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IMPORTANT NOTICE

In the interest of getting greater membership input into APS activities your attention is directed to two questionnaires enclosed with this issue of The Physiologist. They are concerned with the election of officers to the American Physiological Society and with the time and place of future Fall meetings of the Society. We would like to receive the opinions of a large percent of the membership and urge you to take the two to three minutes necessary to read the two enclosed pages, indicate your choice and return the ballots promptly to:

Dr. Ray G. Daggs
Executive Secretary and Treasurer
The American Physiological Society
9650 Rockville Pike
Bethesda, Maryland 20014

Thank you for your cooperation.

Robert M. Berne, M.D.
President

Editor's Page

This is to inform you that the editorship of *The Physiologist* will change with the next issue. Ray Daggs is retiring in December of this year. Orr Reynolds has been selected by Council to replace Daggs not only as editor of *The Physiologist* but as Executive Secretary-Treasurer of APS as well. The Publications Committee voted to continue *The Physiologist* in its present format. It contains official actions of the Society; the Fall Meeting abstracts; education articles; the Bowditch Lecture; the Past President's Address; some of the 30-minute introductory talks given at the Spring Meeting; and other items of interest to physiologists. Several organizations have copied the format, including the IUPS News Letter.

The Physiologist was started in 1957 on a two-year trial basis. It served the purpose of a "house organ" type of publication for the membership and as such was continued. It has been a pleasure for me to be your editor over the years. It is hoped you will support your new editor as you did me and send him articles of interest to physiologists.

APS MEMBERSHIP STATUS

September 1972

Regular Members	3542
Retired Members	219
Honorary Members	15
Associate Members	389
Retired Associate	1
	4166

DEATHS SINCE SPRING MEETING 1972

Jean-Pierre Cordeau - 7/2/71 - Chairman, Dept. Physiol., Univ. of Montreal
 Allan Hemingway - 4/22/72 - Chief, Cardiopulmonary Lab., VA Hosp., San Fernando, California
 Edward C. Kendall - 5/4/72 - Visiting Professor of Chemistry, Princeton University
 Margaret M. H. Kunde - 6/30/70 - Instructor, Dept. Medicine, Northwestern Medical School
 Sergius Morgulis - 12/71 - Professor Emeritus, Univ. of Nebraska
 Horace O. Parrack - 5/31/72 - Physicist, Aerospace Med. Res. Labs., Wright-Patterson AFB, Dayton, Ohio
 I. S. Ravdin - 8/27/72 - Professor Emeritus, Univ. of Pennsylvania
 Harry P. Smith - 4/11/72 - Professor Pathology, Univ. of Missouri Med. Ctr., Columbia
 J. Earl Thomas - 2/2/72 - Emeritus Prof. Physiol. & Biophys., Loma Linda University School of Medicine
 F. J. W. Roughton - (Honorary Member) - 4/29/72 - Professor Colloid Science, University of Cambridge, England

NEWLY ELECTED MEMBERS

The following, nominated by the Council, were elected to membership in the American Physiological Society at the Fall Meeting, 1972.

FULL MEMBERS

ADAIR, Eleanor R. : Assoc. Fellow, John B. Pierce Fndn. Lab., Yale
 ADIBI, Siamak A. : Asst. Prof., Dept. Med., Univ. of Pennsylvania
 AGNEW, William F. : Physiologist, Huntington Inst. Applied Med. Res. Pasadena
 AGRAWAL, Harish C. : Res. Asst. Prof., Dept. Pediat., St. Louis Children's Hosp.
 ANDERSON, Ralph R. : Assoc. Prof., Dairy Husbandry, Univ. of Missouri, Columbia
 AULL, Felice B. : Asst. Prof., Dept. Physiol. & Biophys., NYU
 BAGBY, Roland M. : Assoc. Prof., Dept. Zool. & Entomol., Univ. of Tennessee
 BAKER, Mary Ann : Asst. Prof., Dept. Physiol., USC Med. School
 BAKER, Robert G. : Asst. Prof., Dept. Physiol. & Biophys., Univ. of Iowa

- BANG, Nils U. : Assoc. Prof. Med., Chief, Hematol. Serv., Marion County Gen. Hosp.
- BARKER, Jeffery L. : Res. Assoc. NINDS, NIH
- BARMACK, Neal H. : Res. Assoc., Lab. Neurophysiol., Good Samaritan Hosp. & Med. Ctr.
- BARNARD, Roy J. : Res. Physiologist, Dept. Med., UCLA Sch. Med.
- BENGELE, Howard H. : Sr. Res. Assoc., Dept. Physiol., Univ. of New Mexico
- BERGMAN, Norman A. : Prof. & Chrmn. Dept. Anesthesiol., Univ. of Oregon Sch. Med.
- CASTRO, Gilbert A. : Assoc. Prof. Dept. Parasitology, Univ. of Oklahoma Health Science Ctr.
- CHEN, Stephen S. : Asst. Prof., Dept. Physiol., Univ. of Wisconsin
- CHENEY, Frederick W. : Assoc. Prof., Dept. Anesthesiol., Univ. of Washington
- CHURCHILL, Paul C. : Asst. Prof., Dept. Physiol., Univ. of Michigan
- CLARK, James M. : Res. Med. Officer, USAF Sch. Aerospace Med., San Antonio
- COHEN, Lawrence B. : Assoc. Prof., Dept. Physiol., Yale Sch. Med.
- COHEN, Sidney : Asst. Prof., Dept. Med., Univ. of Pennsylvania
- COLLIPP, Platon J. : Prof. Pediat., State Univ. of N.Y., Stonybrook
- COOKE, Julian P. : Res. Physiologist, Sch. Aerospace Med., Brooks AFB, San Antonio
- COSTILL, David L. : Assoc. Prof., Dept. Physiol., Indiana Univ.
- CURRY, John J. : Asst. Prof., Dept. Physiol., Boston Univ. Sch. Med.
- DAUGHARTY, Terrance M. : Asst. Prof., Dept. Med., Univ. of California, San Francisco
- DAWSON, Christopher A. : Asst. Prof., Dept. Med., Med. Coll. of Wisconsin
- DiSALVO, Joseph : Asst. Prof. Physiol. & Health Sciences, Ball State University
- FABRE, Louis F., Jr. : Head, Mental Retardation Res. Div., Texas Res. Inst., Mental Sci.
- FARIDY, Edmund E. : Asst. Prof., Dept. Physiol., Univ. of Manitoba
- FARNSWORTH, Wells E. : Assoc. Prof., State Univ. N.Y., Buffalo
- FIELD, Michael : Asst. Prof., Dept. Med., Harvard University
- FISCHER, Grace M. : Asst. Prof., Dept. Physiol., Univ. of Pennsylvania
- GAY, Vernon L. : Asst. Prof., Dept. Physiol., Univ. of Pittsburgh
- GEBBER, Gerard L. : Assoc. Prof., Dept. Pharmacol., Michigan State
- GEHA, Alexander S. : Asst. Prof., Dept. Surg., Washington Univ.
- GERLINGS, Eelco D. : Assoc. Prof., Dept. Physiol. & Biophys., Univ. of Nebraska
- GIBBS, Finley P. : Asst. Prof., Dept. Anat., Univ. of Rochester
- GORE, Robert W. : Asst. Prof., Physiol., Univ. of Arizona
- GRAYSON, John : Dept. of Physiol., Univ. of Toronto
- GRAYZEL, Arthur I. : Assoc. Prof. Med., Albert Einstein Coll. Med.
- HALL, Peter F. : Prof., Chrmn., Dept. Physiol., Univ. of California, Irvine
- HAWLEY, Philip L. : Assoc. Prof., Dept. Physiol., Univ. of Illinois
- HELFANT, Richard H. : Chief, Div. of Cardiol., Presbyterian-Univ. Pennsylvania Med. Ctr.
- HELMAN, Sandy I. : Asst. Prof., Dept. Physiol., Tulane Univ. Sch. Med.

- HENRICKS, Donald M. : Assoc. Prof., Dept. Biochem., Clemson Univ.
HERMRECK, Arlo S. : Asst. Prof., Dept. Physiol., Univ. of Kansas
Med. Ctr.
HINKE, Joseph A. : Prof., Dept. Anat., Univ. of British Columbia
HOFFMAN, Julien I. E. : Assoc. Prof. Pediat., Univ. of California,
San Francisco
HOROWITZ, John M. : Asst. Prof. Physiol., Univ. California, Davis
HOVERSLAND, Arthur S. : Assoc. Prof., Dept. Animal Sci., Fresno
State College
HOWELL, John N. : Asst. Prof., Dept. Physiol., Univ. of Pittsburgh
HUBER, Gary L. : Asst. Prof. Med., Harvard Sch. Med.
HUNTER, William S. : Asst. Prof., Dept. Physiol., St. Louis Univ.
INTAGLIETTA, Marcos : Assoc. Prof. Bioengineering, Univ. of
California, San Diego
KALOYANIDES, George J. : Asst. Prof., Dept. Int. Med., Univ. Iowa
KAMMER, Ann E. : Asst. Prof., Dept. Zool., Univ. California, Davis
KASCH, Frederick W. : Prof., Dept. Physical Ed., San Diego State Coll.
KNOX, Charles K. : Asst. Prof., Dept. Physiol., Univ. of Minnesota
KOKKO, Juha P. : Asst. Prof., Dept. Int. Med., Univ. of Texas S.W.
KOOYMAN, Gerald L. : Asst. Res. Physiologist, Univ. of California,
San Diego
KRULICH, Ladislav : Asst. Prof., Dept. Physiol., Univ. of Texas S.W.
LEE, Thomas C. : Asst. Prof., Dept. Human Physiol., Univ. of Cali-
fornia, Davis
LIEBESKIND, John C. : Asst. Prof., Dept. Psychol., UCLA
LOIZZI, Robert F. : Assoc. Prof., Dept. Physiol., Univ. of Illinois
McKEAN, Thomas A. : Asst. Prof., Dept. Zool. & Physiol., Univ. of
Wyoming
MARMOR, Michael F. : Teaching Fellow, Dept. Ophthalmol., Harvard
Med. Sch.
MIROLLI, Maurizio : Assoc. Prof. Neurophysiol., Indiana Univ.
MOORE, Lee E. : Asst. Prof., Dept. Physiol., Case Western Reserve
Univ.
MORIARTY, C. Michael : Asst. Prof., Dept. Physiol. & Biophys.,
Univ. of Nebraska
MUNSON, John B. : Asst. Prof., Dept. Neurosciences, Univ. of Florida
NAGLE, Francis J. : Assoc. Prof. Physiol. & Phys. Ed., Univ. of
Wisconsin
NASJLETTI, Alberto : Res. Assoc., Dept. Pharmacol., Med. Coll. of
Wisconsin
NEMOTO, Edwin M. : Asst. Prof. Dept. Anesthesiol., Univ. Pittsburgh
NEVILLE, Margaret C. : Asst. Prof., Dept. Physiol., Univ. of Colo-
rado Med. Ctr.
NEY, Robert L. : Prof., Dept. Med., Univ. of North Carolina
NICOLOFF, Demetre M. : Assoc. Prof., Dept. Surg., Univ. of Minne-
sota Hosps.
NOVY, Miles J. : Scientist, Dept. Perinatal Physiol., Oregon Regional
Primate Res. Ctr.
NUTTER, Donald O. : Assoc. Prof., Dept. Med., Emory Univ. Sch. Med.
PETERSON, Donald F. : Instr., Dept. Pharmacol., Univ. of Texas
PETROPOULOS, Evangelos A. : Asst. Prof., Dept. Physiol.-Anat.,
Univ. of California, Berkeley
PFAFF, Donald W. : Assoc. Prof., The Rockefeller University

- PHILLIPSON, Eliot A. : Asst. Prof., Dept. Med., Univ. of Toronto
- RAJU, K. G. : Assoc. Prof., Dept. Physiol., Tuskegee Inst.
- RAPER, Arthur J. : Asst. Prof., Dept. Med., Med. Coll. of Virginia
- RAVIN, Mark B. : Assoc. Prof., Dept. Anesthesiol., Univ. of Florida
- REEL, Jerry R. : Sect. Dir. Endocrinol., Parke, Davis & Co.
- RHOADES, Rodney A. : Asst. Prof., Lab. for Human Performance Res., Pennsylvania State Univ.
- ROBERT, Andre: Sr. Scientist, Exptl. Biol. Dept., The Upjohn Co.
- ROBERTS, Jane C. : Research Worker, Dept. Ophthalmol. Res., Columbia Univ.
- ROSSING, Robert G. : Assoc. Chief of Staff for Res. & Ed., VA Ctr., Temple, Texas
- SAXENA, Brij B. : Assoc. Prof. Endocrinol., Cornell Univ. Med. Coll.
- SCHACHTER, David: Prof., Dept. Physiol., Columbia Univ., P & S
- SHEEL, Konrad W. : Asst. Prof., Dept. Physiol. & Biophys., Univ. of Mississippi Med. Ctr.
- STEIN, Jay H. : Assoc. Prof., Dept. Med., University Hosp., Columbus
- STITT, John T. : Asst. Fellow, John B. Pierce Fndn. Lab.
- TANSY, Martin F. : Assoc. Prof. & Chrmn. Dept. Physiol., Temple Univ. Sch. Dentistry
- TYBERG, John V. : Sr. Res. Scientist, Dept. Cardiol., Cedars-Sinai Med. Ctr., L. A.
- VATNER, Stephen F. : Asst. Prof. Med., CV Lab., Univ. of California, San Diego
- VILLABLANCA, Jaime R. : Assoc. Res. Anatomist & Psychiatrist, Dept. Anat., UCLA
- WADDELL, William J. : Prof. Oral Biol., Assoc. Dir. Dental Res., Univ. of North Carolina
- WANGENSTEEN, O. Douglas: Asst. Prof., Dept. Physiol., Univ. of Minnesota
- WEISS, Robert M. : Assoc. Prof., Dept. Surg., Yale Univ. Sch. Med.
- WHEREAT, Arthur F. : Assoc. Prof., Dept. Med., Univ. of Pennsylvania
- WICKELGREN, Warren O. : Asst. Prof., Dept. Physiol., Univ. of Colorado Med. Ctr.
- WILLIAMS, Robert J. : Res. Scientist, Cryobiol. Dept., Am. Natl. Red Cross Res. Labs.
- WOLF, Matthew B. : Asst. Prof., Dept. Biomed. Eng. & Physiol., Univ. Southern California
- WOOD, Stephen C. : Asst. Prof., Dept. Zoophysiol., Aarhus Univ., Denmark
- ZAK, Radovan H. : Assoc. Prof., Dept. Med., Univ. of Chicago
- ZALEWSKI, Andrew A. : Surgeon, USPHS, Lab. Neuropathol. & Neuroanat. Sci., NIH
- ZATZMAN, Marvin L. : Assoc. Prof., Dept. Physiol., Univ. of Missouri

ASSOCIATE MEMBERS

- BAUMGARDNER, F. Wesley: Res. Physiologist, Sch. of Aerospace Med., Brooks AFB
- BOONE, Marshall N. Jr. : Grad Student, Res. Assoc., Physiol., Univ. of Alabama
- BROOKS, George A. : Asst. Prof., Dept. Phys. Ed., Univ. California, Berkeley

