of Chicago
KATZ, Joseph: Sr. Res. Assoc., Cedars of Lebanon Hosp.
KAUFMAN, William C.: Res. Biologist, Aerospace Med. Res. Labs.
KITTLE, C. Frederick: Assoc. Prof. Surg., Univ. of Kansas
KRIEGER, Dorothy T.: Res. Asst. Med., Mt. Sinai Hosp., New York
KRUM, Alvin A.: Asst. Prof. Physiol., Univ. of Arkansas
LANDAU, Bernard R.: Assoc. Prof. Med., Western Reserve Univ.
LAUBER, Jean K.: Asst. Prof. Animal Sci., Washington State Univ.
LAYNE, Donald S.: Staff Scientist, Worcester Fndn. Exptl. Biol.
LEE, James B.: Dir. Metabol. Res., St. Vincent Hosp., Worcester, Mass.
LENDE, Richard A.: Asst. Prof. Neurosurg., Univ. Colorado Med. Ctr.
LEON, Henry A.: Independent Res., Res. Scientist, NASA Ames Res. Ctr.
LILLEHEI, Richard C.: Assoc. Prof. Surg., Univ. of Minnesota
LINDSLEY, David F.: Asst. Prof. Physiol., Stanford Univ.
LINKENHEIMER, Wayne H.: Group Leader, Physiol., Pharmacol., Am. Cyanamid Co.
LODGE, James R.: Assoc. Prof. Physiol., Dairy Sci., Univ. Illinois
LUHBY, A. Leonard: Assoc. Prof. Pediat., New York Med. Coll.
MALLOV, Samuel: Assoc. Prof. Pharmacol., State Univ. New York, Syracuse
McKENZIE, John M.: Asst. Prof. Med. & Clin. Med., McGill Univ.
MELI, Alberto L.G.: Sr. Res. Assoc., Warner-Lambert Res. Inst.
MOSER, Kenneth M.: Asst. Prof. Med., Georgetown Univ. Hosp.
MOSES, Arnold M.: Staff Physician, Instr. Med., State Univ. New York, Syracuse
MOSS, Arthur J.: Res. Fell. & Instr. Med., Univ. Rochester Med. Ctr.
MUNCK, Allan U.: Assoc. Prof. Physiol., Dartmouth Med. Sch.
NELSON, Phillip G.: Physiol., Neurophysiol., NIH
NIKITOVITCH-WINER, Miroslava B.: Asst. Prof. Anat., Univ. Kentucky
NUNN, Arthur S., Jr.: Asst. Prof. Physiol., Univ. of Miami
O'BRIEN, George S.: Res. Assoc., CV Res. Lab., Univ. of Wisconsin
OPPENHEIMER, Jack H.: Endocrine Res. Lab., Montefiore Hosp.
PINNEO, Lawrence R.: Res. Assoc., Head Lab. Neurophysiol., Tulane Univ.
PLAGER, John E.: Res. Dir., Med. Fndn. of Buffalo
RANCK, James B., Jr., Asst. Prof. Physiol., Univ. of Michigan
REED, Donal J.: Res. Instr., Pharmacol., Univ. of Utah
RICHARDS, A. Glenn: Prof. Entomol., Fisheries & Wildlife, Univ. of Minnesota
ROBINSON, Roscoe R.: Asst. Prof. Med., Duke Univ. Med. Ctr.
SALZMAN, Edwin W.: Instr. Surg., Harvard Univ. Med. Sch.
SCHINDLER, William J.: Asst. Prof. Physiol., Baylor Univ.
SCHLAG, John D. A.: Asst. Prof. in Residence, Anat. & Brain Res., UCLA

SCHONBAUM, Eduard: Assoc. Prof. Pharmacol., Univ. of Toronto
SCHREINER, Bernard F., Jr.: Asst. Prof. Med., Univ. of Rochester
SIEGEL, John H.: Clin. Instr., Teach. Assoc. Surg., Univ. of Michigan
SOMJEN, George G.: Asst. Prof. Physiol., Duke Univ. Med. Ctr.
STEINER, Sheldon H.: Asst. Prof. Med., Indiana Univ.
SUTIN, Jerome: Assoc. Prof. Anat., Yale Univ.
TAYLOR, Fletcher B.: Res. Physician, CV Res. Inst., Univ. California
ULVEDAL, Frode: Res. Physiol., USAF Sch. Aerospace Med., Brooks AFB
WALDMANN, Thomas A.: Sr. Investigator, Metabol. Serv., NIH
WEISBERG, Howard: Res. Assoc., CV Inst. Michael Reese Hosp.
WEISSMAN, Sherman M.: Sr. Investigator, Metabol. Serv., NIH
WELTMAN, A. Stanley: Assoc. Prof. Pharmacol. & Res., Brooklyn Coll. Pharmacy
WILLIS, William D., Jr.: Asst. Prof. Anat., Univ. of Texas
WINDHAGER, Erich E.: Asst. Prof. Physiol., Cornell Univ. Med. Coll.
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ASSOCIATE MEMBERS

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FUTURE MEETINGS

1965 Spring - Atlantic City, N.J., April 9-14
1965 Fall - Univ. of California at Los Angeles, August 24-28
1965 IUPS - Tokyo, Japan, September 1-9
1966 Spring - Atlantic City, N.J., April 11-16
1966 Fall - Baylor Univ., Houston, Texas
1967 Spring - Chicago, Ill., April 16-21
1967 Fall - Howard Univ., Washington, D.C.
1968 Spring - New York City, April 7-12
1968 Fall - Will be cancelled because of Congress in Washington
1968 IUPS - Washington, D.C., August 25-30

THE HYPOTHALAMUS IN THE REGULATION OF ENERGY AND WATER BALANCE*

JAMES A. F. STEVENSON

Since the demonstration some 20 years ago that the obesity associated with pathological and experimental lesions in the region of the hypothalamus and pituitary is primarily due to overeating or hyperphagia (19), we have learned a great deal about the regulation of food and water intake by the central nervous system. As our knowledge increases, our explanations may become more precise but they also become more complex. In the middle of the last decade the matter seemed simple. There was a "feeding centre" in the lateral, and a "satiety centre" in the ventromedial hypothalamus (4, 49). The site of regulation of water intake was not quite so clear; in the rat it appeared to be in the lateral hypothalamus (32, 55, 83) but in the goat (11) and dog (43) more anterior and medial. Subsequent investigations have revealed that the neurophysiological systems for the regulation of food and water intake are very complex, being evident as well in other parts of the hypothalamus and, indeed, in other parts of the nervous system.

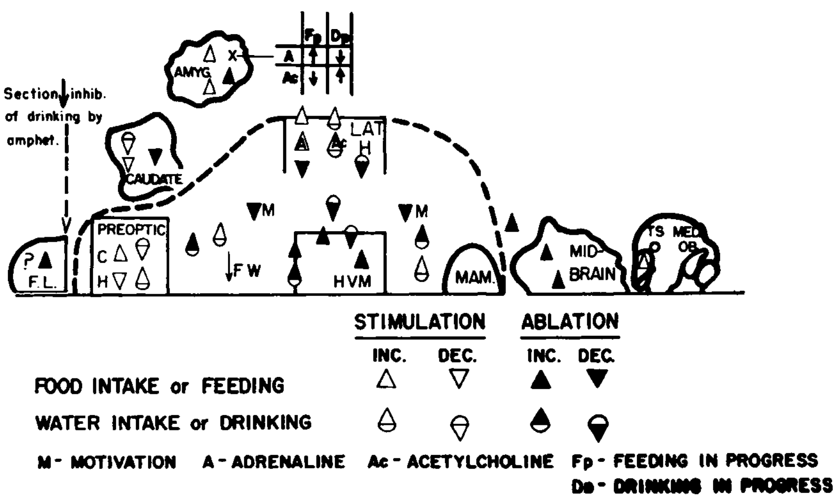

Fig. 1. Diagramatic outline of regions in nervous system that ablation, or stimulation, has shown to influence food and water intake. The broken line encloses the hypothalamic region; F. L. refers to frontal lobe, TS to tractus solitarius, ↓FW to region where ablation impairs food and water intake only in response to variations in environmental temperature.

*Based on presentation at Symposium presented at the Autumn Meeting of the American Physiological Society, University of Miami, Coral Gables, Florida, August 30, 1963.

Fig. 1 provides a diagramatic representation of some of the regions that influence food and water intake significantly according to the results of various ablation and stimulation experiments. In the hypothalamus, ablation in the ventromedial region produces hyperphagia and obesity (19, 20). If the lesions are anterior and ventral, hyperdipsia (44), secondary to diabetes insipidus from destruction of the supraopticohypophyseal tract, may also occur; but, if the lesions are on the lateral aspect, a relative hypodipsia and chronic dehydration are associated with the hyperphagia (83). Slightly more laterally, an absolute hypodipsia without hyperphagia is encountered following ablation (6,56). Stimulation in the ventromedial region tends to decrease food intake (7, 57, 64, 78, 101) while anesthesia of this region prevents the inhibition of feeding by gastric distension (40). Ablation at certain points in the posterior hypothalamus causes significant but less profound changes in food intake (84).

Ablation in the lateral hypothalamus results in adipsia in the rat (55). The aphagia that also occurs following these lesions led to this region being considered a "feeding centre" (4, 5). The argument as to whether or not this aphagia is a truly permanent effect and is due to a regulatory (27) or to a motor deficit (15) remains open. Although the spontaneous intake of water may be regained following such lesions, it is now dependent upon the intake of food - the animal apparently learns to eat water; spontaneous regulation of intake of water per se in response to natural exigencies is not recovered (27, 28). The evocation of feeding and drinking by stimulation in the lateral hypothalamus (24, 32, 35, 39, 47, 79, 95) confirms that important systems for the regulation of food and water intake lie here. The observations of Morgane (58) indicate the complex nature of these systems which apparently involve facilatatory or motivational elements.

As mentioned, stimulation more anteriorly and medially in the hypothalamus of the goat induces drinking, and ablation in this region in the dog causes an adipsia. This may be a true species difference from the rat, but, since Andersson has shown that cooling the preoptic hypothalamus of the goat evokes feeding and inhibits drinking, while warming has the opposite effects (10, 12), one may also postulate, as suggested earlier (85), that this anteromedial site of stimulation of drinking in the goat is part of an important pathway from the thermoregulatory systems in the preoptic area to a fundamental hydroregulatory system in the lateral hypothalamus. The evidence that lesions in this anterior region disrupt adequate regulation of food and water intakes in response to variations in environmental temperature supports this view (38, 85, 87). Thermoregulation requires adequate regulation of water and food intakes; in some species, it may exert the paramount control.

Recent observations suggest that osmoreceptors that facilitate or inhibit water drinking, as well as renal water loss, may be situated in the anterior hypothalamus (80) and there is evidence that osmosensitive elements occur in other parts of the nervous system (92). Water intake is also influenced by other regions of the hypothalamus; both stimulation and destruction in the premammillary area may cause some increase of water intake (48, 70, 72, 76, 84).

Ablations in several other regions of the brain have not produced marked effects on drinking or feeding (8, 9) with the exception of those in the amygdala (31, 46, 59, 60, 61, 62, 100) in the brain stem (1, 75, 82) and in the dorsal longitudinal fasciculus (22), which lead to some degree of hyperphagia, and ablation in the caudate nucleus, which may cause hypophagia or aphagia (8, 9, 85). Excepting the amygdala, it would perhaps be permissible, until shown otherwise, to consider these effects as due to interruption of sensory and motor systems. The inhibition of feeding that has been obtained from stimulation of the caudate (63) could be due to activation of an afferent inhibitory system for which evidence has currently been produced (74). Although it is generally agreed that ablation of the amygdala results in a hyperphagia, the effects of stimulation here on food and water intake vary with the site and type of stimulation as well as with the state of the animal (36, 68, 97). It is interesting that the exhibition of adrenaline in the cortical nucleus of the amygdala enhances feeding and depresses drinking, but only if these activities are already in progress; acetylcholine has opposite effects (36). These same agents have a more powerful influence in the lateral hypothalamus where adrenaline will evoke feeding and acetylcholine drinking, even in the satiated animal (35) - conversely these activities are inhibited by the local application of the appropriate blocking agents (37). These observations have led to the suggestion that the feeding systems may be adrenergic and the drinking systems cholinergic.

Section of the frontal lobes has been reported to increase food intake in both man and animal but in many instances this appears to have been secondary to a change in mood or to an increase in physical activity. However, there may well be inhibitory mechanisms to feeding and drinking in the frontal lobes, for section of these lobes removes the inhibitory effect of amphetamine on water and food intake (13). At the other end of the brain, stimulation in the region of the dorsal motor nucleus of the vagus has elicited feeding, even of contaminated food (47).

At this point it seems reasonable to postulate that the hypothalamus contains the fundamental systems for regulating food and water intake, particularly those related to other vital aspects of homeostasis such as thermo - and osmo-regulation. There is also evidence that chemoregulatory systems to adjust food intake to the needs for carbohydrate and fat may be located in the hypothalamus. The fundamental hypothalamic systems are affected not only by local events and peripheral afferent systems but also by higher systems, particularly in the limbic or visceral brain, with which the hypothalamus has many association pathways. Stimulation along several of these pathways has been found to influence immediate feeding and drinking behavior (29, 67, 69). The circuitry of the neurophysiological and neuroanatomical systems for these regulations appears to be very complex, but this is not surprising when we consider all the factors, with their various priorities, that affect food and water intake in animal and man (2).

Various attempts have been made to construct integrated hypotheses to describe at least the major or fundamental regulatory mechanisms for food and water intake (3, 14, 16, 17, 33, 45, 50, 51, 52, 73, 85, 87, 96). Those for feeding which have received emphasis recently are listed in

Table I. So far, none alone seems adequate to explain all facets of the regulation of food intake.

Table I. Current Hypotheses of the Regulation of Food Intake.

Gastrointestinal	-A. Oral-Pharyngeal B. Distension C. Effects on osmolarity of ECF
Thermostatic	-Peripheral and central heat monitors
Glucostatic	-Specific receptors for glucose
Lipostatic	-Concentration of circulating metabolite
Liponeurostatic	-Innervation of fat tissue
Amino Acid Pattern	-Pattern of amino acids in ECF
Combinations of above	

The inhibitory effect of gastric distension is well accepted. It probable serves as both a safety signal and as a conditioned or learnt cue. Relearning, or adjustment to changes, of this cue probably occur when the caloric density of the diet is varied. Afferent pathways from the stomach travelling via the vagus (41, 42, 53, 65, 91) or sympathetic nerves (34, 42, 94) apparently pass through the ventromedial hypothalamus to reach the lateral systems (40); they may also reach the caudate (74). This gastric mechanism, however, must depend on some more fundamental one, in relation to which it is set or appreciated, e.g. when the caloric density of the diet is varied.

It has long been held that hunger is inversely related to the concentration of blood glucose and Mayer and his colleagues (50, 51) have contributed much to the elucidation of how food intake may be regulated in relation to carbohydrate metabolism. They have concluded that it is the cells' need for glucose, reflected in the rate of uptake and thus in the A-V difference, that signals hunger and, in turn, satiety through specific hypothalamic neurones (49). There is no doubt that hunger and hypoglycemia frequently occur together and that insulin produces hypoglycemia and increases the food intake (50). There are however, many clinical and experimental situations in which the control of food intake shows no obvious correlation with any parameter of the blood glucose (e.g. 30, 66). Further, rats regulate their food intake well over long periods on a carbohydrate-free diet (fig. 2) and show no, or little, difference at a two-hour meal in the rate or amount of intake of such diet compared to those on a normal high carbohydrate diet (fig. 3). Indeed, the rate and amount of food intake at a three-hour meal are almost identical whether the diet be high (60-70% calories) in carbohydrate or fat (fig. 4). It is interesting that a low protein diet (5.9% of calories), which depresses food intake in man and animal, causes an early satiety as far as the consummatory response is concerned if the animals are accustomed to this particular diet. On the other hand, the hypothalamic hyperphagic rat does not show a hyperphagia on a high protein diet (89) although it can and does increase its intake of this diet when exposed to a cold environment, as does the intact animal (85). This inhibitory effect of a protein diet might be attributed to the high SDA of protein, but why then is there also a decreased intake on a low protein diet?