- CARLSON, Edwin L. : Postdoct. Fellow, CV Res. Ctr., Univ. of California, San Francisco
- CASABURI, Richard: Postdoct. Res. Assoc., Biomed. Eng., Univ. of Southern California
- CHAUDHURI, Tapan K. : Asst. Prof., Dept. Nuclear Med., Univ. of Iowa
- COURTNEY, Gladys A. : Prof. & Head, Dept. Gen. Nursing, Univ. of Illinois
- DONOVAN, Francis M. Jr. : Asst. Res. Prof. Engineering, Univ. of Utah
- DURHAM, Beatrice C. : Res. Asst., Dept. Physiol., Lankenau Hosp.
- FLAMENBAUM, Walter: Asst. Chief, Dept. Nephrol., Walter Reed Army Inst. of Res.
- FLOURNOY, Robert W. : Assoc. Prof., Dept. Zool., Louisiana Polytechnic Inst.
- FOLINSBEE, Lawrence J. : Grad. Student, Dept. Human Physiol., Univ. of California, Davis
- FORSTER, Hubert V. : NIH Postdoct. Fellow, Dept. Med., Univ. of Wisconsin
- FRAZIER, Loy W. Jr. : Predoctoral Student, Dept. Physiol., Univ. of Texas S.W. Med. Sch.
- FREDERICKS, Christopher M. : Res. Assoc., Dept. Pharmacol., Oregon State Univ.
- GERIN, Michel G. : Res. Assoc., Dept. Physiol. & Biophys., Univ. of Alabama
- GEUMEI, Aida M. : Postdoct. Fellow, Cardiopulmonary Inst., S. W. Med. School, Dallas
- GONZALEZ, Ramon R. Jr. : Predoctoral CV Trainee, Physiol. Dept., Bowman Gray Sch. Med.
- HEDLUND, Laurence W. : Asst. Prof., Dept. Dairy Husbandry, Univ. of Missouri
- HOLSINGER, James W. Jr. : Res. & Edu. Assoc., VA Hosp., Gainesville, Florida
- IANO, Thelma L. : Asst. Prof. Physiol., Case Western Reserve Univ., Cleveland, Ohio
- JOST, R. Gilbert: Staff Assoc., Lab. Neural Control, NIH, Bethesda, Maryland
- KEIL, Lanny C. : Physiologist, Environ. Biol. Div., Ames Research Ctr., Moffett Field, California
- KLUGER, Matthew J. : Postdoct. Fellow, John B. Pierce Fndn, Yale
- KWAN-GETT, Clifford S.: Assoc. Res. Prof. Surg., Univ. of Utah, Salt Lake City
- NICHOLS, Wilmer W. : Vis. Scientist, Investigator, Inst. Med. Physics, Utrecht, The Netherlands
- McHALE, Janiece S. : Res. Physiol., VA Hosp., Martinez, Calif.
- MASON, Walter H. : Asst. Prof., Dept. Biol., Thiel College, Greenville, Pa.
- MAXWELL, Leo C. : Postdoct. Fellow, Dept. Physiol., Univ. of Michigan, Ann Arbor
- MORGAN, Barbara N. : Fellow in Physiol., Geo. Washington Univ., Washington, D.C.
- MYHRE, Loren G. : Sr. Sci., Physiol., Lovelace Fndn. for Med. Edu. & Res., Albuquerque

- OWEN, Thomas L. : Grad. Student, Dept. Human Physiol., Univ. of California, Davis
- PARKHIE, Mukund R. : Postdoct. Resident Res. Assoc., NASA/Marshall Space Flight Ctr., Huntsville
- PETERS, Jeffrey L. : Asst. Res. Prof. Surg., Univ. of Utah, Salt Lake City
- RAMP, Warren K. : Asst. Prof. Oral Biol., Sch. Dent., Univ. of North Carolina, Chapel Hill
- RICKS, Robert C. : Scientist, Oak Ridge Associated Universities, Oak Ridge, Tenn.
- ROSENBERG, Alberto : Cl. Res. Physician, Atlas Chemical Industries, Inc., Wilmington, Del.
- RUSHMER, Donald S. : Assoc. Dir., Lab. Neurophysiol., Good Samaritan Hosp., Portland, Oregon
- SANDERS, Sue S. : Instr. Physiol. & Biophys., Univ. of Alabama
- ST. JOHN, Walter M. : Asst. Prof. Physiol. & Biophys., Univ. of Arkansas, Little Rock
- SCHATTE, Christopher L. : Postdoct. Fellow, Biochem., Colorado State Univ., Fort Collins
- STILLMAN, Robert D. : Postdoct. Fellow, Callier Hearing & Speech Ctr., Dallas, Texas
- SUKOWSKI, Ernest J. : Assoc. Prof. Physiol. & Biophys., Chicago Med. Sch., Chicago, Ill.
- VAN WYNSBERGHE, Donna M. : Grad. Student, Dept. Physiol., Univ. of Wisconsin, Milwaukee
- WEBSTER, James E. : Res. Assoc. Physiol., Univ. of Alabama
- WEISS, Ira P. : Postdoct. Fellow, Res. Div., Callier Hearing & Speech Ctr., Dallas, Texas

THE AMERICAN PHYSIOLOGICAL SOCIETY

Founded December 30, 1887; Incorporated June 2, 1923

OFFICERS 1972-1973

President - R. M. Berne, University of Virginia School of Medicine,
Charlottesville, Virginia

President-Elect - D. C. Tosteson, Duke University, Durham, North
Carolina

Past-President - J. R. Brobeck, University of Pennsylvania School
of Medicine, Philadelphia, Pennsylvania

Council - R. M. Berne (1974), D. C. Tosteson (1975), J. R. Brobeck
(1973), E. E. Selkurt (1974), Bodil Schmidt-Nielsen (1975), A. C.
Guyton (1976), J. Mead (1973).

Executive Secretary-Treasurer - Ray G. Daggs, 9650 Rockville Pike,
Bethesda, Maryland 20014

STANDING COMMITTEES

Publications - P. F. Curran (1975), Chairman; Paul Horowicz (1974),
A. P. Fishman (1975). Ex officio - J. R. Brobeck, Physiological
Reviews; J. M. Brookhart, Journal of Neurophysiology; J. R. Pappen-
heimer, Handbooks; R. G. Daggs, Executive Secretary-Treasurer,
Editor of The Physiologist and Associate Editor of Physiological Re-
views; Sara F. Leslie, Publications Manager and Executive Editor;
S. R. Geiger, Executive Editor for Handbooks; O. E. Reynolds,
Executive Editor for the Physiology Teacher.

Finance - J. M. Brookhart (1973), Chairman; C. F. Code (1973), E. B.
Brown, (1974). Ex officio - R. G. Daggs, Executive Secretary -
Treasurer; W. A. Sonnenberg, Business Manager.

Education - J. L. Kostyo (1973), Chairman; Leonard Share (1973), D. F.
Bohr (1973), A. Ames III (1974), F. N. Briggs (1974); Representatives
from Society of General Physiologists - B. A. Curtis (1973), P. B.
Dunham, (1973); Representatives from Comparative Physiology Divi-
sion of the American Society of Zoologists - I. J. Deyrup-Olsen (1974),
Patricia Farnsworth (1975). Orr E. Reynolds, Education Officer.

Membership Advisory - J. A. Herd (1973), Chairman; J. Metcalfe (1973)
W. C. Bowie (1973), S. Solomon (1974), J. P. Reuben (1973).

Program Advisory - F. F. Jobsis (1975), Chairman; H. M. Goodman
(1973), D. Kennedy (1973), M. F. Wilson (1973), S. Y. Botelho (1974).

Public Affairs - R. K. Crane (1973), Chairman; A. B. Otis (1973), H. D.
Patton (1974), J. B. Preston (1974), T. Cooper (1974).

Senior Physiologists - D. B. Dill (1974), Chairman; H. S. Mayerson
(1974), H. Davis (1975), M. B. Visscher (1975).

Perkins Memorial Fund - J. R. Pappenheimer (1974), Chairman; H. Rahn
(1974), E. E. Selkurt (1974), B. Schmidt-Nielsen (1974). Ex-officio-
Mrs. J. F. Perkins, Jr.; R. G. Daggs, Executive Secretary-Treasurer.

Porter Physiology Development Program - A. C. Barger (1974) and E. W.
Hawthorne (1974), Co-Chairmen; E. P. Radford (1974), W. C. Foster
(1974), H. V. Sparks (1973), W. Tong (1973), Clem Russ (1975).

Animal Care and Experimentation - H. R. Parker (1974), Chairman; E. T.
Angelakos (1974), L. S. Lilienfield (1974), W. J. Tietz, Jr. (1974).

Legal Counsel - W. H. Pattison, Jr.

REPRESENTATIVES TO OTHER ORGANIZATIONS

- Federation Board - D. C. Tosteson (1975), R. M. Berne (1974), J. R. Brobeck (1973).
Federation Executive Committee - J. R. Brobeck (1973).
Federation Publications Committee - J. W. Severinghaus (1973).
Federation Meetings Committee - D. C. Tosteson (1974).
Federation Program Committee - R. G. Daggs.
Federation Public Affairs Committee - R. K. Crane (1973).
Federation Public Information Committee - R. K. Crane (1973).
Executive Officers Advisory Committee of the Federation - R. G. Daggs
U. S. National Committee for International Union of Physiological Sciences - J. M. Brookhart (1975), A. C. Barger (1975), L. D. Carlson (1973), J. R. Brobeck (1976).
U. S. National Committee for International Union of Pure and Applied Physics - A. P. Gagge (1973).
U. S. National Committee for Engineering in Medicine and Biology - M. L. Wolbarsht (1975).
National Research Council, Div. of Biology and Agriculture - H. Gainer (1973); Div. of Medical Sciences - M. B. Burg (1973).
American Association for the Advancement of Science - W. G. Van der Kloot (1973), E. L. Masoro (1973).
National Society for Medical Research - H. R. Parker (1973).
American Society for Information Science - S. R. Geiger (1973).
Council of Academic Society of the Association of American Medical Colleges - A. B. Otis (1974), L. D. Carlson (1974).

PUBLICATIONS

- Publications Committee - P. F. Curran (1975), Chairman; P. Horowicz (1974), A. P. Fishman (1975).
Publications Manager and Executive Editor - Sara F. Leslie
American Journal of Physiology and Journal of Applied Physiology - Section Editors - D. F. Bohr, F. J. Klocke, W. C. Randall (Circulation); L. E. Farhi, T. C. Lloyd, Jr. (Respiration); W. B. Kinter, E. E. Windhager (Renal and Electrolyte); S. G. Schultz (Gastrointestinal); N. S. Halmi, F. E. Yates (Endocrinology and Metabolism); H. S. Belding, A. P. Gagge (Environmental); L. B. Kirschner (Comparative and General); O. A. Smith (Neurobiology); O. D. Ratnoff (Hematology); F. N. Briggs (Muscle).
Journal of Neurophysiology - J. M. Brookhart, Chief Editor
Physiological Reviews - J. R. Brobeck, Chairman, Editorial Board; D. R. Wilkie, Chairman, European Committee; R. G. Daggs, Associate Editor
Handbooks of Physiology - J. R. Pappenheimer, Chairman Editorial Committee; S. R. Geiger, Executive Editor
The Physiologist - R. G. Daggs, Editor
The Physiology Teacher - Nancy S. Milburn, Editor; O. E. Reynolds, Executive Editor
Physiology in Medicine (in the New England Journal of Medicine) - A. P. Fishman, Editor

PAST OFFICERS

Presidents - 1888 H. P. Bowditch. 1889-1890 S. W. Mitchell. 1891-1895 H. P. Bowditch. 1896-1904 R. H. Chittenden. 1905-1910 W. H. Howell. 1911-1913 S. J. Meltzer. 1914-1916 W. B. Cannon. 1917-1918 F. S. Lee. 1919-1920 W. P. Lombard. 1921-1922 J. J. R. MacLeod. 1923-1925 A. J. Carlson. 1926-1929 Joseph Erlanger. 1930-1932 W. J. Meek. 1933-1934 A. B. Luckhardt. 1935 C. W. Greene. 1936-1937 F. C. Mann. 1938-1939 W. E. Garrey. 1938 W. T. Porter Honorary President. 1940-1941 A. C. Ivy. 1942-1945 P. Bard. 1946-1947 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 H. Davis. 1959 R. F. Pitts. 1960 J. H. Comroe, Jr. 1961 H. W. Davenport. 1962 H. S. Mayerson. 1963 H. Rahn. 1964 J. R. Pappenheimer. 1965 J. M. Brookhart. 1966 R. E. Forster. 1967 R. W. Berliner. 1968 L. D. Carlson. 1969 C. L. Prosser. 1970 A. C. Barger. 1971 J. R. Brobeck.

Secretaries - 1888-1892 H. N. Martin. 1893-1894 W. P. Lombard. 1895-1903 F. S. Lee. 1904 W. T. Porter. 1905-1907 L. B. Mendel. 1908-1909 Reid Hunt. 1910-1914 A. J. Carlson. 1915-1923 C. W. Greene. 1924-1929 W. J. Meek. 1930 A. C. Redfield. 1931-1932 A. B. Luckhardt. 1933-1935 F. C. Mann. 1936-1939 A. C. Ivy. 1940-1941 Philip Bard. 1942 C. J. Wiggers. 1943-1946 W. O. Fenn. 1947 M. B. Visscher.

Treasurers - 1888-1892 H. N. Martin. 1893-1894 W. P. Lombard. 1895-1903 F. S. Lee. 1904 W. T. Porter. 1905-1912 W. B. Cannon. 1913-1923 Joseph Erlanger. 1924-1926 C. K. Drinker. 1927-1936 Alexander Forbes. 1937-1940 W. O. Fenn. 1941 C. J. Wiggers. 1942-1946 Hallowell Davis. 1947 D. B. Dill.

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

CONSTITUTION AND BYLAWS

CONSTITUTION

(Adopted at the 1953 Spring Meeting)

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 1966)

ARTICLE I. Principal Office

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

ARTICLE II. Corporate Seal

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

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

ARTICLE III. Membership

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

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

SECTION 3. 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 regular membership shall be eligible for proposal for associate membership in the Society provided they are residents of North America. Associate members may later be proposed for regular membership.

SECTION 5. Retired Members. A regular or associate member who has reached the age of 65 years and/or is retired from regular employment may, upon application to Council be granted retired member status.

SECTION 6. Sustaining Associates. Individuals and organizations who have an interest in the advancement of biological investigation may be invited by the President, with approval of Council, to become sustaining associates.

SECTION 7. Nominations for Membership. Two regular members of the Society must join in proposing a person for regular membership, honorary membership or associate membership, in writing and on forms provided by the Executive Secretary-Treasurer. The Membership Committee shall investigate their qualifications and recommend nominations to Council. Council shall nominate members for election at the Spring and Fall meetings of the Society. A list of nominees shall be sent to each regular member at least one month before the Spring and Fall meetings.

SECTION 8. Election of Members. Election of regular members, honorary members and associate members shall be by secret ballot at Spring and Fall business meetings of the Society. A two-thirds majority vote of the members present and voting shall be necessary for election.

SECTION 9. Voting. Only regular members shall be voting members. Honorary, retired and associate members shall have the privilege of attending business meetings of the Society but shall have no vote.

ARTICLE IV. Officers

SECTION 1. Council. The management of the Society shall be vested in a Council consisting of the President, the President-Elect, the immediate Past-President, and four other regular members. The terms of the President and of President-Elect shall be one year. The terms of the four additional 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 quorum for conducting official business of the Society shall be five of the seven elected members of Council.

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

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

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

SECTION 4. Election of Officers. Nominations and election of a President-Elect and Councilor(s) shall be by secret ballot at the Spring business meeting of the Society. They shall assume office on July 1 following their election.

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

ARTICLE V. Standing Committees

SECTION 1. Publications Committee. A Publications Committee composed of three regular members of the Society appointed by Council shall be responsible for the management of all of the publications of the Society. The term of each member 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. Council is empowered to appoint and compensate a Publications Manager who shall assist in carrying out the functions of the Publications Committee under the supervision of the Executive Secretary-Treasurer. The President, Executive Secretary-Treasurer and the Publications Manager shall be ex officio members of the Publications Committee without vote. The

Committee shall have the power to appoint editorial boards for the Society's publications. The Committee shall present an annual report on publications and policies to the Council for approval and present an annual budget coordinated through the Executive Secretary-Treasurer, to the Finance Committee for its approval and recommendation to Council.

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

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

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

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

ARTICLE VI. Dues

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

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

quent of his right to request reinstatement.

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

ARTICLE VII. Financial

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

SECTION 2. Publications Operating Fund. The Publications Operating Fund shall consist of all funds that involve receipts, expenses, short-term investments relating to the annual receipts, disbursements and continuing operation of the Society's publications. The Executive Secretary-Treasurer shall be the responsible agent to the Council with signatory powers. Signatory powers may be delegated to the Publication Manager and/or the Business Manager by the Executive Secretary-Treasurer.

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

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

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

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

ARTICLE VIII. Publications

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

ARTICLE IX. Meetings

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

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

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

SECTION 4. Quorum. At all business meetings of the Society fifty regular members shall constitute a quorum.

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

ARTICLE X. Society Affiliations

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

ARTICLE XI. Regulations

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

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

- publishing or distributing of statements) any campaign on behalf of any candidate for public office.
- d. The Society shall not be organized or operated for profit.

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

ARTICLE XII. General

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

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

ARTICLE XIII. Amendments

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

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

THE ANIMAL WELFARE ACT OF 1970

A Report from the Committee on Animal Care and Experimentation

HAROLD R. PARKER

Laws which have been passed in recent years plus suggested amendments to these laws may jeopardize some biomedical research unless all investigators using warm blooded animals take time to learn the implications of the laws and make certain that they and their associates adhere strictly to the new codes.

A brief history regarding recent national legislation is in order. Public Law 89-544 was passed on August 24, 1966. This law was known as the Laboratory Animal Welfare Act. It applied to a limited number of species (dog, cat, non-human primates, guinea pigs, hamsters, and rabbits; rats and mice were excluded) and confined the authority of the Secretary of Agriculture to supervising conditions of housing and care of these species to the periods when they were in stock and storage. The main purpose of the law was to establish definite regulations regarding housing for the species involved as well as to require systems for identification and record keeping. Dealers in the species listed had to be licensed and conform to all regulations.

On December 24, 1970 the President signed Public Law 91-579 which amended PL 89-544. The new law was called "The Animal Welfare Act of 1970." The major changes incorporated in the Animal Welfare Act of 1970 are: 1) It removed the implication that animals used in research were more deserving of humane treatment than animals used for other purposes, and 2) the new act covers animals in zoos, circuses, carnivals, and exhibitions. It also includes all animals held by wholesale pet dealers as well as those used in scientific study.

The major changes affecting laboratory animals in the present law are that it 1) includes all species of warm blooded animals (not just the six species listed under PL 89-544), and 2) it covers conditions for housing and care throughout an animal's stay in a research facility (not just while the animal is in storage). The Animal Welfare Act of 1970 provides a specific prohibition against interference by the Secretary of Agriculture or his representatives with the design or execution of any experiment. There is, however, a clear requirement that all experiments be conducted with the animal under appropriate analgesics, tranquilizers or anesthetics unless the design of the experiment is such that results would be rendered unusable if these agents were used. In cases where the experiments were performed without the use of analgesics, tranquilizers, or anesthetics, a brief explanation is required with the annual report.

The institution housing the research is responsible for the conduct of all experiments. By February 1st of each year, commencing in 1973, a report must be submitted to the Federal veterinarian who represents the USDA in that state. The Federal veterinarian will report to his chief who in turn will report his findings. This report must originate from

the attending veterinarian of the research facility or from an institutional "laboratory animal" committee composed of three persons, one of whom must be a doctor of veterinary medicine. The attending veterinarian or institutional committee must certify that all experimentation was conducted according to requirements of the law. Violation of the law by any segment of a research facility could invoke the penalty provisions of the Act. See Sec. 19(A) of the Act.

It is important that each investigator realize that the law applies to animal care not only during experimentation, but also during any recovery period. It is essential in cases where animals are not euthanized at the termination of an experiment that specific instructions regarding care of the animals during recovery be given to the animal caretakers in writing so that appropriate medication is administered to keep the animals comfortable during the post-surgical period. Records must be available to show clearly that no animal was abandoned after experimentation had been completed, or during post-surgical recovery.

While the Animal Welfare Act of 1970 satisfies most reasonable demands of humane society groups and guarantees against bureaucratic control of research, there are continuing pressures on congress to force through additional restrictive legislature. It appears that opponents to animal research intend to work within the new law by applying their interpretation to certain sections. By continuous persuasion they intend to cause these sections to incorporate requirements which would cripple biomedical research because of expense or technical difficulties involved in meeting the requirements.

The latest pressure is for modification of the law to include a mandatory requirement for daily exercise for dogs and cats outside the cage (see Federal Register, March 1972). Most physiologists will agree that exercise is necessary for good health. Persons with experience raising and handling caged animals also know that animals do exercise within their cages providing the cages have adequate floor space. Regulations issued under the law specifically state the amount of space which must be provided for each caged animal. It is also well known that placing animals in runs does not guarantee they will exercise. It appears that exercise is being equated with "release from confinement", a comparison which has no scientific basis.

The Department of Agriculture realizes there has been little research conducted which indicates that dogs and cats need exercise outside their cages. Its staff also knows that if studies indicate additional exercise beyond that normally obtained in the cage is necessary there are ways and techniques for obtaining it which are more efficient than resorting to runs. For example, by using treadmills or bull-ring type exercises. The Department has already conducted a series of work sessions with various interested groups to determine whether there should be revision of the law. Persons included in the sessions were from the research community, pet industry, humane societies, and exhibitors. A report based on the work sessions will be published as soon as completed, with a target date of December 1972.

The Department would be assisted in its deliberations if every investigator who has objective scientific information relative to comparing the health status of dogs or cats raised in cages, or maintained in cages for long periods without exercise outside the cage, would file a report with the Department based on his experiments. It would be of little value to report subjective observations as the Department already has many reports of this type.

What is needed are hard facts such as hematological data, growth rate comparisons, skeletal development, behavioral studies, etc. At the moment the numbers of observations need not be large but must be based on a sound protocol. In reports or publications submitted the housing utilized must have been at least equivalent to the minimum standards of the current laws. Address all correspondence to Dr. C.O. Finch, Senior Staff Veterinarian, Laboratory Animal Staff, Animal Plant and Health Service, USDA, Hyattsville, Maryland. Replies are urgently needed at an early date to allow Dr. Finch and his staff adequate time to incorporate the information in their report to be published. Impact of this report could have a lasting effect on biomedical research, therefore, it is to the advantage of every investigator to have as much factual information submitted to the USDA as possible.

Scientists interested in conducting studies relative to effects of exercise obtained by caged animals vs. that of animals released into runs, or similar types of experiments on the normal animal may be able to obtain research support for their proposed studies from NIH. The Animal Resources Branch of NIH is willing to consider grant proposals relative to the biology of the dog. Any proposal must use as its baseline the minimum standards of the USDA as defined in the Animal Welfare Act of 1970. Limits beyond the minimum standards would be up to the investigator. Representatives of NIH emphasized that proposals previously submitted but not funded were too inclusive and did not clearly define exercise and how its effects would be determined. It is better to limit the number of parameters and do a thorough job on a few rather than attempt to study all aspects of the animal's physiology. Investigators should compare dogs or cats raised specifically for research as well as those obtained from pounds. Many complaints regarding long term caging are concerned with dogs which have previously been pets and are "house broken." Therefore, random source (pound) dogs should be included in proposed studies. Make certain that exercise is clearly defined and that ways of measuring it are practical and spelled out completely. Do not attempt to generalize.

The committee urges every member of APS involved in biomedical research utilizing warm blooded animals to obtain and study a copy of the Federal Register, Vol. 36, No. 248 dated Friday, December 24, 1971. This includes the rules and regulations of the Animal Welfare Act of 1970 as established by the USDA. It is also advisable to obtain a copy of the Federal Register, Vol. 37, No. 45, dated Tuesday, March 7, 1972 to learn of the proposed new standards with which the USDA is presently concerned. These documents may be obtained by writing the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C. 20402. Cost is 20 cents per copy, or by request from the USDA veterinarian in charge in each state, or from the office of Dr. Finch at Hyattsville, Md. (See above for address).

PAST-PRESIDENT'S ADDRESS

A Reconsideration of the "Biological Clock in the Unicorn"

JOHN R. BROBECK

"We had no pure physiologists, and it was considered that any surgeon or physician was competent to teach the science." Sir Edward Sharpey-Schafer, 1927.

"...every physiologist who has the future of his subject at heart will pursue the science for its own sake...dedicated in the first instance to physiology pure and unapplied." John F. Fulton, 1949.

Sharpey-Schafer was writing of physiology in England in the middle part of the nineteenth century, noting that it was far behind the development of science in France and Germany. More than a hundred years later, however, we hear once more the opinion that almost anyone can teach physiology, and we wonder if a time will come when professional physiologists no longer hold prominent positions on medical faculties.

My remarks tonight have two themes. First, I plan to discuss what John Fulton recommended, the pursuit of the "pure and unapplied" science of physiology; this concept I first heard in the laboratory of Stephen Walter Ranson at Northwestern as a graduate student in 1936. To develop this theme a figure will be used, the ancient and mysterious occupation of entrapping a unicorn. Second, I shall ask you to consider how medical education seems to progress in a manner that shows stages, cycles, or even fashions. The figure is in a paper written by LaMont C. Cole in 1957 under the title, "Biological Clock in the Unicorn." I hope to demonstrate that it is not the unicorn that has the cycles but rather the unicorn hunters.

A young man who was a medical student while I was teaching at Yale has written recently that research was introduced into academic departments in medical schools beginning in 1946, and has implied that modern medical education dates from that time. Most persons in fact will set the date at about 1910 and the Flexner report. My own teachers said it was even earlier, in the eighteen seventies to nineties with the opening of the Johns Hopkins institutions. Yet a hundred years before Johns Hopkins, that is, in the 1760's, John Morgan, Thomas Bond and William Shippen, Jr., well understood the importance of 1) basic science, of 2) bedside teaching, and of 3) a university affiliation when they founded in 1765 what later became the School of Medicine of the University of Pennsylvania (Corner, 1965). And it is a matter of record that the importance of science in medical education was established at least fifty years prior to John Morgan, in the first part of the eighteenth century, when physiology under the title, "Institutes of Medicine" was taught at Leyden by Hermann Boerhaave. In his 1910 report Flexner stated that what was good in early American medical education was derived from the University models in Leyden and Edinburgh. What was bad began in 1810 in the form of proprietary schools that were modelled after the London Hospital schools.

The mailing address of the Department of Physiology at the University of Pennsylvania is the Richards Building -- a unique structure designed by a famous professor of architecture, Louis Kahn. It is named for Alfred Newton Richards, beloved and distinguished physiologist and pharmacologist who honored the University by his presence from 1910 until his death in 1966. The plaque naming the building bears a thistle. This delighted Dr. Richards, because he had received an honorary degree from the University of Edinburgh. The thistle was placed on the plaque, however, mainly to recall the influence of the Scottish university upon this School of Medicine in the years just before and just after the American revolution. It was to Edinburgh, but also to London and to a few of the Continental universities, that young men trained via the preceptorial system of medical education in the colonies went to receive their formal training and their degrees. John Morgan, the first Professor of Medicine, and William Shippen, Jr., the first Professor of Anatomy and Surgery, had studied there, under Alexander Monro secundus in anatomy, John Hope in botany, and William Cullen and Robert Whytt in theory and practice of medicine (Corner, 1965).

In 1789, fourteen years after the medical school was opened and well after the difficulties it suffered during the war, Caspar Wistar was appointed to the professorship of chemistry by the trustees of the College of Philadelphia. He proposed that he be authorized to lecture also in the Institutes of Medicine, the discipline that included physiology and pathology. At Edinburgh at that time Cullen held such a chair. The trustees approved Wistar's suggestion, and he was then appointed as the first Professor of the Institutes of Medicine in the Colonies. He held the position for only two years, however, because two years later when the College of Philadelphia was united to the University of Pennsylvania, Wistar resigned in favor of Benjamin Rush. Wistar had received his M.D. degree from Edinburgh in 1786, Rush in 1768 before the war.

Robert Whytt, Professor of Theory and Practice of Medicine at Edinburgh from 1747-1766, was also a pioneer neurophysiologist. He had been educated at St. Andrews, Edinburgh, London, Paris and Leyden, and he received his medical degree from Rheims. He is remembered for studies of reflex action, including proof that the response of the pupil to light is a neural reflex (Talbot, 1970). Like most of the other members of the Edinburgh faculty, the dominant influence in the medical and scientific training he received came from Hermann Boerhaave of Leyden.

I have taken what may seem a long way around to come to this man, Boerhaave. Nevertheless, I believe that to him can be attributed the concept that physiology is a necessary preparation for medicine. Born in 1669, educated primarily at Leyden, appointed Professor of Medicine and Botany in 1709, Professor of Practical Medicine in 1714, and Professor of Chemistry in 1718, he established the academic discipline we know as physiology through publication of his lectures on the Institutiones Medicae, first made available in 1708. Lindeboom suggested that, "Apparently the author considered that physiology was the most important but much-neglected subject in the medical course. So the physiological part is not only the most extensive but also the best-documented part of the Institutes" (p. 73). As noted above, the title of the volume became

the name of the chair at Edinburgh, and subsequently at the University of Pennsylvania.

I wonder whether Boerhaave ever thought about trying to catch a unicorn?

One should recall that the name, unicorn, appears in the King James translation of the Bible, in a context where more modern versions use the term, wild ox. A head of the animal adorns the badge of the Stewart clan; two white unicorns are supporters on the arms of Scotland, gorged and crowned, with thistles growing from the ground beneath them. One of these beasts is a supporter on the Royal Arms of Great Britain -- on the right side as used in Scotland, on the left in England.

In portraying a hunt for a unicorn that was successful, but that ended in deepest tragedy, T. H. White (1963) has given the following description:

"When the unicorn came, things were different from what had been expected. He was such a noble animal, to begin with, that he carried a beauty with him. It held all spell-bound who were within sight."

"The unicorn was white, with hoofs of silver and a graceful horn of pearl. He stepped daintily over the heather, scarcely seeming to press it with his airy trot, and the wind made waves in his long mane, which had been freshly combed. The glorious thing about him was his eyes. There was a faint bluish furrow down each side of his nose, and this led up to the eye-sockets, and surrounded them in a pensive shade. The eyes, circled by this sad and beautiful darkness, were so sorrowful, lonely, gentle and nobly tragic that they killed all other emotion except love" (p. 258).

T. H. White reported that the four boys, Gawaine, Agravaire, Gaheris, and Gareth, sons of King Lot and Queen Morgause of Lothian and Orkney, followed literally the instructions of the Bestiary called Liber de Natura Quorundam Animalium. The unicorn was swift and timid as the antelope, and could be captured in only one way. You had to have a virgin for bait, and when the unicorn saw that she was alone he would come at once to lay his head in her lap. The boys impressed into their plans a most reluctant kitchenmaid, one Meg, and persuaded her to wait alone for the unicorn by tying her pigtails together around a heather root.

But when the unicorn came, overwhelmed simultaneously with love, with an unconscious sense of destiny, with unrecognized cruelty, and incidentally with a desire to please their mother, they stabbed it to death with boar spears and cut off its beautiful head so as to drag it home as a mangled trophy.

When I arrived in Philadelphia in February 1952, I found that I had not only the oldest chair, but the oldest desk, the oldest benches, the oldest sinks, and the oldest equipment - not only the oldest in the country but probably in the Western World. Then a few months later I discovered that in 1926 my immediate predecessor, Cuthbert Bazett (1885-1950) had described with his typical enthusiasm those same buildings, facilities,

courses, and library as an up-to-date, completely rejuvenated department of physiology. Moreover, Bazett's predecessor, Edward Reichert (1855-1931), had published a similarly glowing account of the new building and his new apparatus just 25 years earlier, in 1901.

One can see some sort of pattern here -- Reichert's paper in 1901, Bazett's in 1926, with Brobeck on the scene ready for a renaissance in 1952, and R. E. Forster taking over in 1970.

Edward Tyson Reichert graduated from the medical school of the University of Pennsylvania in 1879, and then from 1882 to 1885 studied at Berlin where DuBois-Reymond and Helmholtz were professors, at Leipzig under Carl Ludwig, and at Geneva. Upon his return to Philadelphia he was appointed as Demonstrator in Physiology, and then as Professor in 1886. The following year with the formation of the American Physiological Society by Bowditch, S. Weir Mitchell and H. Newell Martin, Reichert was listed as one of the 28 original members (Howell, 1938). His best known publication is an oversize monograph on the crystallography of hemoglobins.

The building originally known as "The New Laboratories of Pathology, Pharmacology and Physiology" was dedicated in 1904 (Anon., 1904). Perhaps carried away by the prospects of the new building, and by the elegance of the instruments he was having manufactured in his own shop, Reichert wrote in 1901: "... in the University of Pennsylvania the teaching of this subject has undergone such progress and reached such standards in methods and equipment as to attract attention in this country and abroad." He stated that in the course were utilized commercial models of muscle and heart clamps, perfusion cannulae, microscopes, live stages, centrifuges, hemocytometers, hemoglobinometers, urinometers, plethysmographs, ergographs, galvanometers, electrometers, polarimeters, artificial eye models, gas pumps, and chemical apparatus. His own attention, on the contrary, had been given to items that could not be purchased, and that included a laboratory table, apparatus for recording, and apparatus for stimulating muscle or nerve. Reichert said that the kymograph was adapted from Ludwig and Sherrington, and the inductorium and other stimulating apparatus from DuBois-Reymond. He chose as objectives for the course, "...the training in the use of instruments of precision with especial reference to clinical and experimental medicine, the cultivation of the individual powers of observation and deduction, the encouragement of and insistence upon accuracy of method and expression, and the prosecution of collateral work with the view of the coordination of facts and their broad application..."(p. 1).