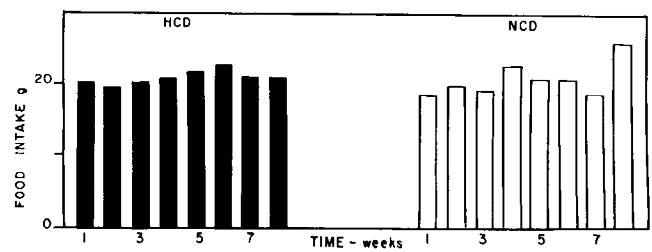

Fig. 2. Average daily food intakes each week over an eight-week period in which one group of six rats was fed a high carbohydrate diet and a second group of six was fed a non-carbohydrate diet, ad libitum.

The effects of environmental temperature on food and water intakes are well known (16) and we have recently found that a high or low environmental temperature even if only for a period of a brief meal will inversely affect the food intake at that meal. These environmental or peripheral effects are paralleled by similar effects of local temperature changes in the preoptic hypothalamus which have been already discussed. Present evidence suggests that it is an integration of information from peripheral, as well as central thermoreceptors that mediates the final influence of temperature on food and water intakes in the healthy animal. Such an integration could provide a measure of the body's insulation, i.e. of the fat stores - a thermolipostatic mechanism. The decrease which some agents cause in food intake has been attributed to their hyperglycemic action, e.g. glucagon (23) and adrenaline (71, 81), but these particular agents also cause an increase in heat production; insulin, which causes an increase in food intake, tends to lower the core and skin temperature as well as the blood sugar (86). Which, if either, of these effects is the critical signal?

The attempt to analyze the signals that affect the hypothalamic and associated regulating systems is not easy. With the present hypotheses, how is one to explain the observation in man and in the rat that irregular bouts of exercise often decrease the food intake on the day of exercise with a compensatory increase one or two days later? We have recently observed that insulin can offset this decrease after exercise (86).

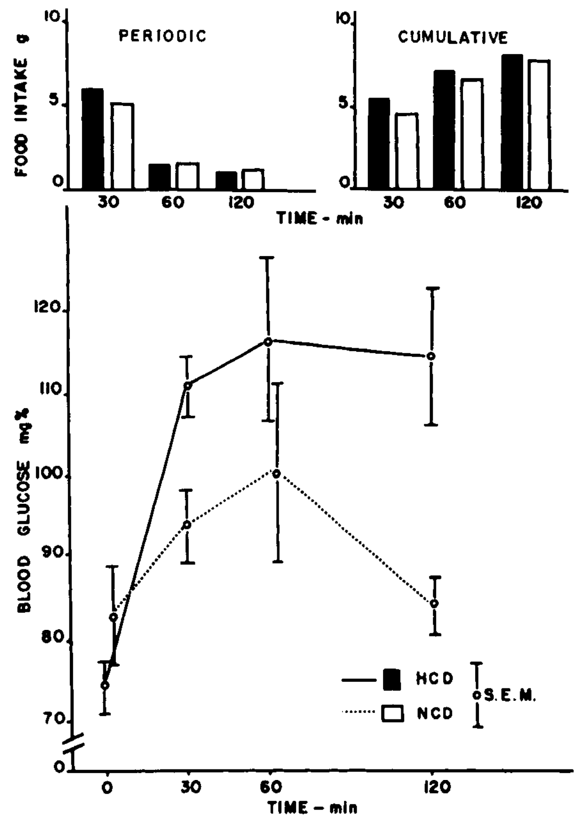

Fig. 3. Periodic and cumulative food intakes of rats for the first two-hour period of ad libitum feeding following a 24-hour fast. The rats had previously been accustomed to the diet on which they were tested. Below are shown the concurrent changes in blood glucose.

The hyperphagia that follows ablation of the ventromedial region has often been attributed to the destruction of a satiety center and while there is much evidence that some inhibitory pathways which subserve satiety are destroyed by this lesion, not all inhibitory systems for feeding run through this region. The sensitivity of hypothalamic hyperphagic rats to aversive qualities of the diet or of the feeding situation has been demonstrated (54, 93). Anorexigenic agents such as amphetamine and phenmetrazine cause an aphagia in hyperphagic obese rats which may persist for some time after the drug is stopped (18, 25, 89, 90). It is possible that the inhibition they produce originates in the frontal lobes

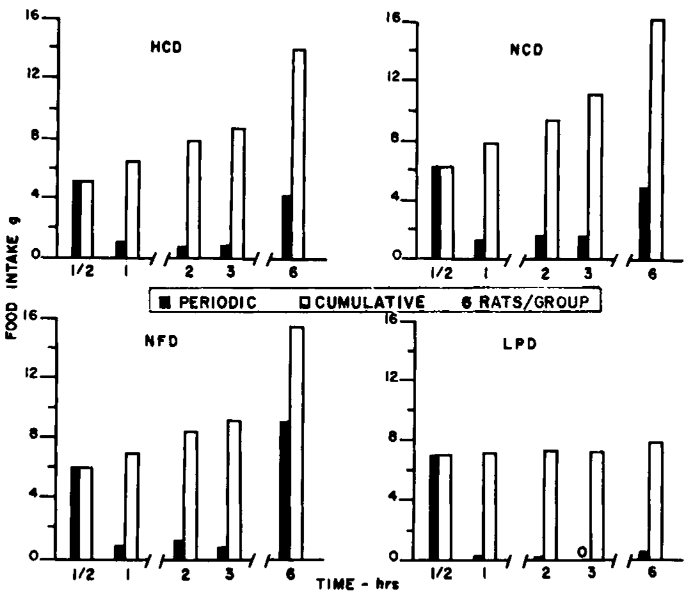

Fig. 4. Periodic and cumulative food intakes for rats on a six-hour feeding regime eating high carbohydrate (HCD), non-carbohydrate (high fat, NCD), low fat (NFD) and low protein (LPD) diets which were all isocaloric.

(13); in any case, the inhibitory system involved is not destroyed by ventromedial ablation. We have recently investigated the effects of another agent in these hyperphagic animals. Chalmers and his colleagues (21) several years ago reported the extraction of a substance from urine of fasting human beings that was similar in its biological activity to the urinary extract from fasting rabbits which Weil and Stetten (98) had found would mobilize fat to the liver. In the intact mouse, the human extract caused transient hypoglycemia, ketonemia, hyperlipemia, and increased mobilization and catabolism of fat, with depletion of fat stores leading to a loss of body weight and, according to these investigators, it did this withour causing any decrease in food intake. Following the extraction procedure of Chalmers and his colleagues, we have obtained a substance from the urine of fasting rats which appears to be similar, on paper chromatography, in amino acid composition and to have the same biological properties as the human extract (88). We have found, however, that, when this material was injected into rats, the reduction in body weight was related to a decrease in food intake, which is easier to measure in the rat than in the mouse (fig. 5). Like the amphetamines, this substance has a much more profound effect on food intake in the hypothalamic hyperphagic than in the normal animal. This substance causes a marked increase in the blood FFA in vivo and in the release of FFA from the rat's epididymal fat pad in vitro. If anything, it reduces oxygen consumption. Upon first examination, these particular observations would fit the lipostatic hypothesis for the control of food intake much more easily than the gluco- or thermostatic hypotheses.

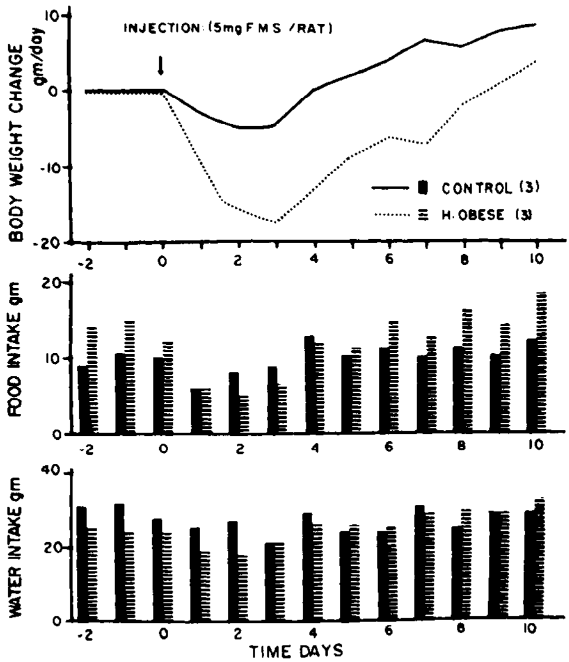

Fig. 5. The effect of one injection (s.c.) of FMS (5mg/rat) on the body weight, food intake and water intake of control and hypothalamic obese female rats. At the time of injection, the control rats weighed an average of 297 gm. and the hypothalamic rats weighed an average of 607 gm.

Further problems arise in explaining the long-term factors that affect food intake. When rats that have had their food intake restricted for a sufficient period during growth are later given food ad libitum, they gain some of the weight they have missed, by over-eating for a short period but then they stabilize at a smaller body size and food intake than the controls that have always eaten ad libitum. The food intake of these animals can be markedly increased by exposure to cold or by administration of insulin but, upon removal of such stimuli. it falls back to its former lower level and these animals do not gain to their normal potential size (86). With insulin, they can be brought to the control weight but this gain is lost when the insulin is stopped (fig. 6). These animals appear to have accepted a new metabolic size, imposed by the previous restriction, and now regulate their food intake in relation to this. What mechanism can explain this regulation? Perhaps a thermo-lipostatic hypothesis may serve, but this is not yet demonstrated.

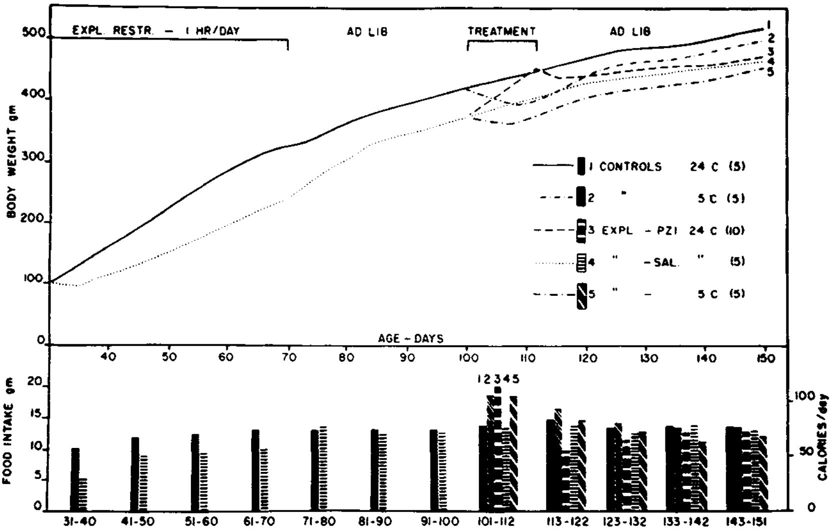

Fig. 6. Body weight curves and average daily food intakes for weanling rats restricted at 30 days of age to a one-hour feeding period per day. At 70 days of age, the rats were allowed to feed ad libitum until 100 days of age at which time the previously restricted group was divided - ten rats received daily injections of protamine zinc insulin, five received daily injections of normal saline, and five were placed in an environment of 5°C along with five of the controls. After 12 days of this treatment all animals were returned to ad libitum feeding at 24°C until the end of the experiment at 150 days of age.

None of the current single-factor hypotheses for the regulation of food intake appears to be adequate alone to explain the apparent variety of controls of food intake (fig. 7). But is this surprising in view of what we now know, particularly from the work of Adolph (2), about the priorities of regulation in the whole animal? Several systems for even the fundamental control of food intake seem appropriate when one considers the several vital aspects of homeostasis which it affects.

The situation with regard to the control of water intake is similar. There is good evidence that osmometric (99), volumetric (77) and thermometric (10) mechanisms are fundamental in this control. Again,

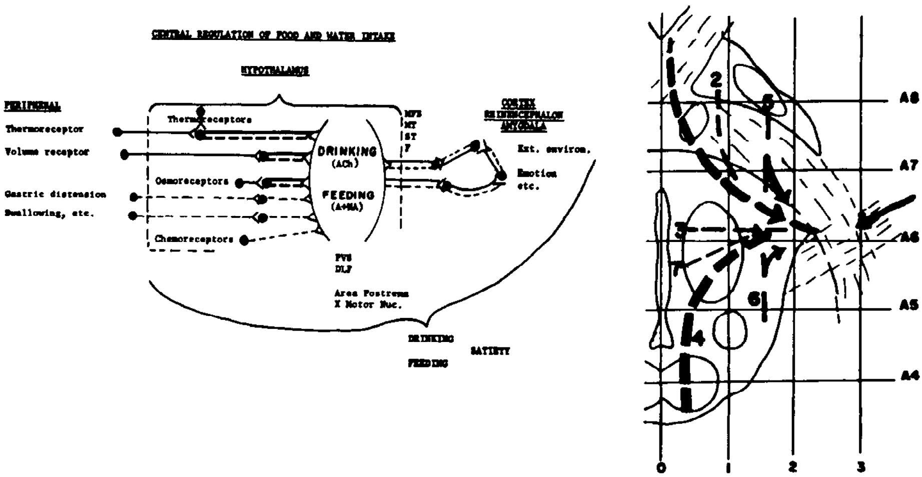

Fig. 7. On the left, a diagramatic working hypothesis of some of the fundamental clues or signals that influence water and food intake. Several of these, such as the temperature, have peripheral as well as central sensors; for others there may be only peripheral or central sensors. Many of the factors in the external environment and the emotional or motivational state of the animal are sensed and integrated through higher systems, particularly the visceral brain-limbic system. There are many association pathways available for transmission of information between the cortical, hypothalamic and lower systems.

The figure on the right demonstrates some of the postulated systems within the hypothalamus involved in the regulation of food and water intake. The grid refers to sterotaxic coordinates 1 mm. apart.

1. Inhibitory and/or facilitatory pathways from the anterior thermoregulatory systems which are activated by thermal stimuli (Andersson) and interfered with by lesions in the anterior (Hamilton and Brobeck; Stevenson) and in the anterior ventromedial (Montemurro and Stevenson) hypothalamus.
2. A pathway inhibitory to water intake from the supraoptic region, perhaps from osmoreceptors as suggested by the observation of Smith and McCann.
3. A possible pathway from chemoreceptors in the ventromedial region.
4. Inhibitory pathways from the gastrointestinal tract, subserving gastric distension, swallowing, etc., and, perhaps, peripheral chemoreceptors.
5. and 6. Motivational systems in the median forebrain bundle (Morgane) and, by an analogy, other association pathways.
7. Some facilitatory pathways for feeding apparently pass through the VM region as suggested by the observations of Miller et al. and of Teitelbaum. These all appear to focus on the fundamental systems for the execution of drinking and feeding behavior in the lateral-far lateral hypothalamus.

several mechanisms would permit the interplay of priorities in the overall regulation. As with food intake the gastrointestinal tract probably provides important immediate cues, which may serve as conditioned stimuli. Dryness of the mouth enhances thirst subjectively, the act of swallowing and gastric distension provide immediate measure of intake (26, 33).

The present discussion has dealt only with some of the fundamental controls of food and water intake which appear to be focused in the hypothalamus. Superimposed on these are the influences of emotion and of the immediate exigencies of the environment. The neurophysiological bases of these secondary influences are now beginning to be revealed. It is apparent, however, that we still have a great deal to learn about both the fundamental and ancillary controls of these intakes.

REFERENCES

1. Adametz, J., and J. L. O'Leary. Neurology 9:636-642, 1959.
2. Adolph, E. F. Physiological Regulations. Lancaster, Pa.: Jaques Cattell Press, 1943, 502p.
3. Anand, B. K. Physiol. Rev. 41:677-708, 1961.
4. Anand, B. K., and J. R. Brobeck. Proc. Soc. Exptl. Biol. Med. 77: 323-324, 1951.
5. Anand, B. K., and J. R. Brobeck. Yale J. Biol. Med. 24: 123-140, 1951.
6. Anand, B. K., and S. Dua. Indian J. Med. Res. 46: 426-430, 1958.
7. Anand, B. K., and S. Dua. Indian J. Med. Res. 43: 113-122, 1955.
8. Anand, B. K., and S. Dua. Indian J. Med. Res. 49: 834-836, 1961.
9. Anand, B. K., S. Dua, and G. S. Chhina. Indian J. Med. Res. 46: 277-287, 1958.
10. Andersson, B., C. C. Gale, and J. W. Sundsten. Acta Physiol. Scand. 55: 177-188, 1962.
11. Andersson, B., and S. M. McCann. Acta Physiol. Scand. 33: 333-346, 1955.
12. Andersson, B., and B. Larsson. Acta Physiol. Scand. 52: 75-89, 1961.
13. Andersson, B., and S. Larsson. Acta Physiol. Scand. 38: 22-30, 1957.
14. Andersson, B., and S. Larsson. Pharmacol. Rev. 13: 1-16, 1961.
15. Baillie, P., and S. D. Morrison. J. Physiol. (London) 165: 227-245, 1963.
16. Brobeck, J. R. Recent Progr. Hormone Res. XVI: 439-466, 1960.
17. Brobeck, J. R. Yale J. Biol. Med. 20: 545-552, 1948.
18. Brobeck, J. R., S. Larsson, and E. Reyes. J. Physiol. (London) 132: 358-364, 1956.
19. Brobeck, J. R., J. Tepperman, and C. N. H. Long. Yale J. Biol. Med. 15: 831-853, 1943.
20. Brooks, C. McC. Am. J. Physiol. 147: 708-716, 1946.
21. Chalmers, T. M., G. L. D. Pawan, and A. Kekwick. Lancet II: 3-12, 1960.
22. Crow, L. T. In: Thirst, edited by M. J. Wayner. Oxford: Pergamon Press, 1964, pp. 473-486.
23. Davidson, I. W. F., J. M. Salter, and C. H. Best. Am. J. Clin.

Nutr. 8: 540-546, 1960.
24. Delgado, J. M. R., and B. K. Anand. Am. J. Physiol. 172: 162-168, 1953.
25. Epstein, A. N. J. Comp. Physiol. Psychol. 52: 37-45, 1959.
26. Epstein, A. N. Science 131: 497-498, 1960.
27. Epstein, A. N., and P. Teitelbaum. Science 132: 1491, 1960.
28. Epstein, A. N., and P. Teitelbaum. In: Thirst, edited by M. J. Wayner. Oxford: Pergamon Press, 1964, pp. 395-410.
29. Fisher, A. E., and J. N. Coury. Science 138: 691-693, 1962.
30. Fryer, J. H. Am. J. Clin. Nutr. 6: 354-364, 1958.
31. Green, J. D., C. D. Clemente, and J. de Groot. J. Comp. Neurol. 108: 505-545, 1957.
32. Greer, M. A. Proc. Soc. Exptl. Biol. Med. 89: 59-62, 1955.
33. Gregersen, M. I., and L. J. Cizek. In: Medical Physiology, edited by P. Bard. 11th ed. St. Louis: C. V. Mosby, 1961, Ch. 17, pp. 317-331.
34. Grossman, M.I., and I. F. Stein. J. Appl. Physiol. 1: 263-269, 1948.
35. Grossman, S. P. Science 132: 301-302, 1960.
36. Grossman, S. P. Am. J. Physiol. 202: 1230-1236, 1962.
37. Grossman, S. P. In: Thirst, edited by M. J. Wayner. Oxford: Pergamon Press, 1964, pp. 487-514.
38. Hamilton, C. L., and J. R. Brobeck. Am. J. Physiol. 203: 383-384, 1962.
39. Hess, W. R., and M. Von Brugger. Helv. Physiol. Acta. 1: 33-52, 1943.
40. Hoebel, B. G., and P. Teitelbaum. Science 135: 375-377, 1962.
41. Iggo, A. J. Physiol. (London) 128: 593-607, 1955.
42. Iggo, A. J. Physiol. (London) 131: 248-256, 1956.
43. Keller, A. D., D. M. Witt, and H. L. Batsel. Federation Proc. 18: 80, 1959.
44. Kennedy, G. C. Colloquia on Endocrinology (Ciba) Vol. 4, edited by G. E. W. Wolstenholme. London: J.& A.Churchill, 1952, pp. 203-212.
45. Kennedy, G. C. Proc. Roy. Soc. Biol. B140: 578-596, 1953.
46. Koikegami, H., S. Fuse, S. Hiroki, T. Kazami, and Y. Kageyama. Folia Psychiat. Neurol. Japon. 12: 207-223, 1958.
47. Larsson, S. Acta Physiol. Scand. 32: 1-40, 1954.
48. Maire, F. W. Federation Proc. 15: 124, 1956.
49. Mayer, J. Physiol. Rev. 33: 472-508, 1953.
50. Mayer, J. Nutritional Abstracts and Reviews. 25: Pt.1, 597-611; Pt. 2, 871-883, 1955.
51. Mayer, J. Am. J. Clin. Nutr. 8: 547-561, 1960.
52. Mellinkoff, S. M. Ann. Rev. Physiol. 19: 193-204, 1957.
53. Miller, F. R. Pfluger Arch. 143: 1-20, 1911.
54. Miller, N. E., C. J. Bailey, and J. A. F. Stevenson. Science 112: 256-259, 1950.
55. Montemurro, D. G., and J. A. F. Stevenson. Can. J. Biochem. Physiol. 35: 31-37, 1957.
56. Montemurro, D. G., and J. A. F. Stevenson. Yale J. Biol. Med. 28: 396-403, 1955-56.
57. Morgane, P. J. Am. J. Physiol. 201: 838-844, 1961.
58. Morgane, P. J. Anat. Record 139: 257, 1961.

59. Morgane, P. J., and A. J. Kosman. Federation Proc. 16: 90, 1957.
60. Morgane, P. J., and A. J. Kosman. Nature 180: 598-600, 1957.
61. Morgane, P. J., and A. J. Kosman. Am. J. Physiol. 197: 158-162, 1959.
62. Morgane, P. J., and A. J. Kosman. Am. J. Physiol. 198: 1315-1318, 1960.
63. Nielson, H. C., R. W. Doty, and L. T. Rutledge. Am. J. Physiol. 194: 427-432, 1958.
64. Olds, J. Science 127: 315-324, 1958.
65. Paintal, A. S. J. Physiol. (London) 126: 255-270, 1954.
66. Penick, S. B., and L. E. Hinkle. Am. J. Clin. Nutr. 13: 110-114, 1963.
67. Robinson, B. W. In: Thirst, edited by M. J. Wayner. Oxford: Pergamon Press, 1964, pp. 411-427.
68. Robinson, B. W., and M. Mishkin. Science 136: 260-262, 1962.
69. Robinson, B. W., and M. Mishkin. XXII Intern. Congr. Physiol. Sci., Leiden, 1962. Abst. 362.
70. Ruch, T. C., F. W. Maire, and H. D. Patton. XX Intern. Congr. Physiol. Sci., Brussels, 788-789, 1956.
71. Russek, M., and S. Pina. Nature 193: 1296, 1962.
72. Scherrer, H. Exptl. Neurol. 2: 97-108, 1960.
73. Shapiro, B., and E. Wertheimer. Metabolism 5: 79-86, 1956.
74. Sharma, K. N., and S. Dua. The Physiologist 6: 273, 1963.
75. Skultety, F. M., and T. M. Gary. Neurology 12: 394-401, 1962.
76. Slusher, M. A., and S. Roberts. Federation Proc. 15: 173, 1956.
77. Smith, H. W. Am. J. Med. 23: 623-652, 1957.
78. Smith, O. A. Anat. Record 124: 363-364, 1956.
79. Smith, O. A. In: Electrical Stimulation of the Brain, edited by D. E. Sheer. Austin, Texas: Univ. of Texas Press, 1961, pp. 367-370.
80. Smith, R. W., and S. McCann. Am. J. Physiol. 203: 366-370, 1962.
81. Soulairac, A. Bull. Biol. Franc. Belg. 81: 273-432, 1947.
82. Sprague, J. M., W. W. Chambers, and E. Stellar. Science 133: 165-173, 1961.
83. Stevenson, J. A. F. Recent Progr. Hormone Res. 4: 363-394, 1949.
84. Stevenson, J. A. F. XXII Intern. Congr. Physiol. Sci., Leiden, 1962, vol. 2, Abst. 359.
85. Stevenson, J. A. F. In: Thirst, edited by M. J. Wayner. Oxford: Pergamon Press, 1964, pp. 553-567.
86. Stevenson, J. A. F. Unpublished observations, 1963.
87. Stevenson, J. A. F., B. M. Box, and D. G. Montemurro. Can. J. Physiol. Pharmacol. 1964. In press.
88. Stevenson, J. A. F., B. M. Box, and A. Szlavko. Proc. Soc. Exptl. Biol. Med. 115: 424-429, 1964.
89. Stevenson, J. A. F., D. G. Montemurro, and L. L. Bernardis. Federation Proc. 17: 156, 1958.
90. Stowe, F. R. Jr., and A. T. Miller, Jr. Experientia 13: 114-115, 1957.
91. Sudakov, K. V., and S. K. Rogacheva. Fiziol. Zh. SSSR Sechenov. 48: 728, 1962. Federation Proc. 22: T306-T310, 1963. No. 2, Pt. II.
92. Sundsten, J. W., and C. H. Sawyer. Federation Proc. 19: 293, 1960.
93. Teitelbaum, P. J. Comp. Physiol. Psychol. 48: 156-163, 1955.
94. Titchen, D. A. J. Physiol. (London) 125: 25P, 1954.
95. Traczyk, W. Acta Physiol. Polon. 13: 239-251, 1962.

96. Van Itallie, T. B. Diabetes 8: 226-231, 1959.
97. Wagner, J., L. Grunden, K. Conrey, W. Mahler, and J. de Groot. Federation Proc. 21: 173, 1962.
98. Weil, R., and de W. Stetten, Jr. J. Biol. Chem. 168: 129-132, 1947.
99. Wolf, A. F. Am. J. Physiol. 161: 75, 1950.
100. Wood, C. D. Neurology 8: 215-220, 1958.
101. Wyrwicka, W., C. Dobrzecka, and R. Tarnecki. Acta Biol. Exptl. 20: 121-136, 1960.

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REGULATION OF PULMONARY VENTILATION*

FRED S. GRODINS

When Dr. Rahn invited me to give this introductory talk, I accepted only because he stated that its purpose was "to bring the non-specialist up to date and make it easier for him to obtain an over-all or more general view of present research trends in the area of control of respiration." This prescription seemed to exactly fit my own needs in this area, and I hope my efforts to educate myself will assist those of you who feel a similar need.

Ever since Legallois (28) discovered a medullary respiratory center in 1812, its responses to various neural and chemical inputs have been studied. Since it was known from the time of Lavoisier that the primary function of respiration was O_2 procurement and CO_2 elimination, it was natural to begin the study of chemical agents with these. It also seemed natural to assume that the effective concentrations of these agents resided in the arterial blood which supplied the center. Controversy is nothing new in this field! In 1882, Rosenthal (46) using only narcotic levels of CO_2 in his experiments, decided that O_2, not CO_2, was the important agent. Miesscher-Rüsch (36), in 1885, using more moderate concentrations of CO_2 and O_2 in man, made the opposite choice.

Miesscher-Rüsch's early decision in favor of CO_2 was adopted and greatly extended by Haldane and his school beginning in 1905. Haldane developed methods for measuring alveolar pCO_2 and was impressed both by its constancy under various conditions as well as by the great sensitivity of ventilation to inspired CO_2. In 1905, he stated that under "normal conditions", the rate of alveolar ventilation depended exclusively upon the pCO_2 of the respiratory center (16). Although his "normal conditions" included muscular exercise they excluded arterial anoxemia. Haldane knew of course that ventilation was increased by arterial anoxemia, but he preferred to regard this as an "abnormal stimulus" to the center. This was the beginning of a trend on the part of various respiratory physiologists to pick out a single factor as the "normal" or "true" stimulus to the respiratory center and to assign all others a secondary role in modifying the response to this true stimulus. At that time, respiratory disturbances in acid-base balance were not understood, and it was believed that the low blood CO_2 content associated with anoxemia was due to a metabolic acidosis resulting from lactic acid production. Since it was also known that fixed acid injection caused hyperpnea, Haldane modified his views somewhat and wrote in 1908 that the activity of the respiratory center depended upon the total acidity of the blood including carbonic acid, and that increased

*Taken from the introductory remarks given at the session on Regulation of Respiration at the 1964 Federation Meetings.

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blood acidity caused anoxic hyperpnea (3, 17). He still insisted, however, that ventilation was always determined by alveolar pCO_2 although oxygen lack and other conditions might alter its threshold exciting value (17).

In 1911, consistent with the then current belief that anoxemia was associated with acidemia, Winterstein (49) proposed his "first reaction theory". He stated that "neither pO_2 nor pCO_2 as such but only the (H^+) of the blood influences the chemical regulation of breathing.... This theory places the whole chemical regulation of breathing (O_2 lack as well as CO_2 excess and deficit) upon a single unitary cause." It is worth noting that Winterstein fully appreciated and eloquently stated the fallacy of arbitrarily choosing a "true" stimulus (49, 50). Although perhaps superficially resembling this, his proposal was really quite different in concept, i.e., it suggested a common chemical path through which each of the different chemical stimuli could operate.

But shortly thereafter another fallacy, that of anoxic acidemia, was revealed by Winterstein himself (50) Haggard and Henderson (15) and others. It turned out that arterial (H^+) was low, not high, in arterial anoxemia! Winterstein's resourcefulness was equal to the challenge, however, for in 1921 he proposed his second reaction theory which retained the importance of (H^+) but now placed its effective concentration inside the cells of the respiratory center and thus beyond measurement (51). This concept was adopted and extended by Gesell in 1925 (10). Then, in the early 1930's, the necessity for postulating an increased (H^+) either in the blood or inside the cells of the respiratory center to explain anoxic hyperpnea was removed when Heymans demonstrated the role of the carotid and aortic chemoceptors (19).

A new period began in 1936 when Nielsen (40) published a monumental study on the chemical regulation of human respiration which aimed, among other things, to decide whether the "true" stimulus to the center was CO_2, as postulated by Haldane, or (H^+) as postulated by Winterstein and Gesell. His conclusion in favor of CO_2 was based on a decision process so strange that it deserves careful description. Nielsen adopted Lindhard's method of measuring the excitability of the respiratory center (32), an apparently innocent procedure illustrated in fig. 1. Under a particular condition (say NH_4Cl acidosis), we measure the subject's ventilation and alveolar pCO_2 when breathing air (point B), and when breathing a CO_2 mixture (point C). We then define the excitability of the center as the slope, not of the line ABC, but rather of the transformed line, OP, in the right hand plot where the axes are now $(\Delta R/R)$ and ΔV. Even this looks innocent enough until we ask what the numerical value of this slope turns out to be. It doesn't take much of a trigonometer to realize that the ventilation at B (i.e. the "initial value" or "Ausgangsversuch") is equal to $R\tan\theta = R\left(\frac{\Delta V}{\Delta R}\right)$, the same as the slope of OP and thus the excitability of the center! We arrive at the remarkable result that the excitability of the center under any condition other than CO_2 inhalation is simply the value of the ventilation! Having defined excitability in this way, we really don't need to do any more experiments or go to the trouble of determining these CO_2 response curves at all, for it is inevitable that anything other than CO_2 inhalation which increases ventilation can only do so by increasing the excitability of the center. Nielsen decided that because a given (H^+) produced less hyperpnea in NH_4Cl acidosis than in CO_2 inhalation despite an increased excitability of the center in the former, H^+ could not be regarded as the adequate chemical stimulus to breathing and this role must be assigned to CO_2.

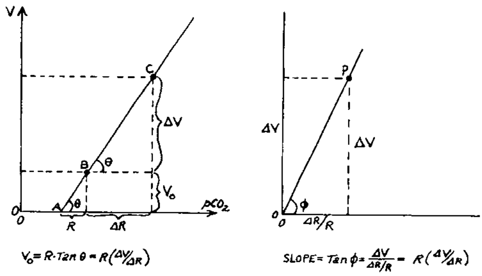

Fig. 1. Lindhard-Nielsen method for measuring the excitability of the respiratory center.

It turned out that this misadventure in definitions had a happy result - it stimulated my colleague, John Gray, to develop his multiple factor theory of respiratory regulation (11), a contribution which has greatly influenced research in this field ever since. This theory had three important features. First, it was quantitative in concept with rigorous definitions and explicitly stated assumptions. Second, it refused to concern itself either with non-measurable hypothetical intracellular mechanisms or with the fruitless subjective game of choosing a single true stimulus from several equally qualified candidates. Instead, like the early German school of Zuntz, it accepted the obvious common sense notion that many different chemical stimuli were carried to central or peripheral receptors by the arterial blood, and that the resulting ventilation was a function of all of them. By restricting itself to steady state conditions, it could measure the effective concentrations of these stimuli in arterial blood without having to worry about the nature of any ultimate but as yet unmeasurable intracellular mechanism. Finally, it recognized that the respiratory system was a closed-loop regulator (fig. 2) in which not only did the chemical stimuli determine the level of ventilation through the controlling system, but the level of ventilation determined the concentration of the chemical agents via the controlled system, and that these concentrations were interdependent (fig. 3).