The next report that a unicorn had been cited in Philadelphia is dated 1926; the author was Henry Cuthbert Bazett, M.D. Oxon., trained in physiology in the department where Sherrington and John Scott Haldane were uneasy professorial colleagues. (Haldane and his teacher and preceptor, Burdon-Sanderson, had both received their medical training at Edinburgh.) Much of what Bazett had was undoubtedly bequeathed to him by Reichert, including "...a large machine shop fitted with three lathes, milling, drilling machines, etc., and a skilled mechanic who gives his whole time to the construction of new apparatus and repairs." Eventually

the Department also acquired essentially a full-time glassblower, "Jimmy" Graham, Sr., now living the year around at Woods Hole. Bazett wrote: "The aim of the Department in teaching may be stated as an attempt to make the medical instruction at once fundamental and yet more medical, the dental work more experimental and more adapted to dentistry, and the scientific teaching as purely scientific and fundamental as possible, rather than to develop a middle course not really adapted to any one of these three groups of students." This means that he had decided that, although it might be possible to pursue a goal of pure science for everyone, the Department would adopt rather a policy that now goes by the epithet, "relevant", for the courses for medical and dental students.

From 1952 until perhaps 1965, by contrast, a search for the unicorn was organized every year when we made our plans for the medical course. My bookshelf contains an appropriate series of oversized laboratory manuals that were the guide books of these expeditions. Every medical student was obliged to participate in a total of 35 laboratory experiments; apparatus nearly the equivalent of research equipment was secured for their use; and they were expected gradually to assume more and more of the responsibility for their preparations until they were, we hoped, performing their experiments as if they were becoming "real" physiologists. Through it all, of course, most of our students were just as reluctant as Meg was. Looking back on it now I suppose that the grading system, which we believed to be fair and even liberal, served the purpose of tying their pigtailed to the heather root. Consequently, when the revolution arrived and the students began to help plan the curriculum, most of the laboratory "exercises" went out the window, along with those of other departments in many of the schools of medicine in this country.

If we had succeeded in catching a unicorn in any of our many attempts, I wonder if we would have followed the experience of the four boys, and killed the lovely beast? To put this question more directly, can pure physiology survive if it is forcibly separated from medical education? Beginning with Boerhaave, physiology has existed in medical faculties for obvious reasons. It is concerned with material that medical, dental, and other students need to learn. It has made important contributions to the improvement in standards and techniques of medical care. The situation has been one, I believe, where conspicuous benefit has flowed in both directions. Medicine has gained from its foundation in, among other sciences, physiology; and physiology has drawn strength from its involvement in the medical enterprise. It is my conclusion that 250 years of history of medical education show that if physiology is to be moved out of medical schools, perhaps into college departments, the medical schools will then have to find some other way to present the material covered by the title, the "Institutes of Medicine" -- that is, what every medical student needs to know about the scientific basis of clinical practice.

Turning now to the second of my themes, what about the possibility of cycles in the unicorn? I noted already what seemed to be a pattern of development as marked by Reichert in 1901, Bazett in 1926, Brobeck in 1952, and now Forster in 1970. Before Reichert there was a long period of more than a hundred years when instruction was didactic,

classes were large, there were many lectures and no practical work nor bedside teaching. William Pepper, a physician who became Provost of the University of Pennsylvania, wrote in 1894 that the bright expectations of prerevolutionary medical educators were not at all achieved in the early days of independence of this country. In fact, he said that in 1846 the University "... made an unsuccessful attempt to elevate the standard of medical education... But the honor of having been the first to adopt the essential reforms... fairly belongs to the Medical School of Harvard College. In 1871 the authorities of that great University... determined that the system of education in the medical department should be reformed, so as to place it on the level of the other departments. There, as elsewhere, the plan met with the strongest opposition... But, in spite of discouragement and opposition, the needful reforms were instituted... Hereafter, when the historian... describes the hard struggle which was needed to establish true scientific medical education, it is to Harvard that he will award the praise of having been the first to step into the arena" (pp. 35-36).

Bowditch returned to Boston to the department of Oliver Wendell Holmes in 1871; by 1883 he had moved into quarters on Boylston Street where, for the first time, he had facilities for instruction of medical students. H. Newell Martin had been called from Cambridge to the chair at Johns Hopkins University in 1876, although the medical school was not opened until 1893. Reichert returned to Philadelphia from the Continent in 1885. In 1904 an anonymous author, who may have been Reichert, wrote: "The completion of the new medical department in West Philadelphia and its active operation date from 1877. The facilities for practical teaching were then unexcelled at any institution... One after another laboratory courses were instituted and enlarged." (From the Program for Dedication of the New Laboratories, Anon. 1904).

Richards H. Shryock (1947), a proper medical historian, has identified stages in the development of American medical education as follows: First, the Colonies received physicians trained where they had grown up, in Europe. Second, young Americans after local apprenticeships went to Europe for their formal education, particularly to Leyden, Edinburgh, and London. Third, from 1820 until 1860 the influence of the French schools was predominant; this coincided with the careers of Magendie and Claude Bernard. Fourth, beginning about 1840 but reaching full development only after the Civil War, the German schools broadcast their scientific achievements throughout the Continent, Great Britain, and the New World.

There is an essential corollary to the attainment of any new stage in medical education that is often overlooked. Pepper said that the University of Pennsylvania in 1846 had failed to elevate the standards of medical education. The American Medical Association had a similar experience. Organized in Philadelphia in 1847, one of its first acts was the establishment of a Committee on Medical Education, to encourage the utilization of "practical demonstration and clinical teaching..." (Johnson, 1949). Twenty-five years later in 1872 the Committee found that it had accomplished little. Simmons concluded, "Of all the resolutions adopted, and there were hundreds of them, not one can be regarded

as resulting in any specific good." (See Johnson, 1949, p.112). Undoubtedly he was correct. One must ask, therefore, when the reform came, what made the difference?

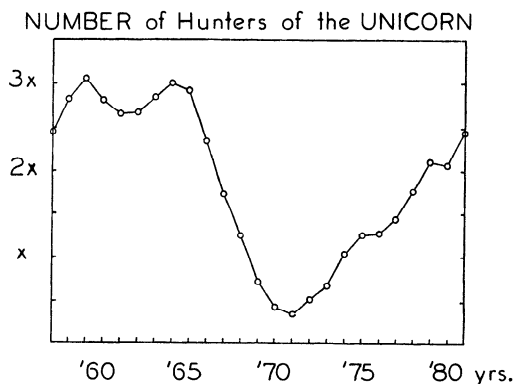
Two factors did, and two men. The first as Pepper noted, was the vision of President Charles W. Eliot of Harvard, who placed the resources of Harvard College behind his move in 1871; the second as recorded by Chesney (1943), was the generosity as well as the foresight of the Quaker, Johns Hopkins, whose will left \$7,000,000 for the endowment of a university and of a hospital, charters for which were granted in 1867. (The School of Medicine was separately endowed by other donors in about 1892, to the amount of \$500,000.) Harvard succeeded, and the Johns Hopkins institutions succeeded, where the University of Pennsylvania and the A. M. A. failed, because they had access to enough money to force the changes.

It is customary to identify the Flexner report No. 4 for the Carnegie Foundation in 1910 as the document that revolutionized medical education in this country. It did provide the philosophy of the revolution; but the battle was not won with documents, as Simmons had earlier recognized. Anyone who is inclined to overemphasize the significance of the Flexner report should read another book by the same author, "I Remember", his autobiography published in 1940. In recounting his association with medical education from 1910 until 1928, Abraham Flexner made it clear and emphatic that the success of the revolution depended upon the interest and commitment of one man--John D. Rockefeller, and the \$50,000,000 with which he endowed the General Education Board for medical education. Many of us come from schools that received significant portions of those funds, whether from Johns Hopkins, Harvard, Yale, Chicago, Rochester, Columbia and Cornell, Western Reserve, Washington University in St. Louis, Vanderbilt, Tulane, among others (but not the University of Pennsylvania because our faculty was opposed to any consideration of a full-time plan for clinical departments). Perhaps there is a law to the effect that academic revolutions always require new funding.

What I say tonight, therefore, will have no impact unless I can point out where the money will come from to finance our next expedition. In limited amounts it will come from individuals and foundations as in the past, and from state governments in the case of state schools. But principally it will come from the federal government, and it will come marked for medical education and health care. Now I have come full circle. Philosophically, I believe that our science must be an integral part of medical education; financially, that integration is our only hope of survival. Physiology is, to use Penfield's apt phrase, the "centrencephalic system" of health care, a principal foundation for improvement and for advancement of health sciences. If we should decide that this is not exactly the role we wish to play, someone else will come along to take it, because the entire production will collapse if this essential core is not preserved and strengthened.

Bob Pitts (1972), in accepting the award for contributions to teaching from the Association of Chairmen of Departments of Physiology, said:

"The situation will worsen over the next few years, but in time there will come another Flexner Report. My advice is salvage as much as possible and save it for the day of the renaissance." That he is right in his prediction can be verified from data published in 1957 by LaMont C. Cole in his paper, "Biological Clock in the Unicorn." Cole discovered his data in a table of random numbers, and then by manipulations that I shall not take time to explain produced an analysis that reveals inherent rhythmicity. I have only one criticism of his graph; he seems to have mislabeled the two axes. I happen to know that the time axis should be calibrated in years, not hours. The ordinate also is incorrectly labeled as "metabolic rate"; it should be rather, "number of unicorn hunters." I have taken the liberty of making these corrections on the accompanying graph. The actual position of the years on the abscissa cannot be taken as exact, and some slippage one way or the other may be required for complete accuracy. The century is not specified, either. The curve seems to fit the nineteenth century fairly well, although it is my judgment that it is intended to be applied to the twentieth. In spite of these uncertainties, the data show clearly that the years we have just finished represent the low point of interest in physiology as a science. Unfortunately, as the curve begins to rise the data do not reveal whether the increased numbers of hunters are licensed physiologists, or whether they are unlicensed, that is, erstwhile clinicians drafted to teach the Institutes of Medicine.



It seems to me that we shall do well to try to make this a self-fulfilling prophecy. We can, and we should, flood the heather with physiologists eager to take part in all of the new proposals and experiments in medical education, and in the creation of new "system" for delivery of health care, as well as in the search for fundamental new knowledge that physicians must have to conquer the most important clinical problems. Instead of being suspicious of what is taking place in medical education and health care, we should join in eagerly, ready to assume responsibility and to provide leadership in changes that must come. We can do this along the lines that Henry Bazett laid out in 1926. He decided to

strengthen the teaching of physiology in relation to medicine and dentistry (and we can now add, veterinary medicine and other related professions) for the benefit of the larger number of students who will enter those careers. At the same time, however, he intended to preserve and to develop opportunities in the science of physiology for students who will become investigators. During the tenure of his chairmanship many students entered physiology as a profession after their graduation from the medical school.

In keeping with these objectives we have seen an interesting change at the University of Pennsylvania since the new curriculum of the medical school was adopted in 1967. We now have a significant number of students who plan to secure really substantial education in a surprising variety of basic sciences and other disciplines. In the classes that entered from 1968 through 1971 there are a total of almost 50 students enrolled for combined M.D. -Ph.D. degree programs. Their fields of study range from biochemistry, physiology, and the other preclinical sciences, through molecular biology, psychology, biomedical engineering, chemical engineering, sociology, business administration, economics and even philosophy. The features of the new curriculum that have made this possible are three, as follows: First, the medical school adopted essentially the same calendar as the rest of the University; second, the required courses in basic science can be completed in two semesters (but can, on the contrary, be distributed over a longer period if a student so desires), and the required clinical clerkships likewise take only two semesters; third, payment of medical school tuition permits students to take courses in other schools of the University during their elective time. In other words, by making the science requirements shorter and more flexible, we are attracting actually more students who intend to secure advanced training in basic medical sciences. They don't need to be tied to a heather root by their pigtails to insure their cooperation in the hunt for the unicorn.

For almost 300 years physiology has been a powerful science. Its strength is drawn in part from the inherent interest of biological mechanisms and processes, but also in part from the utility an understanding of these processes finds in medicine and related professions. We must not be simplistic about our discipline. Intellectual curiosity does not need to be our only reason for existence. Neither is a practical application enough to insure the perpetuation of the science. The two go together -- the history of even our most distinguished forefathers shows that they do. We can well be guided by their experience.

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FUTURE MEETINGS

1973 Spring - Atlantic City, N. J. - April 16-20

1973 Fall - Univ. of Rochester, Rochester, N. Y. - August 20-25

1974 Spring - Atlantic City, N. J. - April 8-12

Biochemists meeting in Minneapolis - June 2-6

1974 Fall - State Univ. of New York at Albany - August 11-15

1975 Spring - Atlantic City, N. J. - April 14-18.

1975 Fall - Michigan State Univ., East Lansing, Mich.

EXCITATION-CONTRACTION COUPLING IN VERTEBRATE
SMOOTH MUSCLE:
CORRELATION OF ULTRASTRUCTURE WITH FUNCTION*

ANDREW P. SOMLYO

Dept. of Pathology, Presbyterian-University
of Pennsylvania Med. Ctr., and
Univ. of Pennsylvania Sch. Med., Philadelphia

Action potentials trigger the contractions of certain types of smooth muscles. This relationship between spike activity and contraction was already recognized through extracellular recording of electrical activity (8); considerable progress has been made in characterizing the action potentials of smooth muscles with the intracellular microelectrode and sucrose gap techniques (2,10,13,17,31,40,41,44,55,62,65, for further reference see 11,38,52). Single action potentials can trigger a twitch, and increases in the firing frequency of action potentials can lead to an increased amplitude of maintained contractions through a tetanic mechanism. Smooth muscle of some small resistance arteries is capable of spontaneous spike electrogenesis (68) and it is possible that the moment to moment regulation of peripheral vascular resistance in these species is regulated through electromechanical coupling of the action potential. A similar action potential-controlled mechanism probably also regulates motility of the gut (7,48).

Graded depolarization without accompanying action potentials is a second type of electrical response to excitatory drugs found in other smooth muscles (34,35,62,65,69,70) that are often more tonic (maintain K-contractions for longer periods) than the relatively more phasic spike generating smooth muscles (53,55,65).

Action potentials and depolarization of the membrane are important, but not essential, links of drug-induced contraction and relaxation, as originally shown by the responses of K-depolarized smooth muscles to drugs (27). The action potentials can also be blocked (with caffeine) in a polarized, normally spike-generating smooth muscle (the rabbit portal vein) without blocking drug-induced contractions (62). Drug-induced relaxation may also occur in polarized smooth (19) and tonic striated (53) muscles, without a necessary change (hyperpolarization) in the membrane potential. The process of excitation-contraction and inhibition-relaxation coupling that is not mediated by a change in membrane potential has been called pharmacomechanical coupling (52,54,62). Although it is probable that both electromechanical and pharmacomechanical coupling contribute to the excitation-contraction coupling process in normally polarized smooth muscles, the relative contribution of the two types of activation may vary and has not been quantitated.

* Taken from the introductory remarks given at the session on Smooth Muscle at the 1972 Federation Meetings.

The unequal maximal contractile response of a given smooth muscle preparation to different excitatory agents (1, 53, 55, 56, 62, 64, 65) is one of the more special properties of smooth muscles, and is not exhibited by fast striated muscles. The unequal maximal contractile responses persist after depolarization of the smooth muscles with high potassium solutions (21, 55, 62) and are, therefore, expressions of the unequal degrees of maximal pharmacomechanical coupling produced by different drugs and hormones. Pharmacomechanical coupling has been considered to be mediated by the unequal changes in membrane ion-permeability produced by different drugs, when it was found that in certain preparations of polarized smooth muscle the drugs producing lesser contractions also produced a lesser depolarization and, probably, lesser inward calcium movement (56, 65). The inequality of the maximal contractions produced by different drugs, however, is not due to comparable differences in the influx of extracellular calcium alone, because they can also be elicited in preparations that have been thoroughly depleted of extracellular calcium by the chelating agent EGTA (21). Some of the earlier observations of contractions of smooth muscle in nominally calcium-free solutions were difficult to evaluate (for review see 52, 54), because, in the absence of an adequate concentration of a calcium chelating agent, the levels of contaminant extracellular calcium may have contributed to contractile activation. Large drug-induced contractions in well-chelated calcium-free solutions were, however, observed in smooth muscle of turtles (9, 59). The lower temperatures used in experiments on the turtle smooth muscles apparently prevented the loss of intracellular activator calcium (59), and experimentation at lower temperatures has also been found to be suitable for demonstrating large drug-induced contractions of mammalian smooth muscles in the virtual absence (i.e. $< 10^{-8}$ M) of extracellular free calcium (21, 39, 59).