Gray first tried to obtain a controller equation restricted to two independent variables, arterial pCO_2 and (H^+), which would work for both CO_2 inhalation and metabolic disturbances in acid-base balance. He started with the simplest guess, namely that the effects of pCO_2 and (H^+) were independent and additive. There was nothing sacred about this guess. It was retained only because it turned out to work! Since its

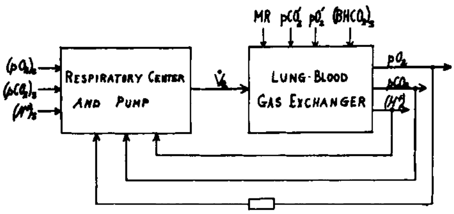

Fig. 2. The closed-loop respiratory chemostat. (From Grodins and James. Ann. N.Y. Acad. Sci. 109: 852-68, 1963).

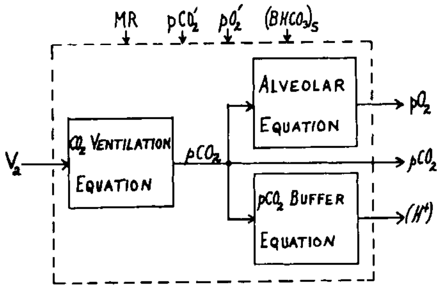

Fig. 3. The interdependence of the arterial chemical agents.

validity was supported by two different conditions in which the pattern of pCO_2 - (H^+) behavior was quite different, faith in its generality was strengthened, and this encouraged Gray to extend it to include arterial anoxemia. This extension was done in such a way that it could not fail to work whether the assumption of independence and additivity were valid or not provided its application was restricted to arterial anoxemia alone, i.e. to the same data on which its derivation was based. An independent test of its general validity would have required data on combinations of anoxemia and CO_2 inhalation or metabolic disturbances in acid-base balance, but such data were not available. This then was the weakest point of the theory.

This brings us to what we might call the present era. We shall only have time to look very briefly at some selected highlights, and I apologize in advance for the unavoidable omission of other equally important contributions. The current research trends we shall consider can be classified under four major headings:

1. Interaction between stimuli and the quantitative approach.

2. Mechanism of central sensitivity - the CSF and intracranial receptors.

3. Dynamic models of respiratory regulation.

4. The hyperpnea of exercise.

Interaction between stimuli. Gray's best tested assumption, i.e. that the pCO_2 and (H^+) effects were independent and additive, appears to have been validated by several workers including Perkins (43), Katsaros (24), Lambertsen (26), and Saito (47), although there seems to be a dissenting note scheduled for presentation here this afternoon (18). On the contrary, his essentially untested assumption that the pO_2 effect was also independent and additive has been consistently denied, first by Nielsen and Smith in 1951 (41) and subsequently by Lloyd and Cunningham (33) and by Loeschcke (35). The crucial data of Nielsen and Smith are shown in fig. 4. If Gray's assumption were valid, the three lines should have been straight and nearly parallel. Cunningham's group (33) confirmed and extended these results and chose to represent the linear portion of such curves as a family of straight lines whose slope parameter was a hyperbolic function of alveolar pO_2 as shown in fig. 5. They then formulated the general problem of respiratory regulation as one of determining the effect of various agents upon the four parameters, A, B, C, and D. This they have proceeded to do over the past several years testing among other things, acidemia, hyperthermia, and norepinephrine. In so doing they have recognized the general importance of a quantitative mathematical approach to complex control problems, but it should be clear that their particular representation is a purely arbitrary one which refuses to break the seal of Pandora's Black Box!

This might be the place for a word of caution about conclusions based on the slope of the so-called CO_2 response curve. Cunningham thought that if pO_2 were an independent and additive stimulus, Gray's theory required these curves at different constant levels of pO_2 to be parallel, but you will note that we said "nearly parallel". Why the difference? The CO_2 response curve is a composite response to pCO_2 and (H^+), and anything that changes the relationship between these two variables through the blood buffer systems will alter the curve. A reduction in O_2 saturation increases the buffer capacity for CO_2 so that a given change in pCO_2 would produce less change in (H^+). Hence Gray's theory really predicts that the slope of the CO_2 response curve should decrease at low pO_2, and thus the discrepancy between theory and observation was even greater than Cunningham thought it was. He was lucky - it might have turned out the other way! I think the moral is obvious - do not neglect the composite nature of the CO_2 response curve.

Mechanism of central sensitivity. Interest in the intimate mechanisms by which changes in arterial pCO_2 and (H^+) ultimately effect the respiratory center received new impetus in the early 1950's when Leusen (29, 30) showed that an increased (H^+) in CSF perfusing the cerebral ventricles stimulated ventilation. It was first believed that this effect was exerted directly upon the respiratory center. However, Loeschcke (34) showed

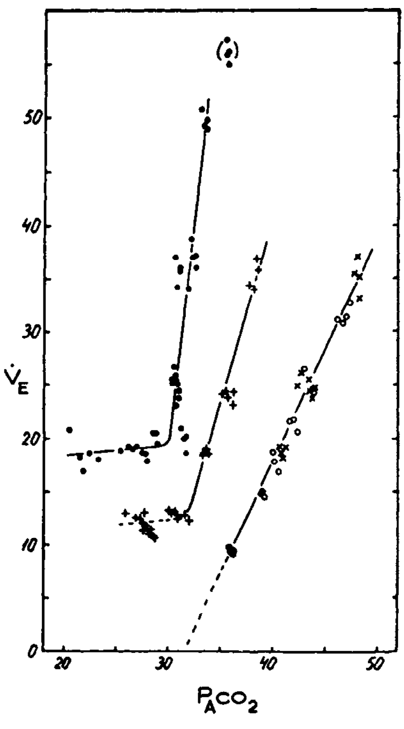

Fig. 4. Ventilation as a function of alveolar pCO_2 at three different alveolar pO_2 values: (X), pO_2=169; (O), pO_2=110; (+), pO_2=47; (.), pO_2=37. (From Nielsen and Smith. Acta Physiol. Scand. 24:293-313, 1951).

that local application of acid to the floor of the fourth ventricle failed to stimulate breathing, and he postulated the existence of a chemosensitive area outside the centers which was bathed in CSF. Extending this work, Mitchell (38) and coworkers identified paired chemosensitive areas on the ventrolateral surface of the medulla in the cat (fig. 6). They are bounded medially by the pyramidal tracts, laterally by the roots of the 8th-11th cranial nerves, rostrally by the pons and extend some 5-6 mm caudally. Local application of pledgets containing CSF equilibrated with high pCO_2 and (H^+) or containing nicotine or acetyl choline produced prompt hyperpnea, whereas local cooling or procaine

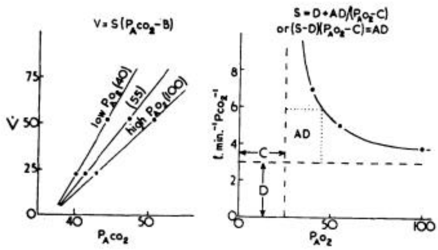

Fig. 5. Dependence of the slope of the CO_2 response curve on alveolar pO_2. (From Lloyd and Cunningham. Regulation of Human Respiration. Oxford: Blackwell, 1963, pp. 331-349).

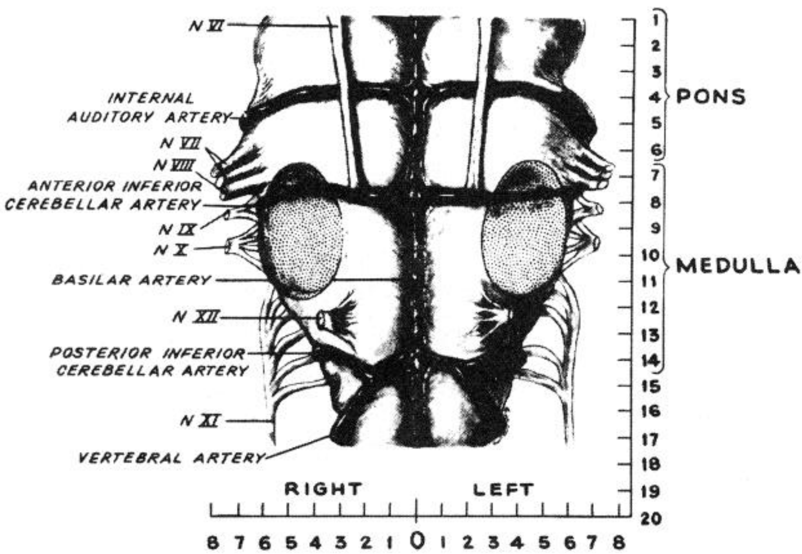

Fig. 6. Location of the medullary chemoreceptors. (From Mitchell, Loeschcke, Severinghaus, Richardson, and Massion. Ann. N.Y. Acad. Sci. 109(2): 661-81, 1963).

application depressed respiration usually to the point of apnea. Similar responses were produced by perfusing the solutions into the subarachnoid space over the ventrolateral surfaces of the medulla. Because proportionate increases in pCO_2 and (HCO_3^-), (i.e. constant (H^+) perfusion), depressed ventilation, these workers believed this sensitive area to be an H^+ receptor. However, since the blood-brain barrier is freely permeable to CO_2 but not to H^+ or HCO_3, acute changes in CSF (H^+) are mainly a reflection of changes in blood pCO_2, and the authors postulated that all medullary CO_2 sensitivity was mediated via these CSF H^+ receptors on the ventrolateral surfaces of the medulla. Thus, just as Heymans showed in the early 1930's that the respiratory response to pO_2 was mediated via "distant" peripheral receptors in the carotid and aortic bodies, it now appears that Loeschke has demonstrated that the response to pCO_2 is mediated via "close", but still peripheral, receptors bathed in CSF.

It is not at all clear to me just what role these investigators assign their receptor in acute metabolic disturbances in acid-base balance. Here several authors have shown that CSF (H^+) changes only very slowly and then in a direction opposite to that of blood (H^+)(5, 31, 45). Do both blood and CSF somehow compete for the attentions of this single receptor, or are there two receptors, one responding to CSF (H^+) and the other to blood (H^+) as suggested by Lambertsen (27)? Some such explanation seems necessary.

Dynamic models of respiratory regulation. Gray's theory was limited to the steady state. As such, it could ignore the ultimate mechanism by which changes in arterial pCO_2, (H^+), and pO_2 influenced ventilation, merely assuming that the arterial concentrations of these agents have a constant relationship to the effective levels of the actual stimuli at the receptor sites whatever and wherever these might be. We hope ultimately to be able to treat such steady state behavior as a special case of a more general dynamic analysis. Such an analysis is very difficult. It requires all of the information needed for a steady state analysis and much more besides. Some 10 years ago when we were considerably more rash and ignorant than we are now, we suggested such a model to explain some peculiar features of the transient response to CO_2 inhalation (14). Although this model ignored many more details than it included, it did assign the effective pCO_2 to the tissues of the respiratory center and was surprisingly successful in accounting for much of the observed behavior. In the last few years, this very crude model has been refined and extended by several workers (6, 20, 37). In general, these models include many of the details neglected in our earlier one. Among these are other stimuli (H^+ and pO_2), "unlumping" of the tissue reservoir, dependence of cerebral blood flow on arterial pCO_2, blood transport lags to and from various receptor sites, the blood-brain barrier, and others. It is obvious that our understanding of respiratory regulation must ultimately be expressed in this form. It is equally obvious that we still have a long way to go, but mutual feedback between models of this sort and experimental results should speed the journey.

The hyperpnea of exercise. Last but far from least we come to the hyperpnea of exercise. I think Carl Schmidt stated the case precisely in his introductory remarks to a New York Academy symposium two years ago (48) when he said that the real test of any concept of respiratory control is its ability to explain the hyperpnea of exercise. Despite 100 odd years of effort, I'm not sure we can pass this test yet!

Let us begin with Haldane's view cast in modern control terminology as our point of departure (fig. 7). If we increase MR_{CO2} without changing ventilation, arterial pCO_2 must rise. This in turn would stimulate ventilation and the final steady state operating point at any given MR_{CO2} would be determined by simultaneous solution of the controller and process equations. Because this is a proportional controller (i.e. its responce depends only on the present level of the input and not at all on its past history), there will be some steady state increase or "error" in pCO_2 whose magnitude will vary inversely with controller gain. This is a very attractive explanation. It is simple, requires no exotic stimuli, and provides an automatic adjustment of ventilation to metabolism. True, the adjustment would fall short of perfection to the extent that the controller gain fell short of infinity, but a reasonably sensitive controller would provide a very satisfactory behavior.

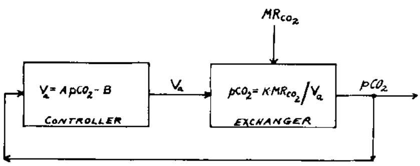

Fig. 7. Closed-loop arterial pCO_2 regulator.

Unfortunately it has turned out that if we judge controller gain by its response to CO_2 inhalation at rest, then the error observed in moderate exercise is nowhere near enough to account for the ventilation (12). The apparent failure of this admirably simple explanation has launched a vigorous search for others.

For a long time such studies moved along lines outlined by Geppert and Zuntz (9) in 1888. If there are other stimuli, they must influence the center via neural and/or humoral paths. If neural, they may originate centrally (e.g. the "cortical radiation" of Krogh (25), or peripherally in the exercising limbs (e.g. in kineceptors, chemoceptors, thermoceptors, 'ergoceptors', 'X-ceptors'). If humoral, they most likely originate in the exercising muscles. Many attempts to explore these possibilities have been made in both animals and man using electrically induced exercise, vascular occlusion, denervation, and cross circulation procedures among others. Investigators most closely involved in such studies include Krogh and Lindhard (25), Asmussen and Nielsen (2, 42), Comroe and Schmidt (4), Kao (21-23), Dejours (7, 8) and others. Despite many errors in interpretation, certain conclusions seemed justified from these studies: 1) A neural factor must be responsible for the initial increase in ventilation simply because it occurs so rapidly, i.e., well within the shortest relevant circulatory dead time (8) (fig. 8); 2) A neural factor must operate in the steady state for its abrupt disappearance is the only way to account for the very rapid fall in ventilation when exercise is stopped (8) (fig. 8); 3) At least part of the steady state neural factor must arise peripherally for cross circulation studies show that a center communicating with an exercising limb only via the blood produces less ventilation than one which has both humoral and neural communication channels intact (21-23); 4) Granting the existence of a peripheral neural stimulus, it might arise in kineceptors (4, 7, 8) or hypothetical 'ergoceptors' (22), but apparently not in thermoceptors (39).

Thus it seemed rather well established that the hyperpnea of exercise depended upon both neural and humoral factors (8). The former certainly had a peripheral component and perhaps a central one as well, while the latter represented the combined effect of all changes in pCO_2, (H^+), pO_2,

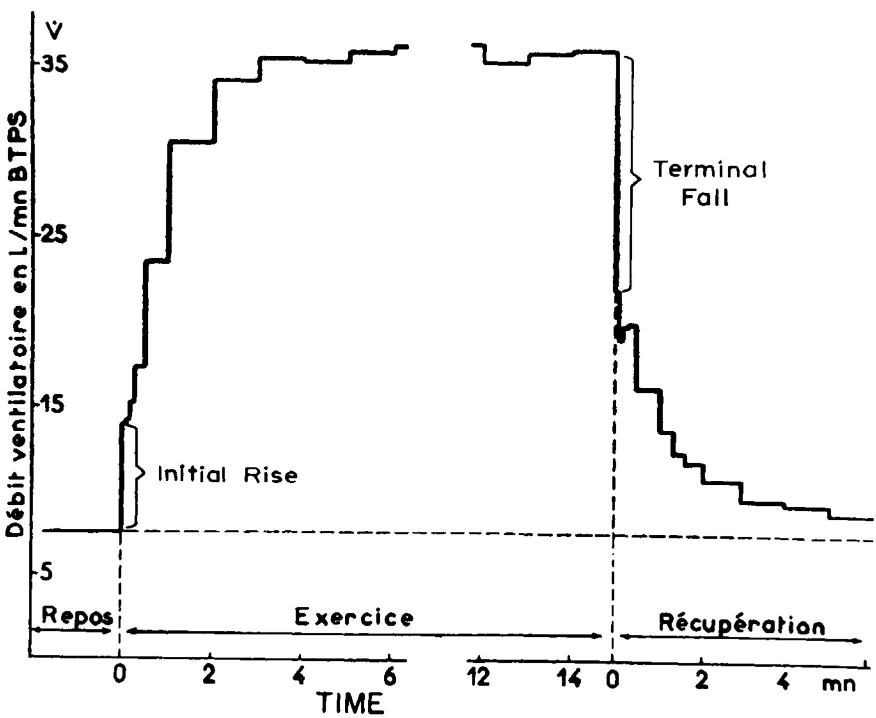

Fig. 8. Time course of ventilatory response to exercise. (From Dejours. J. Physiol. (Paris). 51:163-261, 1959).

temperature, epinephrine, etc. which, although individually small, seemed to be collectively significant. And of course we must always remember that the basic pCO_2 feedback path is eternally vigilant and will provide corrective action or fine adjustment if the combined effect of the other stimuli should miss the mark.

But even though it may turn out to be perfectly correct, the notion that the very accurate adjustment of ventilation to metabolism depends upon a large number of factors which just happen to add up right makes some physiologists feel uneasy! Hence, the search for alternatives has continued, and we shall briefly mention two recent suggestions. One, associated with the names of Armstrong (1) and Riley (44) postulates a mixed venous chemoceptor. Unfortunately, no one has yet been able to conclusively demonstrate its existence, and Kao's cross circulation experiments would seem to deny its importance (22, 23).

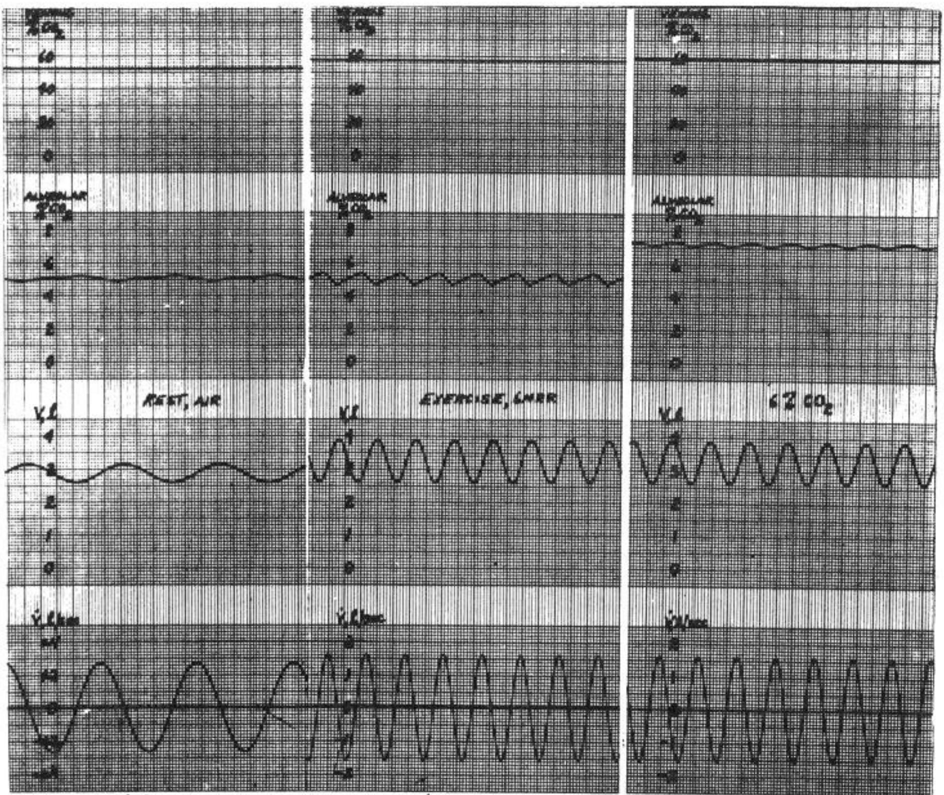

Fig. 9. Theoretical dynamic behavior of alveolar pCO_2 at rest, during exercise, and during CO2 inhalation. (From Grodins and James. Ann. N.Y. Acad. Sci. 109:852-68, 1963).

A completely new and intriguing possibility has been suggested by Yamamoto (52). Its essence is that we may be wrong in judging the pCO_2 gain of the center in exercise by its response to CO_2 inhalation at rest. Yamamoto pointed out that the dyanmic behavior of alveolar pCO_2 is much different in exercise than at rest or during CO_2 inhalation (fig. 9) and that such dynamic information might provide the signal responsible for exercise hyperpnea. Perhaps the most disturbing thing of all about this suggestion was that it was made to account for a crucial experimental observation by Yamamoto and Edwards (53). They had found that if the systemic venous blood of rats were artificially loaded with CO_2, steady state ventilation responded exactly in proportion to the load, just as in normal moderate exercise. This finding directly contradicts the results of a variety of denervation (13) and cross circulation (21-23) experiments. Its implications are so important that I would assign highest priority to resolving this apparent conflict at the observational level.

And so we come to the end of our brief account of past history and current trends in research on the regulation of breathing. Although it is probably safe to say that we know more about it now than we did 100 years ago, it is also true that many of the old problems remain unsolved and new ones constantly arise. There is a lot to be done and we had best get at it.

REFERENCES

1. Armstrong, B. W., H. H. Hurt, R. W. Blide, and J. M. Workman. The humoral regulation of breathing. Science 133:1897-1906, 1961.
2. Asmussen, E., E. H. Christensen, and M. Nielsen. Humoral or nervous control of respiration during muscular work? Acta Physiol. Scand. 6:160-167, 1943.
3. Boycott, A. E., and J. S. Haldane. The effects of low atmospheric pressure on respiration. J. Physiol. (London) 37:355-77, 1908.
4. Comroe, J. H., Jr., and C. F. Schmidt. Reflexes from the limbs as a factor in the hyperpnea of muscular exercise. Am. J. Physiol. 138:536-47, 1943.
5. De Bersaques, J., and I. Leusen. Acid-base equilibrium between blood and cerebrospinal fluid. J. Physiol. (London) 126:14P, 1954.
6. Defares, J. G., H. E. Derksen, and J. W. Duyff. Cerebral blood flow in the regulation of respiration. Acta Physiol. Pharmacol. Neerl. 9:327-360, 1960.
7. Dejours, P. La regulation de la ventilation au cours de l'exercise musculaire chez l'homme. J. Physiol. (Paris) 51:163-261, 1959.
8. Dejours, P. The regulation of breathing during muscular exercise in man. A neuro-humoral theory. In: The Regulation of Human Respiration, edited by D. J. C. Cunningham and B. B. Lloyd. Oxford: Blackwell, 1963, pp. 535-47.
9. Geppert, J., and N. Zuntz. Uber die Regulation der Athmung. Arch. Ges. Physiol. 42:189, 1888.
10. Gesell, R. The chemical regulation of respiration. Physiol. Rev. 5:551-595, 1925.
11. Gray, J. S. The multiple factor theory of respiratory regulation. AAFSAM Project Report No. 386 (1, 2, 3), 1945.

12. Grodins, F. S. Analysis of factors concerned in the regulation of breathing in exercise. Physiol. Rev. 30:220-39, 1950.
13. Grodins, F. S., and D. P. Morgan. Regulation of breathing during electrically induced muscular work in anesthetized dogs following transection of spinal cord. Am. J. Physiol. 162:64-73, 1950.
14. Grodins, F. S., J. S. Gray, K. R. Schroeder, A. L. Norins, and R. W. Jones. Respiratory responses to CO_2 inhalation. A theoretical study of a non-linear biological regulator. J. Appl. Physiol. 7:283-308, 1954.
15. Haggard, H. W., and Y. Henderson. Hemato-respiratory function. III. The fallacy of asphyxial acidosis. J. Biol. Chem. 43:3-13, 1920.
16. Haldane, J. S., and J. G. Priestly. The regulation of the lung ventilation. J. Physiol. (London) 32:225-266, 1905.
17. Haldane, J. S., and E. P. Poulton. The effects of want of oxygen on respiration. J. Physiol. (London) 37:390-407, 1908.
18. Hamilton, R. W., Jr., and E. B. Brown, Jr. Variations in respiratory response to CO_2 at different constant levels of blood pH. Federation Proc. 23:259, 1964.
19. Heymans, C., J. J. Bouckaert, and P. Regniers. Les sinus carotiden. Paris: G. Doin & Cie, 1933.
20. Horgan, J. D., and R. L. Lange. Simulation of the chemical and circulatory factors in the dynamic analysis of the human respiratory control system. Digest 15th Ann. Conf. on Engineering in Med. and Biol., Nov. 1962, p. 53.
21. Kao, F. F., and F. S. Grodins. Regulation of breathing during exercise. Federation Proc. 11:80, 1952.
22. Kao, F. F. An experimental study of the pathways involved in exercise hyperpnea employing cross-circulation techniques. In: The Regulation of Human Respiration, edited by D. J. C. Cunningham and B. B. Lloyd. Oxford: Blackwell, 1963, pp. 461-502.
23. Kao, F. F., C. C. Michel, S. S. Mei, and W. K. Li. Somatic afferent influence on respiration. Ann. N.Y. Acad. Sci. 109(2): 696-710, 1963.
24. Katsaros, B., H. H. Loeschcke, D. Lerche, H. Schönthal, and N. Hahn. Wirkung der Bicarbonat-Alkalose auf die Lungenbelüftung beim Menchen. Bestimmung der Teilwirkungen con pH und CO_2 - Druck auf die Ventilation und Vergleich mit den Ergebnissen bei Acidose. Arch. Ges. Physiol. 271:732-47, 1960.
25. Krogh, A., and J. Lindhard. The regulation of respiration and circulation during the initial stages of muscular work. J. Physiol. (London) 47:112-136, 1913, -14.
26. Lambertsen, C. J., S. J. G. Semple, M. G. Smyth, and R. Gelfand. H^+ and pCO_2 as chemical factors in respiratory and cerebral circulatory control. J. Appl. Physiol. 16:473-84, 1961.
27. Lambertsen, C. J. Factors in the stimulation of respiration by carbon dioxide. In: The Regulation of Human Respiration, edited by D. J. C. Cunningham and B. B. Lloyd. Oxford: Blackwell, 1963, pp. 257-276.
28. Legallois, C. J. Experiences sur le principe de la vie. Paris, 1812.
29. Leusen, I. Chemosensitivity of the respiratory center. Influence of CO_2 in the cerebral ventricles on respiration. Am. J. Physiol. 176:39-44, 1954.
30. Leusen, I. Chemosensitivity of the respiratory center. Influence

of changes in the H^+ and total buffer concentrations in the cerebral ventricles on respiration. Am. J. Physiol. 176:45-51, 1954.
31. Leusen, I. Acid-base equilibrium between blood and cerebrospinal fluid. Am. J. Physiol. 176:513-16, 1954.
32. Lindhard, J. On the sensitivity of the respiratory center in exercise. Arbeitsphysiol. 7:72 -, 1934.
33. Lloyd, B. B., and D. J. C. Cunningham. A quantitative approach to the regulation of human respiration. In: The Regulation of Human Respiration, edited by D. J. C. Cunningham and B. B. Lloyd. Oxford: Blackwell, 1963, pp. 331-349.
34. Loeschcke, H. H., and H. P. Koepchen. Versuch zur Lokalisation des Atmungs - und Kreisaufwirkung von Novocain im Liquor cerebrospinalis. Arch. Ges. Physiol. 266:628, 1958.
35. Loeschcke, H. H., and K. H. Gertz. Einfluss des O_2 Druckes in der Einatmungsluft auf die Atemtatigkeit des Menschen, geprüft unter Konstanthaltung des alveolaren CO_2 - Druckes. Arch. Ges. Physiol. 267:460-77, 1958.
36. Miesscher-Rüsch, F. Bemerkungen zur Lehre von den Athembewegungen. Arch. Physiol. 355, 1885.
37. Milhorn, H. T. Jr., and A. C. Guyton. Mathematical models of the human respiratory control system. Federation Proc. 23(2): 307, 1964.
38. Mitchell, R. A., H. H. Loeschcke, J. W. Severinghaus, B. W. Richardson, and W. H. Massion. Regions of respiratory chemosensitivity on the surface of the medulla. Ann. N.Y. Acad. Sci. 109 (2): 661-81, 1963.
39. Morgan, D. P., F. Kao, T. P. K. Lim, and F. S. Grodins. Temperature and respiratory responses in exercise. Am. J. Physiol. 183:454-58, 1955.
40. Nielsen, M. Untersuchungen über die Atemregulation beim Menschen. Skand. Arch. Physiol. 74, Suppl. 10:83-208, 1936.
41. Nielsen, M., and H. Smith. Studies on the regulation of respiration in acute hypoxia. Acta Physiol. Scand. 24:293-313, 1951.
42. Nielsen, M., and E. Asmussen. Humoral and nervous control of breathing in exercise. In: The Regulation of Human Respiration, edited by D. J. C. Cunningham and B. B. Lloyd. Oxford: Blackwell, 1963, pp. 503-513.
43. Perkins, J. F. Jr. Arterial CO_2 and hydrogen ion as independent, additive respiratory stimuli: support for one part of the Gray multiple factor theory. In: The Regulation of Human Respiration, edited by D. J. C. Cunningham and B. B. Lloyd. Oxford: Blackwell, 1963, pp. 303-317.
44. Riley, R. L. The hyperpnea of exercise. In: The Regulation of Human Respiration, edited by D. J. C. Cunningham and B. B. Lloyd. Oxford: Balckwell, 1963, pp. 525-534.
45. Robin, E. D., R. D. Whaley, C. H. Crump, A. G. Bickelmann, and D. M. Travis. Acid-base relations between spinal fluid and arterial blood with special reference to control of ventilation. J. Appl. Physiol. 13:385-92, 1958.
46. Rosenthal, I. In Hermanns Handbuch der Physiologie. Leipzig, 1882, IV/2:269-286.
47. Saito, K., Y. Honda, and N. Hasamura. Evaluation of respiratory response to changes in P_{CO_2} and hydrogen ion concentration of

arterial blood in rabbits and dogs. Japan. J. Physiol. 10:634-45, 1960.
48. Schmidt, C. F. Introductory remarks - six score years of chemoreflexes. Ann. N.Y. Acad. Sci. 109(2):631-3, 1963.
49. Winterstein, H. Die Regulierung der Atmung durch das Blut. Arch. Ges. Physiol. 138:167-184, 1911.
50. Winterstein, H. Neue Untersuchungen uber die physikalisch-chemische Regulierung der Atmung. Biochem. Z. 70:45-72, 1915.
51. Winterstein, H. Die Reaktionstheorie der Atmungsregulation. Arch. Ges. Physiol. 187:293-298, 1921.
52. Yamamoto, W. S. Mathematical analysis of the time course of alveolar CO_2. J. Appl. Physiol. 15:215-219, 1960.
53. Yamamoto, W. S., and M. W. Edwards, Jr. Homeostasis of carbon dioxide during intravenous infusion of carbon dioxide. J. Appl. Physiol. 15:807-818, 1960.

AAAS MEETING

The American Association for the Advancement of Science will hold its 131st annual meeting in Montreal, Canada, December 26-31, 1964. This year's meeting will be distinctive in several respects; its locale, the proportion of distinguished speakers from abroad, and the overall high quality of the special sessions and symposia. A series of special sessions will be concerned with "Moving Frontiers in Science" with world-renowned speakers. There will be an international conference and a series of sessions on "Communication and Social Interaction in Primates." These special sessions and symposia along with the regular section session papers should make this AAAS meeting most attractive to physiologists.

BIOPHYSICAL SOCIETY MEETING

The 9th Annual Meeting will be held February 24, 25, 26, 1965 at the Sheraton-Palace Hotel, San Francisco, California. Contributed papers plus Symposia on Information Transfer in Biological Systems and Evolution and Exobiology will constitute the program. Further information may be obtained from Dr. William Sleator, Washington University School of Medicine, St. Louis 10, Missouri.

PAST-PRESIDENT'S ADDRESS

HERMANN RAHN

Physiologists and the Information Crisis

Since its beginnings physiology has been in the center of biological foment. It spawned biochemistry, pharmacology, and more recently biophysics and biomathematics. Physiology and its sister sciences have now passed the long lag of the incubation period and are firmly entrenched in the exponential growth phase. Physiology is no longer merely acknowledged, but actively courted by the public, the federal agencies, and the medical profession. The last war was the final turning point and we are now in the saddle as "Physiologists on Horseback" (5).