A rise in intracellular free calcium ion concentration is considered to be the primary event linking both electromechanical and pharmacomechanical coupling to contraction. Glycerinated smooth muscle (29), like glycerinated striated muscle, contracts when the free calcium concentration is raised above 10^{-7} M, provided adequate supplies of magnesium and ATP are present. Nonglycerinated smooth muscle is also contracted by externally added calcium if, by depolarization with potassium, the permeability of the surface membrane to calcium is increased (25, 76, for reviews see 6, 18, 37, 52, 54). A calcium sensitive actomyosin ATPase has been isolated from smooth muscle (67), as has the auxiliary protein (tropomyosin-B-troponin) system that confers calcium-sensitivity to actomyosin by inhibiting it in the absence ($< 10^{-7}$ M) of ionized calcium (24). The possibility that auxiliary mechanisms (changes in intracellular pH, substrate availability, magnesium, etc.) may modulate contraction of smooth muscle has been considered (54, 64), but lacking experimental evidence for this, the present discussion will be confined to activation by free intracellular calcium (Table I).

The physiological observations raise some questions that can be answered by electron microscopic studies. These questions are: 1) is there in vertebrate smooth muscles a sarcoplasmic reticulum that can accumulate divalent cations and function as an intracellular calcium store: b) are portions of this sarcoplasmic reticulum associated with

the surface membrane in a manner that would permit the electromechanical coupling of action potentials to twitch contractions through the release of calcium from the sarcoplasmic reticulum; c) are there any other intracellular organelles that may also contribute to the regulation of intracellular free calcium levels; d) are there significant differences between the distribution of potential calcium-storing sites in smooth muscles that have different functional properties? Another major question, amenable to electron microscopic study, is whether the contractile proteins actin and myosin are organized in vertebrate smooth muscle, as in striated muscles, in two separate sets of filament that contract through a sliding filament mechanism.

TABLE I

EXCITATION-CONTRACTION COUPLING
(leading to increased free cytoplasmic Ca^{++})

1. Electromechanical coupling
 - a. Action potential
 - b. Graded depolarization
2. Pharmacomechanical coupling

SOURCES AND SINKS OF ACTIVATOR CALCIUM

1. Extracellular
2. Sarcoplasmic reticulum [peripheral (junctional) and central including the perinuclear space]
3. ? ? Mitochondria

The presence of a sarcoplasmic reticulum in vertebrate smooth muscles has now been definitely established (21, 22, 59). Studies with extracellular markers (ferritin, colloidal lanthanum, horseradish peroxidase) clearly indicated that the tubular system that occasionally forms fenestrations about surface vesicles is a true sarcoplasmic reticulum that is not in direct communication with the extracellular space. In contrast, the surface vesicles ("Caveolae") are generally in free communication with the extracellular space and, judging from the available evidence (21, 22), cannot be considered as intracellular stores of calcium.

Peripheral elements of the sarcoplasmic reticulum approach the surface membrane over relatively long distances to within 100 Å, and this gap is traversed by electron opaque connections (21, 22, 59). These SR-surface membrane contacts resemble those of cardiac muscle (28, 66) and are the most probable sites of electromechanical coupling of the action potential to the twitch or tetanic contraction of smooth muscles. The possibility that the regions of the SR fenestrated around the surface vesicles (21, 22, 32, 51, 59) also contribute to electromechanical coupling cannot be excluded on ultrastructural grounds alone, but the surface vesicle-SR gaps do not show the periodic connections observed in triads of striated muscle and, in the opinion of the present author, are less likely to have a function similar to the triad.

Accumulation of a divalent cation by the sarcoplasmic reticulum of smooth muscle has also been demonstrated: after preincubation of smooth muscles in a strontium-containing solution, the (electron opaque) strontium is deposited in the sarcoplasmic reticulum (63). Strontium, like calcium, is accumulated by the isolated sarcoplasmic reticulum of striated muscle (45, 75, 77), and reduces the ^{45}Ca space of rabbit aortic strips (36). Microsomal preparations of smooth muscle also bind and/or accumulate calcium (e.g. 3, 4, 14, 30). These isolated microsomes probably contain other membrane (e.g. surface and mitochondrial) fractions in addition to the sarcoplasmic reticulum, and the demonstration of a direct relationship between ATP splitting and microsomal calcium uptake and of the potentiation of calcium uptake by oxalate have met with some difficulties. In combination with the electron microscopy of whole smooth muscle fibers, the studies with isolated preparations do support the view that there is a sarcoplasmic reticulum that can actively accumulate calcium in smooth muscle.

The volume of the sarcoplasmic reticulum is different in the two functionally different types of vertebrate smooth muscle: it is significantly larger in the rabbit aorta and main pulmonary artery than in the taenia coli, small mesenteric artery and portal vein of the same species. The larger volumes of sarcoplasmic reticulum may be related to protein synthesis: the morphogenetic function of smooth muscle (21, 22, 51). It is interesting that the smooth muscles that maintain a significant contractile response (rabbit main pulmonary artery, rabbit aorta) in calcium-free solutions also have the larger volume of sarcoplasmic reticulum than the smooth muscles (portal vein, taenia coli) that do not. While the ultrastructural correlation between a relatively large (central as well as peripheral) SR and maintenance of contractile response in calcium-free solution is seemingly good (21, 59), the possibility that this correlation is fortuitous cannot be excluded.

Mitochondria may be found in very close association with surface vesicles in some smooth muscles, and the average gap distance (40-50 Å) between the mitochondrial outer membrane and the surface vesicle membrane in rabbit portal vein (58) is in fact less than the SR-surface membrane gap at the couplings. This observation raised the possibility that the mitochondrial-surface vesicle relationships may function as ion transfer sites. Mitochondria in smooth muscle can take up the electron opaque divalent cations strontium and barium (22, 46, 51, 58, 63). Strontium, like calcium, can activate the contractile proteins directly (26) and its accumulation by mitochondria in spontaneously contracting smooth muscles (63) suggests that this uptake may contribute to relaxation. It must be emphasized, however, that the existing experimental observation (intra-mitochondrial strontium granules) is not sufficient to prove that mitochondria in smooth muscle play a quantitatively significant role in normal contractile regulation. The surface membrane itself may also bind calcium: direct competition between various cations for surface membrane sites of glutaraldehyde-fixed smooth muscle has been demonstrated by electron microscopy (33). The calcium associated with the unfixed (for red cell membrane see 15) plasma membrane is probably less than what is required (59) for the activation of contractile proteins, but may regulate the permeability properties of the surface membrane and perhaps

serve as "trigger calcium" (5, 22, 58).

Extracellular calcium probably also contributes to activation in smooth muscle, since excitatory agents including acetylcholine (23, 47), depolarization with high potassium solutions (74) and norepinephrine (58, 73) increase the permeability of the smooth muscle membrane to calcium. The presence of intracellular calcium storage sites does not exclude additional activation by extracellular calcium, and the relative contribution of the two sources may vary in different smooth muscles and under different experimental conditions. The ultrastructural findings combined with the contraction of certain smooth muscles in virtually calcium-free solutions clearly indicate, however, that the extracellular fluid cannot be the sole source of activator calcium in these smooth muscles.

The activation of smooth muscle by a mechanism independent of the membrane potential and not requiring extracellular calcium is of considerable physiological interest, as it is a property common to a variety of biological transmitters including amines and peptides (9, 21, 59). One possible mechanism suggested is that excitatory drugs initiate a primary permeability change in the surface membrane that triggers the release of calcium from the adjacent, junctional sarcoplasmic reticulum, and that the change in the calcium permeability of the junctional sarcoplasmic reticulum membrane is propagated to the contiguous central sarcoplasmic reticulum as a local circuit calcium current (22, 58). It must be stated clearly that, for the present, this matter remains speculative. A change in the ion permeability of the surface membrane has also been considered as the primary event initiating excitation-contraction coupling in striated muscle (71).

The rise in intracellular free calcium concentration probably activates a sliding filament mechanism of contraction in smooth muscle. Thick filaments (approximately 155 Å in diameter) have now been observed in appropriately fixed smooth muscles, regardless of whether the muscles were stretched, unstretched, contracted or relaxed (20, 50, 57, 61). In some smooth muscles (e.g. the portal-anterior mesenteric vein of rabbits) the distribution of thick filaments is relatively regular and may form a quasi-rectangular, approximately 600 x 800 Å, lattice (50). The identification of the thick filaments with the organized form of myosin in living smooth muscle has been facilitated by the recognition of the 144 Å meridional reflection characteristic of organized myosin in x-ray diagrams of *taenia coli* (43). The suggestion that myosin is organized into structures that, in transverse section, appear ribbon-like (42) rather than as filaments was, in the opinion of the present author, due to the aggregation of the normal thick filament lattice into ribbon-like structures by the preparatory methods (51, 60, 61). The presence of cross-bridge-like lateral projections on the thick filaments (60) is further indication that they represent a form of myosin organized in a manner qualitatively similar to the thick filaments of striated muscles.

Thin (50 - 80 Å) filaments composed of actin are found in association with the thick filaments, and the thin to thick filament ratio (approximately 15:1) is rather high in all of the vertebrate smooth muscles examined thus

far (20, 21, 60, 61). The approximately 147 Å surface to surface distance between the thin and the nearest neighbour thick filaments (60) is of the magnitude that would permit interaction through cross-bridges between the two types of filaments. The thin filaments enter the dense bodies that are considered to be, by the majority of workers (for review see 12, 52), functionally analogous to the Z-line of striated muscles.

A third type of filament is found in association with the dense bodies in normal smooth muscles and is composed of proteins other than actin or myosin (16, 49, 51). Such intermediate (100 Å) filaments that may run in bundles over several micra long have been likened to the cytoskeleton of invertebrate obliquely striated muscles (61). In developing and in some unusual (perhaps abnormal) adult smooth muscle fibers, large conglomerations of these intermediate filaments may be seen in areas devoid of thin or thick myofilaments (51, 60, 72).

CONCLUSION

A distinct sarcoplasmic reticulum is present in vertebrate smooth muscles, and there are significant differences in the extent of the SR in functionally different types of smooth muscles. The ability of the sarcoplasmic reticulum to accumulate divalent cations and the occurrence of SR-surface membrane couplings, suggest that these organelles function as calcium sources and sinks in the excitation-contraction and inhibition-relaxation coupling mechanisms of smooth muscle. Extracellular calcium probably also makes a (variable) contribution to the activation of smooth muscle contraction. The close relationship of mitochondria to the surface vesicles and the mitochondrial cation uptake of smooth muscles in situ raises the possibility that the mitochondria may also play an ancillary role in contractile regulation, but more direct experimental evidence for this suspicion is thus far lacking.

The organization of actin and myosin into, respectively, thin and thick myofilaments and the presence of cross-bridge-like structures on the thick filaments, in conjunction with the length-active tension relationship of smooth muscles, is consistent with a sliding filament mechanism of contraction in vertebrate smooth muscles.

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SOME PROBLEMS OF HOMEOSTASIS IN HIGH ALTITUDE EXPOSURE*

J. CLIFFORD STICKNEY

Dept. of Physiology & Biophysics
West Virginia Univ. Med. Ctr., Morgantown

Human beings live at various altitudes between sea level and about 5,300 meters. Ambient oxygen tension ranges roughly between 160 torr at sea level and 80 torr at the high altitude. One may go above the higher altitude to work or explore. However, he is limited in duration of stay or height in the absence of extra oxygen. Any appreciable ascent above the altitude where one is accustomed requires homeostatic adjustments. These are needed to insure an adequate and continuous flow or transport of oxygen between the environment and the tissue mitochondria. Lenfant and Sullivan have recently presented an excellent account of adaptation to high altitude, and many of their thoughts as well as illustrations have provided the backbone of this presentation (in the *New England Journal of Medicine*) (8).

The gradient of oxygen partial pressure or tension between the environment at sea level and venous blood is about 120 torr (Figure 1).

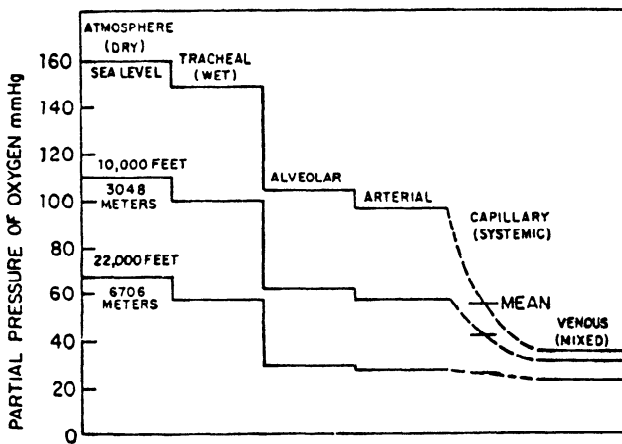


Fig.1. Oxygen gradients at various altitudes (7). From *Aerospace Medicine*. Baltimore: Williams & Wilkins Co. (2nd Ed.) 1971. Used by permission.

*Taken from the introductory remarks given at the session on Altitude at the 1972 Federation Meetings.

That is simply the difference between 160 torr and 40 in the mixed venous blood that comes from the tissues. Since as one goes as high as 3,048 meters or higher the ambient oxygen tension is below 120 torr, the gradient must be greatly reduced to prevent an intolerable condition. Since the absolute lower limit in venous blood is just above 20 torr, the body's defense against reducing the tissue or venous oxygen tension much below 40 is of prime importance. The lower limit at the altitude of 6,706 meters can be tolerated for only brief times in unacclimated man. Another fine review by Holmstrom has provided these facts (7).

How the organism achieves an adequate flow of oxygen in order to prevent intolerable low tissue oxygen tensions is a marvelous feat of adjustment and response. The response involves primarily the ventilatory and circulatory systems, but hemopoietic, renal and neuroendocrine systems play fundamental roles. Let us consider in turn several of the major adaptations, and finally, attempt to evaluate the quality of homeostasis achieved.

Some of the peripheral chemoreceptors in carotid and aortic bodies are stimulated in the unacclimated subject even at sea level. However, no increase in ventilation is seen during short exposures on the average before an elevation to about 3,000 meters is reached. A brief stay and acclimatization of four days at high altitude is sufficient to activate the ventilatory response at around 1,000 meters. A lowering of the threshold ventilatory response to hypoxia has occurred.

There is evidence that a part of this lowered threshold is due to an increased hydrogen ion concentration of the cerebrospinal fluid. In this way the inhibitory effect of alkalosis resulting from hyperventilation and other causes is prevented at the level of central control. The result is a more active respiratory response to ventilatory stimuli. This concept has been challenged as being active during moderate hypoxia (4).

After a prolonged exposure of a year or more to high altitude the sojourner's threshold for ventilatory activation has been reduced to sea level oxygen tensions. The threshold is the same as for the native resident at high altitude, but the sojourner's response is greater. The lesser ventilation of the native is referred to as a blunting of the hypoxic hyperventilation response.

So far the blunting has been seen only in humans. It is apparently due to a combination of early exposure to hypoxia of sufficient degree and of adequate duration. In spite of blunting, the average ventilatory rate in the native remains about 15 percent higher than the resting rate of the sea level resident, as shown in Figure 2. In any case the hyperventilation makes it possible for alveolar oxygen tensions to be considerably higher than they would otherwise be (as seen in Figure 3). This in turn leads to higher tissue oxygen tensions.

The diffusing capacity of the lung is that property of the lung which describes its gas transport capabilities. It is a quantitative measurement of the amount of oxygen or carbon monoxide which can be diffused from alveolar air to pulmonary capillary blood under standard conditions.