This rapid growth has brought on many adjustments but all the kinks have not been straightened out. Compared with the meager pre-war days when research was done at the enthusiastic amateur level, it has become now an assembly line geared to production. This rapid development has been precipitated by non-university support of biological research. Since 1945 this support has increased 20-fold. Today we may appear to be affluent; to paraphrase Will Rogers, "It is easy to be a gentleman when you have a grant."

However, a gentleman has a conscience and assumes responsibilities. These I should like to discuss. Fortunately I am allowed to give you my uncensored version, for you will recall a statement in the Preliminary Announcement of the Fall Meeting, "Children will be entertained elsewhere during the Past-President's Address."

Affluence, in terms of research support and respect, has, however, created new problems. Before the war you discharged your responsibilities to the university by teaching. Universities never planned research as is commonly done in industry. What you did beyond your teaching was of relatively little concern. Today, universities need outside research support in order to survive, and frequently this tail wags the dog. Support is equivalent to survival. Deans become haunted businessmen appeasing the president. Departmental chairmen have become ornery, hard-boiled production managers more familiar with airline schedules than teaching schedules. Their prestige is proportional to the number of days spent in Washington. At home there is only time for reports and indulging in toothpaste containing food particles advertised for "People who are too busy to eat between brushings." This description fits to some degree all members of a faculty. No wonder that the serenity of the pre-war days is gone and that our personalities have changed. Professors are only a shade better than departmental chairmen, who in turn are only slightly better than deans. These facts are now commonly recognized, but that they have penetrated into the wildest places of New Guinea was quite a shock.

Three summers ago I had joined Pete Scholander on an expedition in the Coral Sea. We had caught a very large sea turtle on one of the islands and were anxious to bring it back to camp. Only he could have persuaded me to hang onto it in the bow of an eight-foot dinghy while he manipulated an outboard motor at the stern. I never did manage to pull it on board; so I was left hanging over the bow with a struggling 200-pound turtle in my arms while Pete tried to run the surf. How we made it I will never know. However, the small boat was so unbalanced that we missed the channel, lost our way, and hours later reached a strange coast where we were welcomed by natives who carried us exhausted into their hut. When we recovered I motioned with my hands that I was hungry. To my great surprise they answered in English, "Here is a menu." When I read the bill of fare, unfortunately quite legible, I lost my appetite:

Fried Instructor of Physiology......	$1.00
Broiled Assistant Professor........	1.25
Sauteed Full Professor.............	1.50
Stewed Departmental Chairman.....	10.00

After recovery from my initial shock I became intrigued by the great price junp from $1.50 for Full Professors to $10.00 for Departmental Chairmen. I finally screwed up my courage and in a rather tremulous voice inquired why departmental chairmen were so expensive. A rather tall man only returned a smile and finally said, "Have you ever tried to clean one?" For several years thereafter I wondered what the price of a dean would have been.

Thus the outside support has changed our personality. It has also split our loyalty between the university where we feel secure and the federal agency which we must acknowledge. And finally, it has produced an information explosion. What we are now beginning to feel is the last phase, as a necessary consequence, the communication crisis.

Having accepted this natural development, we must also ask what our changing responsibilities are. Our divided loyalties between the university which allows us to teach and the federal agency which allows us to experiment have slowly been acknowledged as a new way of life for the academician. The information explosion we must welcome as scientists. That it produces good, bad, and indifferent research I believe is inevitable as long as the support is so large.

What we have not faced is the matter of comprehending and digesting the ever growing accumulation of facts. The natural reaction is a greater and greater compartmentalization of men and ideas with ever growing specialization. This tendency is fostered and encouraged today by an ever increasing number of symposia, colloquia, study groups, meetings, personal communications, exchange programs, postdoctoral training programs, and travel grants. Specialization does not proceed with equal speed on all fronts. It tends to foster cliques and prestige groups and encourages their growth, while other areas suffer and shrink. This is what Price called "Little Science, Big Science" (9).

There is no question that we are all erecting higher and higher walls of communication barriers around our own fields. This is not to keep others out, but to remain undisturbed. This Tower of Babel must eventually collapse and expose the nakedness of our splendid isolation. Even within small departments these tendencies develop. Only last week when the members of our staff were rehearsing their papers for these meetings, I overheard one man remark to another, "Hermann Rahn speaks only to Leon Farhi and Leon Farhi only to God."

The Role of the Documentalist. And how will the communication crisis be solved? To many this seems a straightforward problem. We build machines, computers, scanners, automatic printers, translating machines. These in turn will be linked to smaller centers strategically placed throughout the country. The traditional handlers of scientific information, our librarians, editors, and publishers, have already been reenforced by the information processors, the documentalists, computer designs, computer engineers, information system designers, audiovisual experts, document analysts, and a variety of other information specialists (3). These are today a formidable group of highly skilled experts who talk a new language, using such words as "dowsing," "normalization," "intelligence," "L-indexing," "morpheme," "semoglyphs," "retrieval language," and "associative memory," and have acronyms and abbreviations which today outnumber the governmental alphabet of the Rooseveltian era.

Our colleagues in the new field of scientific documentation are forging ahead with incredible speed. Their total budget last year for documentation research alone was approximately 25 million dollars. They are just beginning, their goals are concrete and well described, their promises tempting. The big monsters of their dreams will answer all your questions. By pushing the right buttons you will obtain all you ask fôr and even more. Your problem will be to avoid drowning in the flood of information of categorized facts. This will undoubtedly be a godsend for the librarian and certainly impress the graduate student. The Medical Literature Analysis and Retrieval System, MEDLARS, of our National Library of Medicine is probably the first big machine which will cover annually about 150,000 articles, and 250,000 by 1970 (1). It will print out for you the information requested. While this is obviously an important and necessary step in the communication problem, will it really solve it? To this I must say emphatically no.

First let me remind you that in the strict sense these machines do not handle information, but documents. What to do with this information once it arrives at your desk is the real problem. Here we encounter a biological computer whose efficiency, versatility, and memory storage are of a different order of magnitude. It is, however, uniquely endowed with certain unknown networks which will sort, select, reject, and associate to feed into the output on occasion, and only on occasion, new concepts, ideas, and even dreams which never existed in the primary data which it digested. These occasional flickers can burst into the strong light of new concepts, and in the long run only these will justify the whole development of our automation effort.

Today plans are big and clear, well supported and well directed with respect to the development of mechanical computers which will categorize the primary information. Plans are weak and ill-defined for the most important final step of evaluation and digestion by the biological computer of our central nervous system. These must go in step or we shall eventually reach the stage where the former will control the latter. This is really not as far-fetched as it may seem. The documentalist will obtain the necessary data, shuffle, sort, and come up with conclusions of the state of the art in any area which you name. The next step is obviously to point out the weaknesses in certain fields of research, advise the federal agencies, which in turn will provide or deny financial support in these areas. The documentalist is unable to differentiate between good, bad, or indifferent research. It is all equally acceptable to his machine. Nevertheless, he can be easily tempted to assume the role of interpreter. His rather precise, overwhelming statistics based upon innumerable bits of information can be most convincing even though it may or may not be based on "garbage."

The Role of the Physiologist. At this juncture the scientist, the consumer of the product, must step in and assume a role not yet crystallized by our planners. What we need is perhaps best illustrated by the philosophy of a certain career medical officer in our Navy who was in charge of younger men putting in their two-year service requirements in the Medical Corps. They were enthusiastic, eager, and at times frustrated, trying to keep up with the most recent advances of the medical field. One afternoon at the bar the Captain was drinking with his junior officers when one of them said, "Say, Captain, how do you manage to keep up with the literature?" This was obviously a very loaded question since all realized that, although the Captain did a fine job, he probably glanced at few journals and probably had not read a medical book in years. The bar suddenly became silent and then he said, "Jim, that's really not very difficult. You see, I have a 'garbage sifter.' When it has digested the whole goll-darned medical literature for the year and done its sifting, there are only one or two articles that are really worth reading."

While on the subject of garbage, I am reminded of an ambassador from one of the undeveloped countries who had recently taken up his residence in Washington. When confronted by a local women's club he was asked, "Mr. Ambassador, what has impressed you most about our country?" He reflected a while and answered, "The size of your garbage cans!" While our western prosperity has indeed allowed us to enjoy this domestic privilege, we are extremely undeveloped in this respect in the area of science. Our garbage cans are too small and unless we make an effort to increase their size for scientific garbage we shall not only remain undeveloped but must eventually retrogress.

Others, long before, have voiced concern about the new role that we as scientists must assume in order to rise adequately to the challenge of the information explosion. Maurice Visscher (12) warned that the information problem cannot be turned over to the documentalist but requires the active participation of the research scientist. Ellis Kelsey (7) suggested that the NIH set up a senior reward system to finance individual, outstanding scientists for increased production of critical reviews. Julius Cahn (2) warned us that the information problem is not a housekeeping job, but must mobilize the best minds of our ablest scientists. The Surgeon General of the Public Health Service, Luther Terry (11) aptly phrased it this way, "In our rush to embrace the glories of automation, let us not slight the need for improvements in traditional methods of communication - for example, more and better qualified evaluators, or synthesizers, who will help us translate papers into useful information." Finally I like to quote the first recommendation from President Kennedy's Science Advisory Committee (10), an excellent document which I recommend to all. "We shall cope with the information explosion, in the long run, only if some scientists and engineers are prepared to commit themselves deeply to the job of sifting, reviewing, and synthesizing information. Such scientists must create new science, not just shuffle documents. Their activities are as much a part of science as is tradional research. We urge the technical community to accord such individuals the esteem that matches the importance of their job and to reward them well for their efforts."

The all-important role of the research man is clear and fortunately has been recognized by our leaders and experts in this area. However, the concrete proposals to enlist the support of the scientist are unclear, vague, and unsure.

The Growth of Physiology. Before making a positive recommendation let me refer to Figure 1 which shows the growth of physiology. According to our surveys it doubles approximately every ten years. The first complete ring represents the whole area of physiology thirty years ago, the wedge merely a particular area. Each decade new land was put into cultivation doubling the area of the previous decade. This expansion is obviously due to the increasing number of physiologists (6). Every one physiologist in a given area in 1934 (see innermost dot) was joined by one additional man in 1944 and has seven colleagues today helping him dig new holes for the proverbial cat described by Wallace Fenn (5). In 1974 we may expect sixteen experts in this same area since our exponential growth curve shows no sign of decline (6). You will also notice that each white field under cultivation by each physiologist is equal when you extrapolate it to the center of the circle. Only the shape is changed. While we may take pride in this continually expanding system, it also presents cause for alarm.

Let us now consider comprehension of an area of physiology by the average physiologist. This is based upon his ability to read, digest, and distill. This faculty, I believe, is limited and relatively fixed by his central nervous system and therefore does not change from decade to decade. With this assumption, comprehension of a particular area must be reduced by one-half each decade. If each white area represents also his approximate area of comprehension, then you can see easily what frightful prospects we face. Our task is to expand each decade the central black area in our figure. This black wedge represents the solid, basic, digested facts and becomes the foundation of our science. While you may quarrel with my quantitation effort, I believe the general issues are clear.

I also want to draw attention to the task of the teacher who not only must keep up in his reading but digest and render succinctly the advancing front of physiology. If he spends all his efforts in this direction you

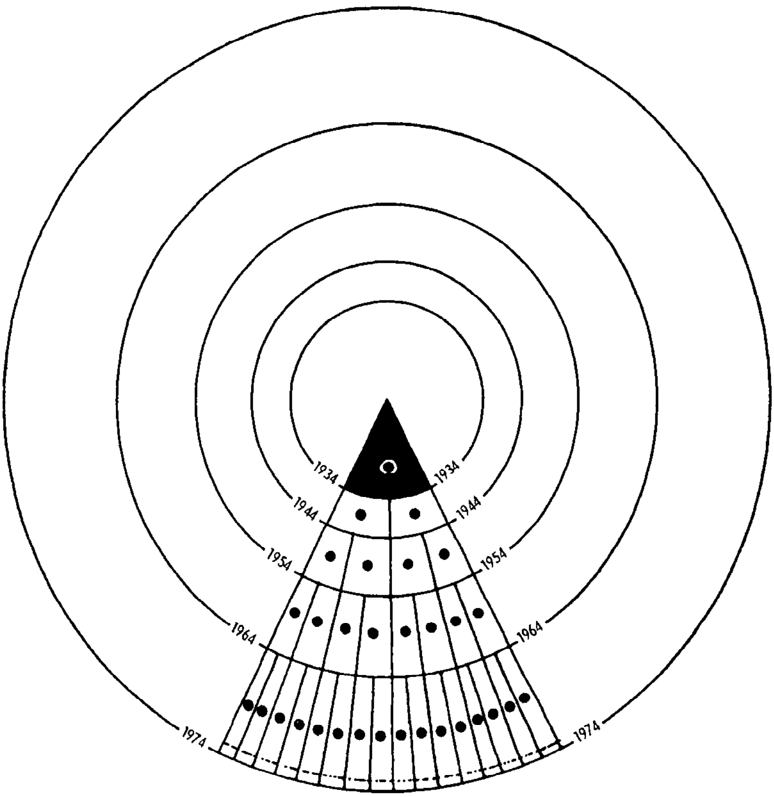

Fig. 1

can see, for example, what he faces ten years hence. I have allotted him the area between the outer circle and the dotted line. If he must teach more than one conventional area, his task becomes insurmountable.

What can we do? Obviously the documentalist can help in the mechanical delivery and sorting of information. But the final goal can only be achieved by the scientist. As Hallowell Davis stated (4), "There will be an increasing need for men who can put ideas together effectively and write well. These will not be a new breed of scientists. There is no one else but ourselves." Thus we must increasingly depend upon others for critical evaluation, and in our own field of specialization we must perform this function for others.

While I have quoted to you the concern of various study groups and leaders in the documentation area for greater participation of the scientist, there are to my knowledge no active, concrete plans. It therefore behooves us to take some action, as individuals, as members of our universities and institutes, as members of our Society. I am sure that our Government is willing to support sound plans. They feel a great responsibility for they have contributed so much to the advancing frontier and simultaneously to the information explosion. As David Price from the Office of the Surgeon General, Public Health Service, states (8), "Federal Agencies have a responsibility in furthering the communication process. However, the Government's role should not be a commanding one, but a supporting one. Scientific societies must initiate and lead and define the role they will play."

A Recommendation. My own suggestions are that foundations and federal agencies such as the National Science Foundation and the National Institutes of Health, with the advice of consultants, initiate two plans of action. One would concern itself with the training and establishment of Career Literature Research Investigators; the other would be the development of new experimental publications devoted to synthesizing information in a manner not practiced today by reviewing journals or handbooks.

We all know talented scientists as well as teachers who excel naturally in such reviewing and who are actually more productive in this endeavor than in bench research. These are the people, found in every laboratory, whose advice is continuously sought by the active bench worker and who frequently contribute more to the research of others than to their own. Unfortunately they are continuously prodded to do experimental work instead and publish, because this is fashionable, recognized by deans, and helps in promotions. To my mind this is a tremendous waste of some of our best talent. These people could become respected leaders in their fields, publish magnificent reviews, solidify vague concepts, and shore up the foundations of our science. However, they must be well supported and their professional work accorded the same respect and esteem as that of the bench worker.

Another, additional plan might be to elect each year a few of our best and most active bench workers. Let them go into a retreat at their home institution or elsewhere for a period of two years. Relieve them of all their usual responsibilities, and give them free reign to express themselves in their search for shoring up our foundations. Reward them well and develop this type of award into the most coveted prize in physiology.

Some of you will say that such work would not result in creativity. If this were the case I would not suggest such a plan. Creativity depends not on what you do but where you find it. An Annual Review type article does not require much creativity. A Physiological Reviews article requires considerable talent. What I am looking for is a step beyond this stage, which doubly and triply distills the available information and renders the simple, comprehensible essence. This can only be done by our best scientists, but they need not be bench workers. If out of every three or four career investigatorships we select the best man as a literature investigator, we can make a real step forward. As the President's Science Advisory Committee indicated (10), "Such a position in science is comparable to that of a theoretical physicist in modern day physics."

My second proposal would be to provide new publication vehicles for some of the reviews which would be forthcoming under this system. I have in mind a format similar to that of the Scientific American. Instead of covering all sciences it should be started in a restricted biological field and at a different level of sophistication. If successful, it can enlarge its role. Many of you will say that this is far too extravagant and gilds the lily. However, at the moment I am not concerned with cost. This is simply an experiment no more costly than others which the taxpayer supports. It certainly does not gild the lily. If you have read Ray Zwemer's review (13) of the reading habits of physiologists, you will be impressed with their limited capacity. If the format and style and illustrations of a publication today are not attractive, it simply does not get the attention. We are innundated with so much reading material that we instinctively select, and not always on a scientific basis. For example, I have the Scientific American on the table next to my bed, but not Physiological Reviews. This is largely a matter of competition. The former is so attractive in format, style, and illustration that it actually competes for my sleeping time. If one could develop, at a large cost I must admit, a similar review in physiology, it might also keep me awake at night. This might produce sleepy physiologists; however, a sleepy one, well-informed, is possibly better than a wide-awake one, uninformed.

And now I have had my say. I can leave you with good conscience to carry on. "Old physiologists never die, they just slowly lose their grants." And with farewell to this great office to which you elected me, let me once more reiterate: - If you are to stay on top and not become inundated in the flood of good, bad, and indifferent information, and if you care to direct and develop your own research area as you see it and without pressure from the documentalist's statistics, then you must seize the initiative. No one else can or will do it. You must begin to train some of the best physiologists to act as synthesizers, catalysts, and evaluators, colleagues whom you will trust, respect, and accord all the honors of a bench scientist. To remain a well-rounded scientist you will need their help. You must also develop new types of publications which will meet the needs and supplement our traditional approaches; and, finally, you must show your affluence as physiologists by building bigger garbage cans.

REFERENCES

1. Adams, S. The MEDLARS System. Federation Proc. 22: 1018, 1963.
2. Cahn, J. Closing the Gaps in Biological Communications. Federation Proc. 22: 993, 1963.
3. Communication Problems in Biomedical Research. Natl. Acad. Sci., Natl. Res. Council. Oct. 31, 1963. (Report of a Study).
4. Davis, H. The Physiologist. 1: 43, 1958.

5. Fenn, W. O. Physiology on Horseback. Am. J. Physiol. 159: 551, 1949.
6. Fenn, W. O. The Third Quarter Century. History of the American Physiological Society. The American Physiological Society, Washington, D.C., 1963.
7. Kelsey, F. E. Government Responsibility for Science and Information. Federation Proc. 22: 975, 1963.
8. Price, D. Challenge to the Primary Journal. Federation Proc. 22: 1008, 1963.
9. Price, D. J. de Solla. Little Science. Big Science. Columbia Univ. Press, New York, 1963.
10. Science, Government, and Information. A Report of the President's Advisory Committee. The White House, Jan. 10, 1963.
11. Terry, L. Surgeon General's Conference on Health Communications. Nov. 5-8, Dept. HEW, 1962, p. 63.
12. Visscher, M. B. Retrieval and Evaluation of Information. The Physiologist. 7: 29, 1964.
13. Zwemer, R. Approaches to Keeping up with the Literature. Federation Proc. 22: 984, 1963.

FOR TRAVELERS TO THE FAR EAST

The Department of Health Education and Welfare wishes to remind travelers that the Division of Foreign Quarantine has issued two leaflets that are helpful to persons planning trips to the Western Pacific and the Far East. One is entitled, "So You're Going Abroad: Health Hints for Travelers" (PHS Publication No. 748A); the other "Health Information for Travel in Asia (PHS Publication No. 748C). Each lists the vaccinations required and recommended for travel in that part of the world as well as health protection hints, such as what not to eat or drink. Copies can be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402, for 5 cents apiece.

AIBS

JOHN R. PAPPENHEIMER*

More than two years have elapsed since you have had a report from your representative to the American Institute of Biological Sciences. Most of you are aware that recent officers of the Institute inherited some extremely complex administrative and financial problems. The financial difficulties arose mainly from mismanagement of funds allocated by the National Science Foundation for the production of the AIBS Educational Film Series prior to 1962. Little is to be gained by reviewing the details of this mismanagement except to emphasize that it involved nothing which could be construed as dishonesty on the part of any individual. Nevertheless it left AIBS in desperate financial difficulties (see Science, 139:317-21, 1962) and seriously threatened the unity and healthy development of biology in this country. The new officers of AIBS faced these problems intelligently and courageously under the leadership of Frits Went, President during 1962, James Ebert, President during 1963, Paul Kramer, President during 1964, and John R. Olive, the new Executive Director of the Institute. AIBS has emerged from its period of trial stronger, wiser, and better equipped than previously to serve the needs of biological sciences. The lessons learned were bitter ones and they are not likely to be lost upon the officers of many scientific societies and universities which accept funds from government agencies. Conversely, the government granting agencies also learned something from this experience which in the end helped to clarify their function in supporting the biological sciences. All of us owe a debt of gratitude to those who weathered the storm so resolutely.

Much remains to be done, but at this time we can say that AIBS will enter 1965 with a balanced operational budget, a practical long-term schedule for payment of its debts and above all with the confidence and enthusiasm of most of its members. Before 1962 there were 27 societies affiliated with AIBS; now there are no less than 43 adherent societies representing some 70,000 biologists. At the same time, the number of individual dues-paying members has increased to 12,000 and hopefully this number will increase as the results of the AIBS programs come to be more widely known and appreciated.

During this two-year period of administrative stress, some of the long-term programs of AIBS came to fruition and it is now possible to point to accomplishments which can hardly fail to strengthen biology as a whole and physiology in particular. In recognition of these accomplishments the Rockefeller Foundation has recently awarded $50,000 to AIBS to aid in initiation of new programs. Some of the solid accomplishments of AIBS may be summarized as follows.

1. The Biological Sciences Curriculum Study Program. Many of you will have seen the new textbooks and laboratory manuals of biology which are now being widely adopted in high schools throughout the

*APS Representative to AIBS Board of Governors.

United States. The preparation of these books through the cooperative efforts of leading research biologists on the one hand and high school teachers and students on the other, was a most interesting experiment initiated by AIBS five years ago. The final results based on three years of practical experience in more than 1,000 high schools are now available in the form of bound volumes published on a large scale. Three versions of the textbooks are available, the "Blue Version" (Molecules to Man), the "Yellow Version" (An Inquiry into Life) and the "Green Version" (High School Biology). The emphasis of each book is slightly different as suggested by the titles, but each provides the basis for a comprehensive and thoroughly modern course in biology. The presentation is challenging to the imagination and often proceeds rapidly to current problems. A substantial fraction of the material is concerned with the functional approach to the study of living things, including general, systemic and mammalian physiology. The balance between Molecular Biology, Biochemistry, Cell Biology, Genetics, Microbiology, Animal and Plant Physiology, Ecology, etc. seems very good and one emerges from each book with a strong sense of the unity of biology as a whole. Each of the three books is supplemented by laboratory guides and a program of films which were designed in conjunction with the laboratory material and texts. Each film lasts about one-half hour and there are 120 films covering 10 major subdivisions of biology. The effects of this enterprise must surely be to revolutionize the teaching of biology in secondary schools and in colleges. The implementation of this new program in high schools throughout the country can be expected to capture new talent and to raise the caliber of the students whom we shall see in graduate schools of Physiology and Medicine. In the words of James Ebert "there can be no doubt that the (BSCS-AIBS) program has brought new spirit and vitality, a new sense of urgency, to biology teaching; the great wave of interest in teaching modern biology spearheaded by BSCS is now overflowing into elementary and college teaching ranks, engendering comprehensive studies and constructive criticism by the schools themselves and by national commissions."

The initiation of the program and the impetus for transforming it into reality came primarily from AIBS and in my opinion this accomplishment alone merits our admiration and firm support both as members of APS and as individual dues-paying members of AIBS.

2. Publications. AIBS publishes two journals, Bio Science and the Quarterly Review of Biology. The quality of the first journal has improved enormously during the past two years, and there is every indication of further improvements under the leadership of the new President of AIBS, Professor Kenneth Thimann of Harvard. Bio Science is published monthly; it describes the activities of AIBS and also contains primary papers, original essays and reviews. Special issues are devoted to particular subjects in Biology such as Ecology, Marine Biology, Biology of the Arctic, Etc. You will not receive this journal unless you have joined AIBS as an individual member.

3. Symposia and Publications. AIBS has sponsored and arranged more than 25 symposia during the past two years. The proceedings of these symposia are usually published as books. Recent examples of special

interest to physiologists include Marine Biology; Brain and Behaviour; The X-Chromosome of Man; Radiation Biology; Small Blood Vessel Involvement in Diabetes Mellitus; Fructose-1; 6-Diphosphate and its Role in Gluconeogenesis; and Sharks and Survival. AIBS has also arranged for the translation and publication of Russian monographs. In addition to arranging for relatively small symposia and conferences, the AIBS is gradually accumulating experience in the management of large international congresses. In 1969 it will undertake management of the International Congress of Botany which is at least as large as our International Congress of Physiology.

4. Annual Meetings of AIBS. For many of the 43 adherent societies, the annual meeting of AIBS in August is the principle scientific meeting of the year. At the 1964 meetings in Boulder, Colorado there were about 4500 registrants and more than 1500 scheduled papers. Twenty-eight of the societies were represented on the program and most of them held their own business meetings and arranged banquets and social functions similar to those normally held by APS at its regular Fall meeting. In addition, however, there were many cooperative and intersociety programs. Your representative spent a most interesting and enjoyable day on Mt. Evans on a field trip symposium on Physiological Ecology of Alpine Environments arranged jointly by the Division of Comparative Physiology of the American Zoological Society and the Ecological Society of America.

The responsibility for arranging these large and invaluable annual meetings is shouldered by the staff of AIBS and this is one of its continuing important functions.

PLANS FOR THE FUTURE

1. Administrative Reorganization of AIBS. The Constitution and Bylaws of AIBS are still under study and a stable version may require some years of further experience. Two years ago the fundamental change to individual, rather than to Society membership, was implemented. Under this system the adherent societies each pay relatively small annual dues. For example, the annual dues of our Society are now $750 per year (approximately 30 cents per member) instead of $2,000 prior to 1962. The principal membership income of AIBS is derived from individual members who pay $10 each and who receive full voting and other privileges of AIBS, including subscription to Bio Science. Each adherent Society appoints one representative to the Board of Governors of AIBS for a four-year term. In addition there are 12 representatives to the Board of Governors from members-at-large. This Board, totalling more than 55 members meets semi-annually with the elected President and other members of the Executive Council, to discuss and determine policy and new programs.

2. The Future Home of AIBS. AIBS is about to move into new headquarters at 3900 Wisconsin Avenue, Washington, D.C. This move does not provide for expansion, but rather consolidation into a more pleasant building with more economical and efficient use of floor space.

Consideration is being given, however, to a permanent home for AIBS in keeping with its national importance to biology. It is entirely possible that means will be found to consolidate with various "umbrella" organizations such as the Federation of American Societies for Experimental Biology and the Society for Experimental Biology and Medicine. In many areas the activities of these organizations overlap and much would be gained by improving communications between them. This is especially true in the fields of publication, visiting scientist programs, science communication studies, symposium service facilities, national roster of personnel and placement services and other large scale national and international enterprises. At the present time representatives of both AIBS and FASEB are exploring the possibility of combining their facilities to establish a national center to represent all of the biological and medical sciences.

SUMMARY

AIBS has emerged from its administrative and financial difficulties greatly strengthened and better equipped than ever before to serve the biological sciences. It now comprises 43 adherent societies representing 70,000 biologists. There are 12,000 dues-paying individual members.

The Biological Sciences Curriculum Program, initiated by AIBS five years ago, has borne fruit with a series of integrated textbooks, laboratory guides and films for comprehensive and thoroughly modern courses in Biology. This program has been widely adopted in schools throughout the country and is generally regarded as the most important event in the history of biology teaching. The program can hardly fail to raise the number, caliber and level of training among students entering graduate schools of Physiology and Medicine.

AIBS has initiated or sponsored some 25 symposia during the past two years. It has published several excellent books of special interest to physiologists. It has also transformed the AIBS Bulletin into a monthly journal called Bio Science which is rapidly becoming as important as Science or Nature for the general biologist. The annual meeting of AIBS has become the principal meeting of many of the adherent societies.

The solid accomplishments of AIBS merit our admiration and support. The Institute will enter 1965 with a balanced operational budget but many years may be required to repair the effects of mismanagement in the past. The chief source of income derives from the $10 annual dues of individual members. As your representative to AIBS I have studied its programs and accomplishments during the past two years and am convinced, as was my predecessor Dr. Fenn, that the interests and work of AIBS contribute to the goals and purposes of the American Physiological Society. I have no hesitation therefore in urging you to join AIBS as individual members if you have not already done so.

COUNCILMAN TOUR

ROBERT E. FORSTER

Some Aspects of the Future of Physiology

A recurring concern about the future of physiology is its relation within a university to the clinical departments of the medical school on the one hand and to the natural sciences and general biology departments on the other, a gap which physiology is called upon to span in explaining function in the higher animals. With biology becoming more "molecular", and with lessening interest in organ and system physiology, this gap has appeared to grow, and with it the problems of the physiologist in performing his integrative and pedagogic function. One department with interests in organ physiology may be considered too "clinical", and the next with research intersts closer to the cellular level may be accused of being too esoteric to be of help in preparing medical students for the care of the sick. Some have suggested that physiology as a separate discipline will disappear entirely, its area of instruction and research being divided amongst biochemistry, molecular biology and the several clinical departments.

Another concern is the training of future physiologists. In the face of the enormous overload of pertinent information, what should be taught? Should the cellular, biophysical and molecular biological material be organized outside the physiology department? How much physiology should be taught medical students primarily by clinical departments?

It occurred to Council that an excellent way to investigate the present status of these problems and existing thoughts about their solution, would be to visit several departments of physiology in which new chairmen had recently been appointed. These individuals could be expected recently to have given a great deal of thought, not only to the immediate present, but to the future of physiology, as the success of the department under their leadership depends in no small way on its organization and its teaching functions. They would also in general be of a newer generation of physiologists as compared to those guiding other departments.

This is a report of visits to departments of physiology in five medical schools in the central and southern eastern seaboard and in the southwest. These departments were selected as noted above, because they had new chairmen. One chairman had been in office long enough to influence the organization of the department. An effort was also made to visit departments with a wide geographic distribution, and departments that had not been visited by a President or Councilman recently. Owing to the pecuniary structure of the tour and the large distances involved, these visits were combined with other business and could not be made contiguously. I was deeply impressed, and grateful for the esteem in which the membership holds their Society, as demonstrated by their efforts on my behalf and the time they spent, usually at inconvenient hours, to inform me.

Innovations in the instruction in physiology of two of the schools visited were presented at the Teaching Session at the Federation Meetings at Chicago in 1964.

As one could have predicted there were as many ways of handling the teaching responsibilities and intra-university relationships of a department of physiology as there were departments and universities visited. However the following changes were seen in more than one department and might be considered as illustrative of widespread responses to currents of change.

1. Faced with the inexorable expansion of scientific information within the finite limits of curricula, there is a general tendency to decrease the number of topics covered in the medical school physiology course, and to increase the detailed consideration of the basic processes and of areas in other sciences pertinent to each topic. The subject matter set aside is that which is less general in its usefulness, that retained provides a background for general medicine and surgery. In other words the physiological background for the lesser medical specialties is getting shorter and shorter shrift in the medical curricula. One form of curriculum reorganization is to provide a core course, made up of the most fundamental and general topics, which is taken by all students and at the same time offering instruction in specialized topics, which may be elected, in such subjects as biophysics, cellular physiology and endocrinology. This increased flexibility is a small recompense for the drastic choice forced on the physiology staff but does help the graduate students and those medical students who are so prescient as to know the medical specialty they will eventually elect.

2. The proportion of teaching time devoted to laboratory experiments over the past quarter of a century is now generally considered too large and the number of experiments has been decreased, with an increase in the time given to conferences and small discussion groups. It is felt that the laboratory is not necessarily the most efficient mechanism for teaching, that in fact it can get in the way, but that a balance between the various methods of instruction has to be sought.

3. A greater effort is being made to provide the students with the opportunity to experience the satisfaction of a scholarly or experimental investigation, rather than to be told about it. These opportunities range from literary research and presentation before small groups on one hand to guided laboratory investigation on the other. The object is not to make investigators out of each student, but to give them a feeling for the research process.