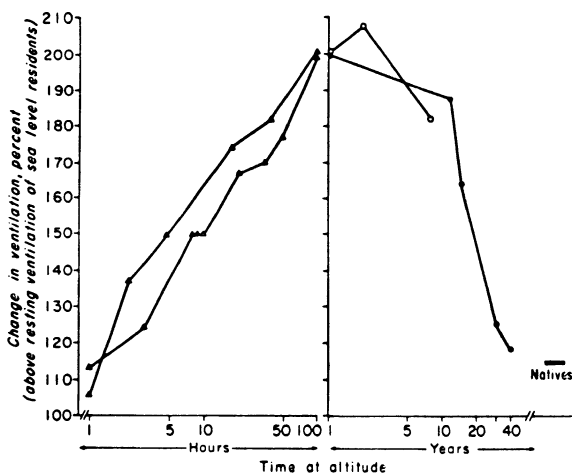


Fig.2. Change in ventilation in percentage of average value at sea level as a function of duration of residence at altitude (8). From the New England Journal of Medicine. Used by permission.

Determinations of diffusing capacity in native residents at high altitudes have revealed a 20 to 30 percent increase in this function. Part of the diffusing capacity depends upon the membrane characteristics of the lungs, and a part upon pulmonary capillary volume. In the high altitude resident apparently greater alveolar area, better distribution of ventilation and perfusion, and increased hematocrit all contribute to the membrane property. The capillary volume of the lung also seems to be increased at high altitude.

Particularly in the early phases of exposure to high altitude, circulatory adjustments leading to increased cardiac output are helpful. Figure 4 indicates that the elevated cardiac output is a result of an upturn in heart rate with stroke volume remaining constant. During even fairly short sojourns at high altitude the cardiac output slowly returns to the sea level value. This is apparently accomplished by maintenance of an increased heart rate while stroke volume diminishes. The role of adrenergic mediation of heart rate is of interest here.

The maximum cardiac output which can be attained during exercise at high altitude is definitely limited below the sea level value for both sojourners and native residents. This is apparent from Figure 5.

The initial exposure to the hypoxia of high altitude causes the kidney to release erythropoietin. As is now well known, this hormone is responsible for increasing the hemoglobin concentration of the blood, the number of red blood cells and the hematocrit. The result is a greater

oxygen capacity of the blood which is proportional to the duration and degree of hypoxia.

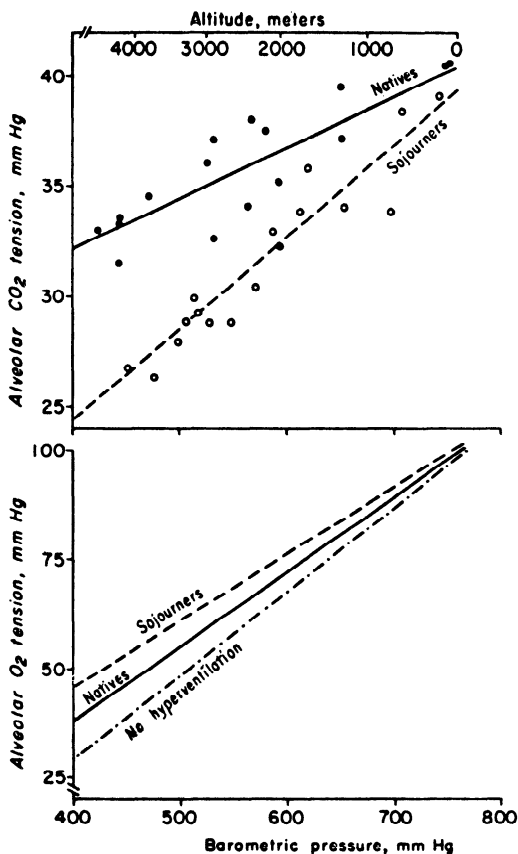


Fig.3. Alveolar gas tensions as a function of altitude in natives and in long-term sojourners (8). Used by permission of the New England Journal of Medicine.

The extent and mechanism of hypoxic adaptation at the tissue level are still incompletely known. There is probably involved an enhancement of capillary vascularization of myoglobin concentration of mitochondrial density and of enzyme activity.

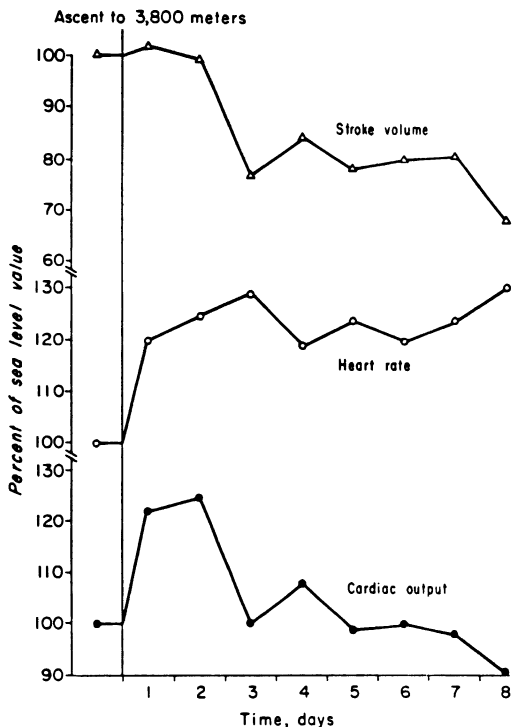


Fig.4. Cardiac output, heart rate and stroke volume in percent of sea level values during the first eight days at 3800 meters (8). Used by permission of the New England Journal of Medicine.

Now let us pause for a review of the adaptations so far discussed to see how well homeostasis is achieved, and how. The question of the blunting of the ventilatory response seems at first glance to be self-defeating for the high altitude resident. However, Dempsey has reported recently some findings at the threshold level of 3,100 meters that suggest otherwise (3). The lowered ventilation during exercise in the resident is associated with a higher arterial carbon dioxide tension. The latter is postulated to lead to a distinguished increase in diffusing capacity. The result is that the residents achieve higher arterial oxygen tensions than sea level visitors in spite of the greater ventilation of the latter, as shown in Figure 6. Furthermore, the energy saved by the reduced respiratory muscle activity is certainly a benefit.

Besides blunting, another anomaly of the acclimated state is the pulmonary arterial hypertension. For an insight here I call attention to the fact that Dawson and Glover (2) have found that the hypertension

produces a more uniform distribution of blood flow to the lungs of native high altitude residents. This probably contributes to the superior diffusing capacity already noted before.

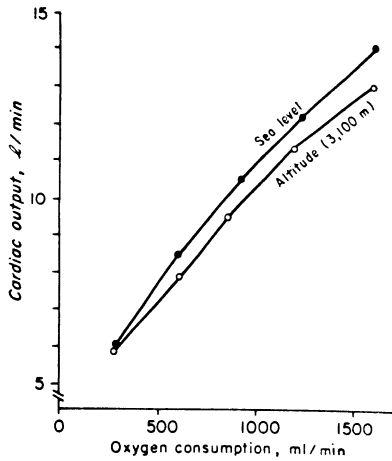
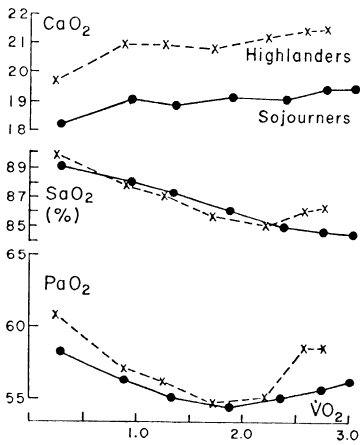


Fig.5. Cardiac output as a function of exercise oxygen consumption at sea level and at 3,100 meters (8). Used by permission of the New England Journal of Medicine.

Fig.6. Arterial oxygen content, oxygen saturation and oxygen tension from above down at rest and during work in sojourners and residents at 3,100 meters (3). By permission of Acta Paediatrica Scandinavica, Stockholm, Sweden.



Although cardiac output is elevated in initial high altitude exposure, the precise mechanisms accounting for the increase remain unclear. So also is the mechanism of exercise limitation. Finally, much more should be known about the distribution of blood flow throughout the body.

The increase of oxygen capacity brings with it the threat of increased viscosity of blood which is bad for unacclimated dogs, but apparently not for acclimated man. The shift in the oxy-hemoglobin dissociation curve toward the right, that is, toward lessened affinity, is not beneficial at all degrees of hypoxia. These problems along with those of tissue adaptations still await thoroughgoing solutions.

Finally, I would like to pose the question of how well the hypothalamus, the ultimum moriens of homeostasis, is doing its job in high altitude exposure. We note that the hypothalamus belongs to the brain which is particularly susceptible to hypoxia. Although the hypothalamus appears not to be the most vulnerable part, yet as a final integrating center it depends for its input upon higher centers which may be extremely vulnerable.

It is well known that the pituitary-adrenal axis is early activated in hypoxia, and we know from the newer knowledge of releasing factors that the hypothalamus is in control. Although the heightened demands upon glucocorticoid secretion fade rather early in continued high altitude exposure, the hypothalamus may still be involved in other functions. It is apparently responsible for continued levels of catecholamine secretion by way of the sympathetics which may maintain an elevated heart rate.

Figure 7 shows that there is an early reduction of aldosterone level as judged from urine values. This is associated with an increased Na/K ratio in both saliva and urine. At one time these changes were thought to spring from the ventilatory increase in venous return (16). The persistence of these responses into the completely acclimated state remains to be clarified (14).

There is evidence of the perturbation of other hypothalamic functions involving sleep, body temperature and water regulation (5, 12) and the thyroid (15) during early phases of chronic high altitude exposure. We know little of the fate of these functions in the acclimated state.

Another area of hypothalamic control involvement has been the anorexia induced by acute and chronic hypoxia. A plethora of papers has appeared in the literature recently documenting the fact. Although the anorexia is partially ameliorated by presentation of a more appetizing diet, or by previous bouts of physical training, or by food deprivation the anorexia does not go away, at least in the acute exposure (1, 13). Does it ever go away, even for the high altitude resident?

Some recent excellent studies of the Quechua Indians of southern Peru who live at altitudes between 4,000 and 5,500 meters have been reported. Frisancho and Baker (6) who point out that although the dietary intake of this population seems to meet accepted dietary standards, there remains a failure of normal growth rate. Studies of body weight gain and increase of postural height show a retardation in childhood

years, a delayed adolescent growth spurt (Figure 8) and a failure to ever reach body postural height of low altitude controls (Figure 9). Body chest size is a notable exception, for this dimension is significantly increased over controls. Although the diet was stated to be ample, one wonders whether altitude anorexia and growth retardation would occur if the diet were as affluent as that so prevalent in the United States, where postural height averages around 180 cm. as compared to 160 cm. in the residents at high altitude.

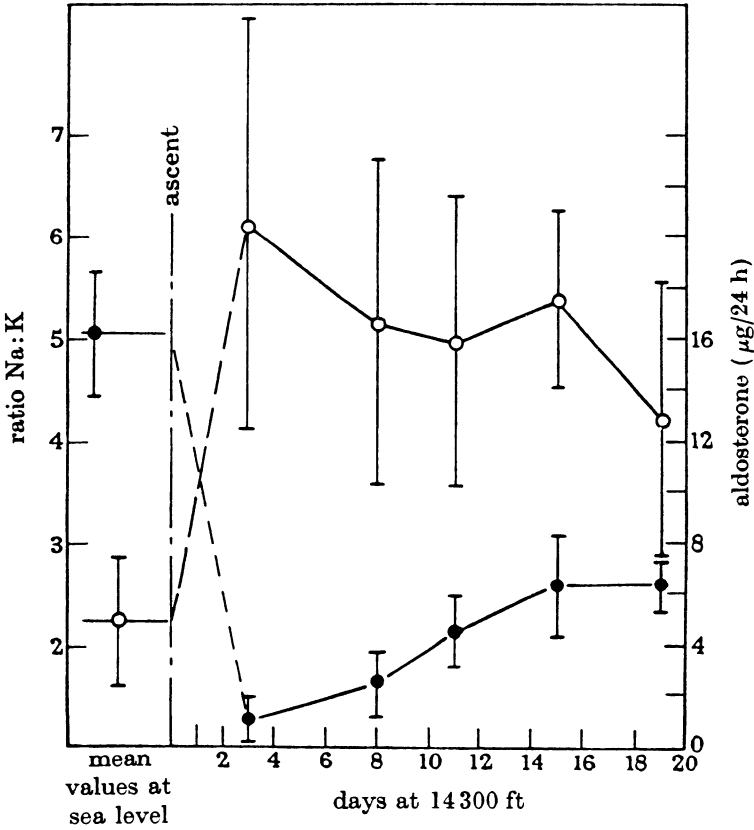


Fig.7. The mean value of urinary aldosterone (filled circles) in seven subjects living at 14,300 ft. compared with the mean urinary Na/K ratio (open circles) with limits of one standard deviation indicated (16). By permission of The Royal Society and the author.

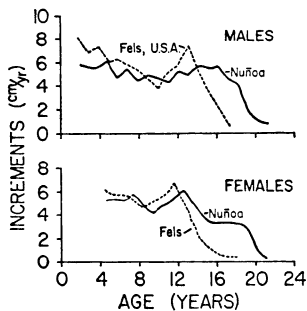


Fig.8. Stature growth rate of Quecha Indians residing in Nunoa to 5,500 meters compared with the U.S.A. Fels Standards (6). By permission of the Wistar Press.

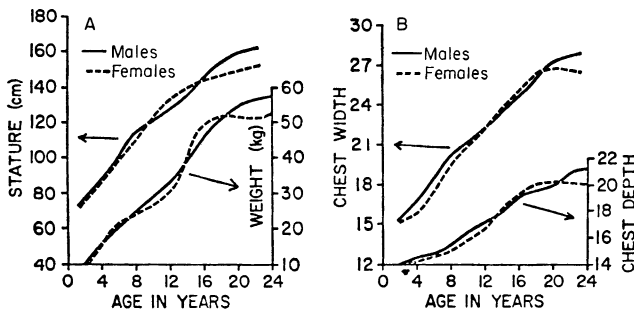


Fig.9. Development of stature and body weight A and in chest size B in the high altitude residents of Figure 8 (6). By permission of The Wistar Press.

Finally, turning to higher mental functions, I note that Lenfant and Sullivan point out the lack of competitive spirit among high altitude dwellers (8). An important question is whether this is due indeed to social and cultural factors or is there a failure of complete acclimatization. I would like to see more studies on short-term memory in this connection. Both McFarland (10), and Malmo and Finan (9) have documented the fact that short-term memory is blunted by acute exposures to high altitude, as shown in Figure 10. The return to normal during chronic exposure as in native highlanders has yet to be put in evidence.

In conclusion I think that this brief survey has demonstrated that there is still plenty of work to do in contributing to our more complete understanding of the problems of high altitude exposure.

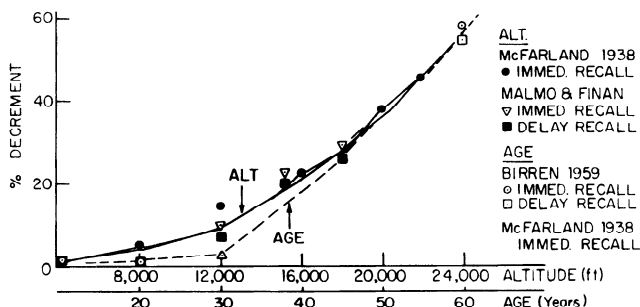


Fig.10. Percent decrement in memory-paired association (short-term memory) due to acute exposures to high altitudes compared with the decrement due to age (11). By permission of the author.

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CEREBRAL CIRCULATION AND METABOLISM

An International Symposium on Cerebral Circulation and Metabolism will be held in Philadelphia, Pa. at the Marriott Hotel, June 6-9, 1973. General topics include the control of cerebral blood flow and metabolism and the pathophysiological and chemical substrates of abnormal function in experimental and clinical pathology. The deadline for submission of abstracts is January 15, 1973. Correspondence should be directed to Thomas W. Langfitt, M.D., Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, Pa. 19104.

COMPUTER-ASSISTED SELF EVALUATED TESTS FOR MEDICAL PHYSIOLOGY

D. T. FRAZIER

At the University of Kentucky College of Medicine, Medical Physiology is a first year course with approximately 180 student contact hours. It covers sequentially the physiology of the various systems of the human body, i.e., nerve-muscle, cardiovascular, respiratory, renal, endocrine, and gastrointestinal. Evaluation of a student's performance is based primarily on the results of two exams; a mid-term and a final with some additional consideration given to student conduct in the laboratory.

Over the past couple of years, students have complained about the amount of time that elapses between examination periods. Frequently, students have requested some means by which they could gauge their progress in the course. In the student's mind is a lingering doubt that, for example, he just didn't learn enough respiratory physiology. He would certainly like to feel more confident about respiratory physiology before embarking on the study of a different system. The notion of more frequent formal exams was rejected by both faculty and students.

The Physiology Department attempted to resolve this difficulty by giving the students a set of review questions on each system and some take-home tutorial examinations. Published answers to the tutorials were provided after allowing the students a few days to work on the material on their own. In general, the students simply waited for the answers to arrive before even reading the questions. They then added the correct answers to their repertoire of facts, going through a minimal deductive process of their own. The faculty had no way of following the progress of individual students since they couldn't observe the students attempt to answer the questions. Review sessions scheduled to discuss this material were poorly attended.

This past year the Physiology Department decided to try a new approach. Sets of multiple choice questions covering most of the physiological systems in depth were programmed into a computer. Students were informed that a satisfactory performance on these exams indicated a thorough knowledge of the material expected of the student by the various instructors. The students were allowed to take the exams as many times as they wished on a totally volunteer basis. The unique feature of the computer exams was that a student received only an evaluation of his overall performance with no feed-back with respect to individual questions.

Purposes of the Project

The specific purposes of this project were to answer the following questions:

1. If computer-assisted self-evaluation tests (CASETS) are available, will the students take them?

2. Do the students who take the CASETS perceive them to provide an on-going evaluation of their knowledge of the various sections of the Medical Physiology course?
3. Do the CASETS stimulate students to study, in greater depth, the material presented in Medical Physiology?
4. Do the CASETS stimulate students to increased tutorial contact with the teaching faculty of the course?
5. Will the CASETS enable the Class of 1972 to score higher on the formal examinations of the course than the Class of 1971 who did not have access to the CASETS?
6. Do the CASETS aid the instructors in course development and in the counseling of students?

Description of the Project

The project was designed around six multiple choice examinations with 31-36 questions per exam. Two exams covered the nerve-muscle section of the course and the other four covered the cardiovascular, respiratory, renal, and gastrointestinal sections. No exam was developed for the endocrine section.

The computer used was an IBM 1800 interfaced with an IBM 1053 typewriter and a special answer box designed to receive student responses to the questions. The answer box included a dial access system for entering student and test identification numbers. Also, the answer box had five toggle switches which allowed the students to enter their choice of the four alternative answers to the test question. The fifth switch permitted a student the opportunity not to guess at a particular question. He would, therefore, receive two evaluation statements. One concerned with his total performance, and one with the '5' answers excluded. This allowed the student a means by which he could evaluate himself on the material he thought he knew. In this initial project only one computer terminal was provided.

The computer in most computer-based examinations prints out each question, receives an answer, and reacts immediately to each answer. In this project the computer was programmed only to do the following:

1. Receive student and test identification numbers.
2. Accept one student response per question.
3. After completion of the exam, print the results of the student's performance and a comment. The comments given the student were as follows:

90% or more correct - "Congratulations, Excellent Performance, Proceed with Confidence."

80-89% correct - "Good Performance - Be Vigilant."

70-79% correct - "Satisfactory Performance - Be sure to study this section in depth before next exam. Suggest you retake this exam until you can answer better than eighty percent of the questions."

69% correct or below - "Unsatisfactory - A similar performance on the mid-term or final will put you in great jeopardy. Suggest you ,

1. Review all sections of the system covered on this tutorial.
2. Make arrangements to discuss lecture material with appropriate faculty members.
3. After reviewing material, retake tutorial."

4. Instructors were provided with the following:

- a) An analysis of each question as to how students answered that item. This was used to determine validity of question.
- b) Record of each student's performance on every attempt at an exam.

Students obtained a copy of each exam from a clerk, proceeded to the computer terminal, dialed in his identification and the test identification number and began to answer the questions. In case of an error, a student could abort the answers at any time and start again. If the student preferred to remain anonymous, he could dial in a special number which, as an after-thought was designated as "chicken." The fact that he took the exam was recorded but his score was not identified with his student number. Many students chose this option, at least on their first attempt.

The decision to have the CASETS in handout form rather than stored in the computer was based on several factors. First, the cost for storage of a bank of questions in the computer was considerable, and, secondly, revision of stored test questions required a computer programmer's efforts. The handout form allows for revision of questions by an instructor with no involvement of the computer as long as the correct answer position within the four alternatives remains the same. A third reason for the decision was based on the time involved for the computer to type out each question, wait for a student's answer, and type the next question. Having multiple printed copies of the exams allowed several students to take the exam simultaneously. They would first put their answers on a sheet of paper and subsequently, enter them in the computer whenever the input terminal was available. Entering the answers in this fashion was very rapid and made more efficient use of the terminal.

At the end of the semester, a questionnaire designed to evaluate the project was given to each student who had taken any one of the six tests. The questionnaire revealed that the most common complaint by students was the lack of direct feed-back as to which questions they had missed or what the correct answers were. A few examples of students comments

are given below:

"The biggest problem with the tests was the unavailability of the answers. I realize that you were trying to give us some idea of what we knew as compared to what we should know. At the same time, it's pretty damn distressing to carefully work through a test with no guessing, and to make mistakes - there's no way to tell where you are deficient."

"The answers should have been gone over at some time, maybe two weeks after a section. The faculty was too hard to pin down and if we can't have copies you can't remember the question."

"There is no feedback on what specific areas on the section one is having trouble with, so studying cannot be directed in a profitable manner."

To answer the students complaints, there were two major reasons for deciding against giving the correct answers. First and foremost, this project was designed for student self-evaluation. Withholding the answers encouraged the students to make repeated attempts after more intensive study. By giving the answers on the first try, the CASETS would become merely a one-shot trial. Secondly, the CASETS were intended to stimulate review of an entire area, rather than simply to teach answers to a few isolated questions. Too frequently, students have a tendency to memorize the correct answers with little regard as to why the other possibilities are wrong. It was hoped that by using this method the students would discover the correct answers on their own in an observable situation.

Results of the Project

It was easy to determine if students used the CASETS since each time a student took an examination the computer made an account of it. Of the 98 students enrolled in the Medical Physiology course, 80 of them took at least one test. Thirty-three of the 80 took three or more and 18 of the 80 took all six exams. Many of the students who took the CASETS, took each one several times; the number of tests taken totaled 390. A complete breakdown of the tests and how often they were taken can be found in Table 1.

The student questionnaire referred to earlier was designed to assess several aspects of the CASETS project. One question asked if the students felt that the CASETS provided an ongoing evaluation of their knowledge of various sections of the course. Eighty-two percent of the class indicated that it did provide a good self-evaluation.

The questionnaire also asked the students if the CASETS stimulated them to broaden the scope of their study and to extend their study time for the course. Eighty-four percent felt that the CASETS did encourage them to study more, and 63% indicated that the project stimulated them not only to study more, but to study more than just their lecture notes.

ANALYSIS AND RESULTS OF CASETS

TABLE 1

Systems	Total Number of Exams Taken	Number of Individual Students Who Took An Exam	Number of Identifiable Students Reaching a Satisfactory Criteria on an Exam	Number of Those Students Scoring Satisfactory on Formal Exams	Mean Class Performance 1972	1971
NERVE-MUSCLE	155	69	18	18	83	71
CARDIOVASCULAR	76	55	21	20	74	78
RESPIRATION	30	23	14	11	69	69
RENAL	68	53	25	22	72	76
G. I.	61	47	15	15	75	71
ENDOCRINOLOGY	--	--	--	--	78	79
TOTAL	390	(80)*				

* This total represents the number of individual students from the Class of 1972 who took at least one exam.

A few general student comments concerning the value of the project follow:

"At first, the tests were a big ego deflator because you thought you knew the material, took the test and got a 60%. Then you went back and studied and when you finally got a good score it was great!! They really kept up my interest by providing a constant challenge to see if you could beat them! I think they're great and I appreciate the effort that went into setting it up and keeping it going."

"I got a feel for the level of knowledge and understanding required by the department."

"They give you a little confidence that you know something, if you take them enough times to know the answers. I think it is a good idea not to distribute answers. It's annoying when you want to know right then whether you're right or not, but the reinforcement is greater if it nags at you a while and you ask around and painstakingly eliminate answers and come up with the right one, but it's the most effective method for helping the student learn. You tend to take it less seriously if you know you have the answers handy."

In order to determine if the CASETS prompted students to seek more conferences with their professor, each instructor was asked to write his comments about the project. The statements of the five instructors follow:

"Feedback concerning the computer-assisted evaluations was generally good. Participating students seemed to study more and engaged in more frequent discussions of physiological problems. I recommend continuing the project next year."

"I am sure that it provoked an 'agonizing reappraisal' of what the students thought they knew. I held a seminar of about 45 minutes with about 60 of the class, because so many of them had questions. Believe it's worthwhile."

"I feel the project was successful and should be continued. I feel I saw more students this year than ever before, but can't attribute this solely to the computer test."

"From the results on the final examination, as well as remarks of the number of students, I feel that the computer examinations not only helped them to obtain a better grade but also led to their retention of some of the more important information in gastrointestinal physiology."

"I feel the project was successful in that the students really worked to raise their scores on the exam and did provide for some students self-evaluation. They studied, talked to faculty, talked to each other, and that's the name of the game. I feel as we go along giving out more detailed lecture outlines and streamlining our courses the student becomes a very passive member of the academic environment. From time to time he needs to have the spoon removed and his mind tweaked."

A valid statistical procedure to determine the value of the tutorial exams would have been to take the scores of the students who had reached a predetermined criteria on the CASETS and compared these to the remainder of the class, or to their own performance on that system on the formal exams. However, due to several technical problems, the statistics required were not available. One of the main difficulties was that many students chose not to be identified and entered the anonymous student number. This made it impossible to follow the progress of these students. The exams they took could be tabulated but not their scores. This option was provided to allay fears of some students that the results might be used by the department for evaluation purposes. First and foremost, we wanted the students to use the exams and weren't particularly concerned with experimental protocol. Another problem was that after several attempts on an exam, some students would begin to try to figure out an answer to a specific question. They would use the '5' switch ("I don't know") answer on all questions with the exception of the one which concerned them. Their total performance on that occasion, therefore, would be reflected, at best, as only one correct answer. The computer is now programmed to respond to a student's attempt to work out an exam key. A series of '5' answers will result in a message from the computer which informs the student that there is an easier and less time consuming way to find the information sought.

The computer print-out revealed that 43 students using their number reached satisfactory criteria on at least one of the systems covered by tutorials. In over 92% of the cases (86/93 exams), a satisfactory performance on the individual tutorials correlated well with satisfactory performance on formal exams in that area.

A comparison was made between the means of the overall performance on each system for the Class of 1972 and those of the Class of 1971. The results indicated that the Class of 1972 scored significantly higher ($p > .005$) than the Class of 1971 on both the Nerve-Muscle and Gastro-intestinal sections (Table 1). On the Endocrine section, there was no significant difference between the two classes which was expected since there was no computer test offered for this section. Also, there was no significant difference when the mean performance of the two classes were compared with respect to the respiratory system. These results could be attributed to the fact that less than one-fourth of the class took this particular section of the CASETS with few reaching a satisfactory criteria. Various factors made a valid comparison of the Cardiovascular and Renal sections impossible. The Cardiovascular system was taught by two professors during 1971 and by only one in 1972. Therefore, orientation and depth were quite different between the two years. The Renal section

showed a negative trend which might be explained by the fact that twice as many multiple choice questions were asked on this system this year as compared to last. In 1971 most of the performance evaluation was based on the students response to several discussion questions rather than multiple choice. The results, therefore, are not readily comparable.

At this point one might ask how the 18 students who didn't take any of the CASETS performed on the mid-term and final examinations in the course. Fifty percent scored in the lower third of the class and with the exception of one student who ranked twenty-first in the class, the remainder of the students scored in the middle third of the class.

The answer to the question referring to the use of the CASETS as an aid to professors, is a definite "yes." A computer print-out showing the number of times a particular student took an exam and his score was available to the professor. This allows him the opportunity to follow the progress of that student and be in a better position to advise. Item analysis of each question by the computer program permitted revision of the question, thereby, improving the overall quality of the exam. In addition, the CASETS helped build a library of tested questions for future use on formal examinations. At the same time, the item analysis provided the professor with feedback as to areas in which his lectures seem to be deficient.

Additional Developments

The students were asked if the project should be continued and possibly expanded to other courses. Ninety-four percent of those who had used the CASETS indicated that it should be continued and 88% stated that other courses should use this procedure. In this regard, the faculty of the first year Gross Anatomy course have begun to develop questions and make plans to implement the CASETS in their course. The Biochemistry Department requested a seminar on the subject and is considering utilizing the technique in their medical teaching.

Another fringe benefit of the project has been that several sophomore students have taken the CASETS as practice for the National Boards. It will be interesting to learn whether or not they feel it was of value.

SUMMARY

In summary, the project, despite a few technical problems, was a useful tool for student self-evaluation in the Medical Physiology course. As evidenced by their responses to questionnaires, both faculty and students believe the CASETS Project to be of value and worth expanding to other areas. There was a good correlation between a satisfactory performance on a tutorial exam and the individual student's performance on that system in the formal Physiology evaluation. Although impossible to quantitate, the CASETS did stimulate a great deal of student concern and, hopefully, interest in Medical Physiology.

REPLIES FROM SENIOR PHYSIOLOGISTS

Our inquiry this year followed the usual pattern including a personal note from one of the four members of the committee, Drs. Dill, Davis, Essex, or Mayerson. Mayerson has replaced Landis on the committee and this year Visscher is replacing Essex. Of the 415 members born from 1893 through 1907 about 42% replied. Their answers to our questions cover a wide gamut: philosophy, contemplation, reverie, history, accounts of current activity and practical advice on second or third careers. One quoted Benjamin Franklin on retirement, "There is nothing wrong with retirement as long as one doesn't allow it to interfere with one's work." The original letters will be deposited in Society Archives for the use of historians.

Replies from those born in the years 1893 through 1900 are recorded in this issue. The replies of those born in the years 1901 through 1907 will appear in the next issue of "The Physiologist."

Born in 1893

Ernst Gellhorn to Hi Essex:

I have several scientific papers in press, the most important will appear in the J. Nervous & Mental Dis., 1972. I am working on an invited paper for a book edited by J. W. Cullen. Finishing it will mark the end of my scientific career.

I am still available as a consultant but do not plan to give lectures any more.

A major event in my life is that I just finished a little book which will now go to the printer. Its title is: "The Time Concertina - Meditations of a Humanist." Several pieces from it have been published in scientific journals - Divine Humor, Humility etc. I have added a second section which deals with "Human Implications of Biomedical Research."

Lester Dragstedt to Hi Essex:

Thank you very much indeed for your letter and more particularly for being interested in the old physiologists and for providing such pleasure. I no longer operate on patients, but keep active in teaching and research. I came to the University of Florida as research professor of surgery, but after having been here several years, was made professor of physiology in addition. I have the fun of teaching gastrointestinal physiology to the medical students, as well as giving some lectures on the ulcer problem to the seniors. The young Swedish surgeon Dr. Gunnar Wickvorn has come to spend a year with me in full-time research. We are presently studying the digestant effect of bile, a pancreatic juice, and intestinal juice on the legs of living frogs by the method that Claude Bernard used many years ago. You will be interested to know that whereas the legs of living frogs introduced into the dogs stomach, are promptly digested away, no digestion occurred when the frogs are exposed to the digestant action of the duodenal juices. We enjoy our life in the sunny

south very much indeed, and continue to recommend this to all senior citizens.

William Buchbinder to Hi Essex:

Who retires? I still practice medicine and am living quite well off a few old codgers who believe I'm not expendible. How mistaken they are. I am also a consultant with the Veterans Administration. Perhaps the most rewarding part of my life is spent with my new Steinway piano.

My only advice for those approaching retirement is - have fun and enjoy yourself while it lasts. If you so wish, go to the horse races and cultivate the game of gin. Perhaps you didn't know that Mozart, while he could have been doing better things, played pool for higher stakes than he could afford; and Robert Schumann always had an eye on some broad with a little pulchritude. Finally, don't have your prostate out until your BUN is over 175. Old physiologists never die; neither do they fade away - it seems.