4. Increasing assistance in the teaching of physiology is being obtained from members of clinical departments with special training in physiology. These individuals may have joint appointments, and in effect provide a larger faculty whose specialized interests cover a wider area. There is however an attendant danger that those less directly associated with this teaching or in administrative posts may conclude that all of physiology can be taught by the staff of clinical departments. It may be freely admitted that specialized topics can be well taught by clinicians interested in the pertinent medical specialty. However applied topics of physiology are supported by the basic physiology of

yesterday. Individuals whose interests include the clinical care of patients cannot keep up with advances in the more fundamental areas as well as the professional physiologist. A clinician who teaches in association with physiologists has pertinent advances in distant fields brought to his attention. If he does not have this help, tomorrow will find his teaching falling behind. Turning over the responsibility for the teaching of physiology to a clinical department in a medical school might produce short term organizational savings, but would lead to eventual bankruptcy.

5. The relationship between a department of physiology in a medical school and the rest of the university is becoming closer; some are becoming "university" departments in the true sense. While this has many advantages and is symptomatic of a growing sense of unity in biology, it does put increased stress on the physiology department in its relations with the medical school and its clinical departments. This shift in the center of gravity towards the university biology department, is necessary in view of advances in cellular and molecular physiology but can be expected to exacerbate the "hands versus brains" debate (E. G. Dimond, Science, 142:445, 1963) that will always exist in medical schools and to place the physiology department between the warring extremes.

CONCLUSION

The organization of the curricula of physiology appears to be undergoing changes, as indicated by a sampling of five departments, that are reasonable responses to the overwhelming increase in the amount of information to be taught and to the exciting advances in molecular and cellular biology. Physiology is more of a bridge between basic biology and clinical medicine than some of her sister basic medical sciences and is feeling the divergent pulls more acutely. Knowledge of the function of living matter is still the ultimate goal which should not be lost sight of along the way. This will certainly require the techniques and disciplines of the more rapidly expanding segments of biology.

To those physiologists of faint heart, have faith. Consider "Biochemistry" nee "Physiological Chemistry." Certainly structure and function has not been a major concern of this daughter science, where the chemical reactions of individual molecules in solution have. In recent years it has become increasingly necessary for the biochemist to study the spatial organization of reacting systems of molecules in order to interpret their importance in living cells, a pursuit which the unindoctrinated would have little difficulty discerning as physiology.

NEWS FROM SENIOR MEMBERS

Ira A. Manville, 901 S.W. King Ave., Portland, Oregon 97205

I am on the Board of Governors of the Physicians and Surgeons Hospital of this city. I am engaged in a two-year research program for the Oregon-Washington-California Pear Bureau trying to find new nutritive and therapeutic uses for pears. With the practice I have and the interests just mentioned, I am very happy. I hope to do some writing so that my work will not be entirely self-centered.

Bruno Kisch, 71 Maple St., Brooklyn 25, N.Y.

I am still involved in research work in the field of electron microscopy of the heart, which in my age I would not like to interrupt for half a year or a year. But I would gladly be available, if ever the possibility arises, to deliver a lecture or two somewhere on my special working field, for instance the sarcosome theory of muscle function, or on my latest discoveries concerning the perinuclear space as a focus of high enzymatic activities. I am invited to give such a lecture in the fall at the meeting of Electron Microscopists in Prague.

William R. Amberson, Marine Biological Lab., Woods Hole, Mass.

We have had an active and, I hope, successful experimental program here. The major advance has come through our 1960 discovery that muscle enzymes unite with the fibrous proteins, in loose complexes which are nevertheless tight enough to detect and study in electrophoretic patterns. Most recently we have been able to show that enzyme activities in our type of press juice are much lower than those in homogenates of the same muscles. This observation demonstrates that much of the glycolytic series is bound to the ultrastructure and is not free in the sarcoplasmic matrix, as has been long believed.

H. B. Van Dyke, P.O. Box 7432, Taipei, Taiwan (Dept. Pharmacology, College of Physicians & Surgeons, 630 W. 168th St., New York 32, N.Y.)

I am in Taiwan for a year as Visiting Professor of Pharmacology under the auspices of the China Medical Board of New York, Inc. My principal assignment is in the National Defense Medical Center. However I shall also have a close relationship with the College of Medicine of the National Taiwan University. I expect to return to the United States in the autumn of 1964.

H. S. Forbes, Association on American Indian Affairs, Inc., Committee on Alaskan Policy (71 Forest St., Milton 86, Mass.)

I am spending full time working on committee of the AALA, particularly on Alaska problems. At the request of the Eskimos and Indians we try to help them carry out their own plans in adjusting to changing

*Supplied by the APS Committee for Senior Physiologists.

conditions. It is intensely interesting but not easy. Dr. Laurence Irving at the University of Alaska is Director of the Zoophysiology Department and is continuing his studies on adaptation to cold. Also he has been a very helpful member of this committee. A little native paper which I helped to start is doing a valuable service of information and communication, and its circulation is increasing. If you know of anyone who might be interested in seeing it, and even to subscribe, please tell them to write to me.

Maurice L. Tainter, Sterling Drug Company, New York 18, N.Y.

I reach retirement age next June but the company has asked me to carry on for an indefinite period thereafter. For the moment therefore I am not considering any alternative ways of occupying my time.

H. A. Abramson, Editor, The Journal of Asthma Research (South Oaks Hosp., Amityville, L.I., N.Y.)

The Journal would be glad to print papers dealing with any aspect of lung and skin physiology and pathology. We are also interested in having papers dealing with immunological mechanisms.

Stanley P. Reimann, Director Emeritus, The Institute for Cancer Research (703 W. Phil-Ellena St., Mt. Airy, Philadelphia 19, Pa.)

My own retirement has been pleasant even though I have no formal classes to help teach. With Dr. Grace Medes I have just had a book published by J. B. Lippincott Company on "Normal Growth and Cancer." At the moment I am writing another. These activities, with letters to colleagues in various parts of the world, have kept me comfortably busy. I do, however, miss close contact with young people, a need which I fulfill unofficially in the Institute for Cancer Research of which I was director for many years.

Lester R. Dragstedt, Research Professor of Surgery, University of Florida, Gainesville, Fla.

I am at present Research Professor of Surgery at the University of Florida, so that, following my retirement from the University of Chicago, I found myself fully occupied in teaching and research. This past June I was made very happy by receiving the Distinguished Service Award of the American Medical Association, for research, teaching, and surgical practice.

Earl A. Hewitt, Iowa State University (Deceased Dec. 29, 1963) formerly reported that:

A Biomedical Electronics program at Iowa State University was initiated jointly in 1957 by the College of Engineering and the College of Veterinary Medicine. The Program is sponsored by the Departments of Electrical Engineering, Veterinary Anatomy, Veterinary Physiology and Pharmacology, the Engineering Experiment Station and the Veterinary Medical Research Institute.

The primary purpose of the graduate program is the training of engineering graduate students in advanced methods of designing instruments for bio-medical measurements, in applying engineering principles and methods to the study of anatomy and physiology and of training graduate students in Veterinary Medicine specializing in advanced methods of using modern instruments for solving medical research problems.

A Biomedical Electronics Laboratory building has been erected which contains an electronic shop, small animal quarters, a fully shielded and instrumented surgery room, radiotracer laboratories, drug and chemical rooms and laboratory space. The program is supported by research and training grants.

E. Gellhorn, 2 Fellowship Circle, Santa Barbara, Calif.

P. B. Hoeber (New York) published my book "Emotions and Emotional Disorders" (in collaboration with G. N. Loofbourrow) in 1963.

I made a bequest to the University of Chicago for a prize in Neurophysiology. The sum has been matched by contribution of friends and former students. The first E. Gellhorn Prize was awarded last June.

K. K. Chen, Dept. of Pharmacology, Indiana University Medical Center, Indianapolis 7, Ind.

I am thoroughly delighted with my full time position in the department of Pharmacology on the Indianapolis Campus.

Franklin C. McLean, Dept. of Physiology, Univ. of Chicago, Chicago 37, Ill.

All is well with me, and I am still on an NIH grant. A new book, "Radiation, Isotopes and Bone" by McLean and Budy, as one of a series sponsored by AEC will be out before January 1, 1964.

Samuel E. Pond, Proj. Coordinator, Rehabilitation Research, Bureau of Vocational Rehabilitation, Hartford, Conn. (53 Alexander St., Manchester, Conn.)

I transferred from laboratory work on brain-barrier biochemistry and college counseling to critical studies of administration and operations in state-agency services which utilize expanding physical medicine and psychiatry, associated with educational guidance counseling to re-motivate and re-direct individuals with disabilities which handicap them in their professional, semi-skilled and even unskilled activities or employment.

A. E. Livingston, 120 W. Wayne Ave., Wayne Pa.

Having been head of Pharmacology at Temple Medical from 1929 until their retirement age, was made head of Pharmacology at Temple Pharmacy until retired at age 70 in 1954.

St. John's asked me to be head of their Pharmacy department of Pharmacology and after four years was made Coordinator of Science Laboratories until retired, August 31, 1963.

J. F. McClendon, R. F. D. Route 1, Box 393, Norristown, Pa.

I have been retired two years and have used the time writing a book on the history of medicine from the physiologist's viewpoint with special reference to new drugs obtained from Latin America.

Alex Forbes, The Biological Laboratories, Harvard University, Divinity Ave., Cambridge, Mass.

I am still doing research. It is on the color sense of the allcone retina of diurnal lizards.

Charles H. Best, 112 College St., Toronto, Canada.

I am just going to chair a seminar by one of my pupils, D. G. Baker, who has recently accepted a fine position as Senior Scientist at the Brookhaven National Laboratory.

Laurence Irving, Institute of Arctic Biology, Univ. of Alaska, College, Alaska 99735.

A study of some simple considerations like age relations to research and premature cessation of research may show how scientific accomplishment can be increased without the new machinery and personnel that may increase the overhead costs of science and introduce risk of diminishing the effectiveness of the existing social scheme in which science operates.

Curt P. Richter, Phipps Psychiatric Clinic, Johns Hopkins Hospital, Baltimore 5, Md.

At the moment I am working full time at my old job - harder and longer than before retirement - and having a lot of fun. Hope, however, to finish a monograph within the next few months based on last 8 years work.

A. Baird Hastings, Scripps Clinic and Research Foundation, 476 Prospect St., La Jolla, Calif.

I gave my first paper before the American Physiological Society at the Baltimore meeting in 1919. It was entitled: "The effect of fatigue on the bicarbonate content of blood plasma." (Paraphrased, this might have been: "The effect of metabolism on the CO_2 concentration of an extracellular fluid.")

My first paper before the Federation, after my return to laboratory work in 1959, was given at the 1962 meeting and the title was: "Effect of CO_2 concentration on carbohydrate metabolism in rat liver."

I have thus gone full circle in 43 years - and find myself engaged in one of the most interesting problems I've ever encountered.

H. E. Essex, President, National Society for Medical Research (Plummer Bldg., Mayo Clinic, Rochester, Minn.)

I have my hands full at present with the affairs of the National Society for Medical Research.

Stuart Mudd, VA Hosp., University & Woodland Aves., Philadelphia 4, Pa.

I am greatly enjoying my Emeritus status, working half time as Chief of the Microbiologic Research Program at the U.S. Veterans Administration Hospital, Philadelphia. This program is supported by grants from the National Institutes of Health and the Veterans Administration Central Office Research Service. Our program concerns Pathogenesis, prevention and treatment of staphylococcal infection.

In the other half of my time I have been much preoccupied during the past two and a half years with editing volume II of the World Academy of Art and Science, "The Population Crisis and the Use of World Resources," which should be published by Dr. W. Junk, of the Hague, next month. An American edition will be published by the Indiana University Press in April 1964.

Roberta Hafkesbring, Dept. of Physiology, Woman's Medical College of Pennsylvania, East Falls, Philadelphia, Pa.

Dr. Dong J. Kim, of Ewha University, Seoul, Korea, has invited me to teach for a year in the Medical School associated with that University. I have promised to stay at Woman's Medical College through the Spring of 1964 and am planning to go to Korea during the Fall.

Arthur H. Steinhaus, George Williams College, 5315 Drexel Ave., Chicago 15, Ill.

The year 1962-63 provided me with an interesting opportunity to serve in the Department of Physical Education of Tokyo University. My assignment was to teach physiology as it applies to physical education, to graduate students. Since my invitation was jointly from the University of Tokyo and the Japanese Olympic Committee, much of my activity took place outside the University. It was my privilege to lecture in some twenty-three universities and a large number of conferences. Outside of my regular assignment at the University I was permitted to make a total of 156 talks in the ten months.

Harry Goldblatt, Mount Sinai Hospital, University Circle, Cleveland 6, Ohio.

Although I was obliged to retire from my position as Director of Laboratories of Mount Sinai Hospital, I was permitted to remain as the Director of L.D. Beaumont Memorial Research Laboratories of this institution, and am gainfully employed.

F. D. W. Lukens, Cox Institute, University Hospital, 36th & Spruce Sts., Philadelphia 4, Pa.

I had the pleasure of working with Fred Hitchcock in Iran last year. He was Visiting Professor of Physiology while I was Visiting Professor of Medicine. He is doing a fine job.

Edward J. Van Liere, School of Medicine, Univ. of West Virginia, Morgantown, W. Va.

I still have two years at this University (mandatory age of retirement is 70).

Our monograph, "Hypoxia", published by the University of Chicago Press is just out.

C. I. Reed, 1816 B. Riverside Drive, Columbus, Ohio 43212

I'm trying to finish up a History of Physiology in North America that has been brewing for twenty years. Part of it will be in the nature of elaboration of the installments previously published in "The Physiologist."

Walter C. Alvarez, 700 Michigan Ave., Chicago, Ill.

I am glad I had some seventeen years in physiology because I think I am still thinking as a physiologist in regard to many problems of disease. For years I could not make up my mind whether I should try to stay in physiology which I loved, or to stay in clinical medicine, which I also loved. Finally the depression of 1929 solved the problem because I lost the appropriation for my lab.

Anna Goldfeder, Cancer and Radiobiological Research Laboratory, New York (99 Ft. Washington Ave., New York 32, N.Y.)

I have a civil service position with the Department of Hospitals, City of New York, an associate professorship at the New York University and am in charge of this laboratory. I am very pleased to say that I have good facilities to continue my research work here.

R. G. Hoskins, 86 Varick Rd., Waban 68, Mass.

I resigned my post as what amounted to the job of Medical Consultant of the Boston Branch Office of Naval Research on my eighty-third birthday 1963. My collaborators at the office gave me a heart-warming going away party and subsequently, a birthday party at which the office of the Secretary of the Navy presented me with a very attractive plaque and commendatory citation.

Eleanor D. Mason, Dept. of Physiology, Harvard School of Public Health, 665 Huntington Ave., Boston 15, Mass.

From the Fall of 1964 I plan to go to England as one of a small ecumenical community, which we shall be starting there. One is a doctor, one a nurse, and I a physiologist - but we join as a religious community. We've all been in India. I expect we'll all miss our professional lives - but are thankful for going where we can continue, though older, to do, we hope, creative and useful work through prayer.

Oscar Riddle, R. F. D. 4, Plant City, Fla.

In "The Third Quarter Century" (History of the American Physiological Society, 1937-1962) Dr. Fenn properly notes the important role of the Society in the founding of both the Union of American Biological Society and its successor, the AIBS. It is little recognized, but here notable, that the Union - through sponsorship of a self-sustaining committee - became the foster-parent of the National Association of Biology Teachers, now apparently the largest (over 8,000 members) of our independent biological societies.

G. H. Wang, 283 Medical Science Bldg., Univ. of Wisconsin, Madison, Wis. 53706.

'The University of Wisconsin Press will publish in April 1964 G. H. Wang's "The Neural Control of Sweating." This monograph summarized the work of Wang and his associates up to July 1962 on the control mechanisms of the neural control of sweat secretion in anesthetized and non-anesthetized cats."

Eleven "over-eighty-five" members were heard from. We note that some of them were adolescing when our Society was founded in 1887.

W. H. Lewis: No comment.
C. D. Snyder: "In good health".
P. M. Dawson: "Thanks"
E. L. Opie: "Thank you for the opportunities suggested."
T. Sollman: "I am 89."
P. B. Hawk: "I have retired."
A. N. Richards: "If I should say 'Yes' to any of these questions, you would say 'No' - and you would be right."
E. L. Scott: "No outside activities."
O. Riddle: "Most answers must be 'No'. (Also see news item).
T. S. Githens: " I am over 85 years old."
G. H. Whipple: "No plans to leave Rochester."