Jane Johnson wrote to Hi Essex about her travels to India and Mexico and to visit their six families that have presented them with 17 grandchildren.

Frieda Robscheit-Robbins Sprague lost her husband three years ago and now is in a rest home with nurses on a 24-hour schedule.

Theodore Boyd to Hy Mayerson:

Except for skimming through "Science" each week, I have been almost completely out of touch with scientific affairs for nearly five years. I retired in 1967 not from an active research laboratory but from an administrative job I had held for 20 years. When you have spent that much time dealing with applicants for grants you don't mind thinking about something else for a change. I always looked forward to ending my life here, where I was born and grew up. This county was then one of the most thinly settled in Tennessee. Now it is becoming more and more like the Bronx. So far I find the crowding uncomfortable but not yet intolerable. I have ground enough to give an old man all the physical work he needs. I have done an occasional bit of writing, such as the sample enclosed. I have more books than I can ever re-read. Now and then there is something on TV or radio that is worth listening to. We have congenial neighbors. On my present income I should be pinched if I tried to live in Scarsdale as I did for 20 years. I get along comfortably here. To senescent physiologists I commend the example of the emperor Diocletian. He bowed out of a career too strenuous for his taste and took up gardening. He is said to have taken special pride in his cabbages.

Hi Essex to Hal Davis:

After completing some unfinished papers soon after my retirement, I interested myself in the history of medicine. Currently the career and publications of Dr. John C. Gunn are claiming my attention. He

was the author of "Gunn's Domestic Medicine" which was the chief source of medical information of the pioneers of the Middle West. The book went through more than a hundred editions and was probably a must in pioneer homes. However, today if one has a copy of this book he has a rare volume. Information about the author is likewise rare. You can understand the challenge that search for facts about this pioneer doctor and author presents. Regarding how I am spending the time I find available for other pursuits let me say that the days are too few in number and too short for me to get all the tasks completed that I attempt to do. Perhaps it is not the increased number of duties and commitments I take on but rather a slowing down in the rate of their execution compared to my earlier years. Be that as it may, this Spring I am completing my efforts as chairman of a drive to raise \$500,000 for the River Trails Girl Scouts Council. It was not exactly the right time for the campaign considering the state of the national economy the past two years. In spite of that we are only about \$50,000 short of our goal and optimistically it shall be reached this year. My interest in painting continues. Last year I gave a collection of my work to my Alma Mater, Knox College, at her request. It is hung in the new Science-Mathematics Building in what is called, "Hiran Essex Hall." From "culture" I can turn to "agriculture." Our 320 acre farm furnishes an opportunity for the application of my early training in genetics in the breeding of Holstein cattle. As a physiologist one contemplates the possible limits of production that might be reached. Heredity, of course, is a very important factor but given the highest genetic potential in the members of the herd, the proper management - handling, feeding, etc. is required for the production of the quantity of milk. Every cow in the herd is a factory to whom we give the raw materials such as hay, silage, grass, various grains, water and minerals and from whom we obtain twice each day the finished product: nature's most nearly perfect food - milk.

Born in 1894

Erma Smith to Bruce Dill:

I am pursuing scientific activities, part time. I should be interested in an administrative position preferably in Kansas. Words of advice: Work full time as long as possible.

William Amberson to Hi Essex:

We have extended our electrophoretic studies of muscle proteins, publishing a series of papers. The latest paper took years to complete. I consider it to be my most important contribution. Some others working in the field have thought well of it. I am now working on a final manuscript. It will deal with the effect of temperature change upon complex formation between the muscle enzymes and the fibrous proteins. I have other unpublished material but composition becomes more and more difficult for me. I think that I must stop. I remember Fred Steggerda very well but have rarely seen him over the years. He was on my staff when I arrived in Memphis in 1930. Arthur Mulder was also with me. Both are now gone. Both were younger than I. You may have known Walter Root, my first Ph.D. student at Pennsylvania. He died here on March 30 by heart failure. He was 69. He left Baltimore in 1937 when

I took over the department and went to Columbia with Gregerson. He published many papers, some with Gregerson, and did much editorial work. We are trying to comfort his second wife, Polly. So many other colleagues have recently gone. I lost my first wife in 1957, a cardiac death. I then married my long-time secretary, Christiana Bond, 17 years my junior. More and more she takes care of me. I look forward to receiving your summary of the present state of colleagues.

Grace Roth to Hi Essex:

This Spring I was taken into the Catecholamine Society with the Nobel Prize boys in Atlantic City. They will meet there next year and after that in Sweden. I have been completing my studies on five hundred men, 250 Airline Executives with stressful jobs and 250 men from Edwards Air Base who were moved from the B70 planes into the X15 planes. I need some further help with a computer. I am interested in a position that would enable me to continue scientific activities. I am free to move to another area.

I. S. Ravdin's secretary reported to Hy Mayerson that Dr. Ravdin has been ill and is unable to answer his mail.

Curt Richter to Hal Davis:

I still work full time - have the same lab, space and help as before - the only thing that I don't have is enough time for work, tennis and squash. I have a book and monograph in the offing and couldn't be having more fun.

Born in 1895

Edward Van Liere to Bruce Dill:

Am still engaged in biologic research, and presently working on the possible mechanism of cardiac hypertrophy produced by hypoxia. The Medical Center is flourishing. There are about 1200 students working toward a degree in medicine, dentistry, nursing, pharmacy etc. There are about 15,000 students enrolled on the campus. Time continues to fly.

Carl Dragstedt, Society Poet, sent Hi Essex a recent creation:

COMPUTER-AGE DOCTOR

I wasn't well,
I had a spell
Of virus overdoses;
But in his eyes,
I was a prize
For modern diagnosis.

We took some blood,
Also my cud,
And then some spinal fluid;
Some urine too,
The whole darn stew
To a white-robed Druid.

He flipped a switch,
and took a hitch,
In something made of pewter;
Then fed my things,
With garnishings,
Into a big computer.

Out came a check-
"This guy's a wreck,
And here's the diagnosis-
He has to have
His gonads out,
Since he has halitosis."

It seems it was
Perhaps because
Some juice fouled the computer;
Or else a fuse
Was the excuse,
But nonetheless, I'm neuter.

Jeno Kramar to Hi Essex:

I am very grateful for your interest in my present status and future plans. Please be informed that I am still active and working as professor of pediatrics but intend to retire this summer. Being 77, I am not interested in any professional obligation any more except for tidying up the results of my unpublished research.

Emmett Carmichael to Bruce Dill:

I retired as professor of biochemistry in 1960 and then served six years as Assistant Dean of our School of Medicine and School of Dentistry. While serving as Assistant Dean, I started "The Alabama Journal of Medical Sciences" in 1964, a quarterly journal of 500 pages per year. My administration requested me to continue on as editor (with the title Consultant to the Editorial Board because of state auditors), and the ninth volume is in the process of being printed. I still am chairman of the Alabama Science Talent Search under the auspices of the Gorgas Scholarship Foundation, Inc., which was begun in 1947. I am a philatelist and I take care of a large yard which has many varieties of flowering shrubs; varieties of flowering bulbs, iris and day lilies. I publish at least two biographical sketches about chemists and physicians each year. I collect documents of deceased members of the health team for our Historical Library. My advice for those who are approaching retirement is that they should plan two things: 1) Collect and arrange

their scientific highlights in an orderly form and place them in either the library or registrars office and 2) start a hobby if you do not have one and at least one should be physical in nature.

Norman B. Taylor's son Eric wrote as follows to Hi Essex:

I am writing for my father, Dr. N. B. Taylor, in response to your recent letter concerning his book, "The Physiological Basis of Medical Practice." Dr. Taylor has not been in the best of health over the past 1-1/2 years, and actually has little to do with any revision work of the book. As you might suspect, all this is now in the hands of the publisher, Williams & Wilkins Co., 428 E. Preston St., Baltimore, Maryland.

Hugh Dukes to Hi Essex:

Several years after retirement I went to London to give the inaugural Sir Frederick Smith Memorial Lecture at the Royal Veterinary College, University of London. This lecture was under the auspices of the British Equine Veterinary Association. Sir Frederick Smith was a father of veterinary physiology in the English-speaking world. His "Manual of Veterinary Physiology" was used throughout the English-speaking world for several decades. While abroad I visited veterinary colleges throughout the British isles. Later, the Film Production Unit of Iowa State University and I made 21 short motion picture films based on the demonstrations in physiology. These are now available from the Film Production Unit. Some years ago I was especially fortunate in persuading Dr. Melvin Swenson of the College of Veterinary Medicine, Iowa State University, to take over the responsibility for the "Physiology of Domestic Animals," 7th edition of which appeared in 1955. Dr. Swenson accepted the editorship and enlisted the aid of some 40 authors. The results, "Dukes' Physiology of Domestic Animals," 8th edition, edited by Melvin J. Swenson, and published by Cornell University Press, appeared in 1970. It has been well received. A Spanish edition is in preparation.

Isaac Starr to Hy Mayerson:

I am indeed continuing my scientific activities, and have never been busier. I still publish about two papers a year, and I am reading a paper before the Association of American Physicians at its meeting in May. Retirement has made little difference to me, as far as spending my time is concerned. Because of the absence of teaching and committee work, I have more time to spend on research than I ever had before. My advice to everyone is to keep working as long as he can! Again, it was a pleasure to hear from you.

Edward Adolph to Hy Mayerson:

Have laboratory, do work. Attend meetings, do listen. Do visit, by invitation, physiologists in near and distant places. Do enjoy acting as though I contribute to a lively science. To which fields of physiology? Developmental, adaptational, regulatory. For those who enter them, these fields are Elysian.

Walter McClellan to Hy Mayerson:

I have read with interest the replies of senior physiologists to the request for information from your committee in "The Physiologist." I have been physically unable to participate in any active teaching. A little reading is all I can do. Retire to some activity and location you can enjoy during this pleasant time of life. Do not just retire from your present position. Then by all means keep well to be able to carry on the chosen retirement activity.

Baird Hastings to Hal Davis:

Except for acquiring a cane, I have no physical complaints. My appointment as research associate in the department of neurosciences at UCSD was renewed for 1972 and I am still housed among the oceanographers. In spite of my preference for association with medical and graduate students, the past year has found me identified with "the aging." There were the planning meetings of the National Advisory Committee to the White House Conference on Aging, and then the conference itself last December. There was also a week last September when I participated in a teaching conference on the Biology of Aging at Bar Harbor, Maine. My most fun was the days I spent on the Alpha Helix doing some work on squid "blood," while neurophysiologists studied action potentials of the axon. Though I have no lab, my life is full with writing, a little teaching, the companionship of students and colleagues and fishing on Sundays. As for words of advice to those approaching retirement: Aging can be fun - if you never look in a mirror!

Larry Irving to Hal Davis:

It may be surprising and it is certainly a pleasure for me that Alaska is quite considerate in allowing its old people to continue their degree of useful work. If it were not immodest I would say that the old ones must behave in seemly manner. I continue in scientific activities with a certain wastage of words and paper. My participation in research is through listening to what the active young fellows are about. In these days of intensive communication, listeners are in short supply. As I contemplate the activities of my contemporaries, who are mostly still useful, well satisfied with their past and present and uniformly cordial to each other, I think that they stand out as an amiable section of society whose company any young fellow might look forward to enter.

Ernest Spiegel to Hal Davis:

I am editing Progress in Neurology and Psychiatry.

Born in 1896

Cowles Andrus to Hi Essex:

I still maintain a (diminishing) consultant practice, periodically re-examining patients whom I have seen over the years, and advising on cases referred because of special cardiovascular problems. I am

"hooked" on satisfaction of medical service to individuals, but on the whole I play more (travel and golf) and work less than I used to.

Walter Fleischman to Bruce Dill:

I am continuing as consultant in pathology at the VA Hospital Mountain Home in Johnson City taking part in the C. P. C. program among other duties. I do some abstracting of American literature for the Naturwissenschaftliche Rundschau in Stuttgart. I spend more time on my hobbies than on scientific activities: gardening and playing the organ daily. In addition I read a lot.

Arthur Gilson, Jr. to Hy Mayerson:

Thank you for the greeting to which I send a reply to Touro with some sentiment. It was almost exactly forty-seven years ago that we paced the floor there waiting for our first-born to arrive. For ourself there is little to report. We move slowly forward with head held high, at least fairly so. I am not doing scientific work of any significant proportions but manage to find enough activity around the house and grounds to keep in motion.

Dick Whitehead to Hy Mayerson:

I have a part time administrative position as assistant to the Dean for Alumni affairs and Executive Secretary of the Colorado Medical Alumni Association. I have also collaborated in the writing of "A History of Medical Education in Colorado" written for the Colorado Medical Society in honor of the 100th anniversary of the founding of the Society. The article appeared in the June 1971 Rocky Mountain Medical Journal (Supplement) and was published, together with other articles in a book entitled "A Century of Colorado Medicine 1871-1971." About the only work for which I feel qualified now is in an administrative capacity. I am or would be free to move to a warmer climate. The only advice I have for those approaching retirement is to keep busy and have a hobby or two which you can enjoy. Mine are medical history, especially therapeutics, and trout fishing.

H. C. White to Hy Mayerson:

I am not continuing scientific activities: I am working with ghetto school children on health problems; I am not interested in any other position. I was a pediatrician before I was a physiologist, and am merely confirming the old saying that "On retourne tojòurs à son premier amourer."

Joseph Hayman to Hal Davis:

I do some teaching of 3 and 4-year students at Case Western Reserve and make ward rounds for a few months in the year at University Hospitals and the VA Hospitals.

Ernst Fischer to Hal Davis:

I decided to resign my half-monthly job with the department of physical medicine and rehabilitation, Albany Medical College. I liked my activities there very much, and I enjoyed particularly to have again direct contact with patients, which I did not have for 45 years since my internship. This decision has been made easier for me by the fact that my successor as chairman of my old department had left Richmond in the meantime and had been replaced. I believed and still believe strongly that a retired chairman should keep out of sight from his successor as long as possible. The new chairman offered me desk and working space. In consequence I am studying again birefringence of smooth and striated muscles, I give a few lectures to professional and to graduate students and give occasional lectures or participate in workshops out of town. Last summer I attended the International Meeting of Physiologists at Munich, Germany, and enjoyed very much meeting old friends from various countries. Prepare yourself early for a "second career" away from your old place of residence. My two attempts to do this were very satisfactory as far as it concerned adjustment to a new job, to new associates, and to a new environment. Unfortunately, I had the misfortune that I could not move my family. In consequence, I had first to return from Turkey to USA and finally even from Albany to Richmond.

Peter Karpovich to Bruce Dill:

I continue some scientific work but not at my usual speed. I have calculated the imminent records in weight lifting and am trying to develop a formula for determination of the total of three classic lifts if the lean body weight is known. My back trouble has made my research work very difficult and I decided to retire at the age of 73 (3 years ago). When my arthritis (right knee, shoulders and hands) eases up I do a few things in my workshop at home and even paint landscapes. I have been offered jobs and had invitations to lecture outside of Springfield, but I gratefully declined them and lecture occasionally only in Springfield. If it were not for Josephine, whom I call my Florence Nightingale, life would have been unbearable. I published an article last December about mechanism of rising on the toes. It has been a controversial topic for more than 100 years. I reported my findings 20 years ago and have been asked to do more.

Born in 1897H. Necheles to Hi Essex:

It makes me feel good that older members remember one. Concerning myself, I am continuing my previous scientific activities as Head of Research Department of Gastroenterology at Michael Reese Hospital. I have an assistant, a surgeon, an internist-gastroenterologist, and a chemist working with me. I come to the laboratory every day, although I am retired and do not receive a salary anymore. I live on my annuity and my social security besides a little that my wife earns. Thus, presently I am not interested in a position, but I may be because in July I will be 75 and I do not know whether the hospital will continue to permit me to pursue

my present activities. In that case I would like to find some income producing activity either through teaching or experimental, or otherwise, in Chicago. We are working on a factor in the blood of patients with duodenal ulcer that contracts the guinea pig ileum and which is not present, or only in small amounts, in the blood of persons without ulcer. We are also doing work in prednisolone-produced ulcer in the rat and using new approaches in its prevention. As you can see I am quite happy and I hardly feel the weight of my years. I have two lovely grandchildren who live near us with their parents. We have helped them buy a nice little house and with that we feel we have fulfilled a duty to our coming generation. I have a small fund which has been supplied by friends and by wealthier members of my family. Since I use only guinea pigs and rats and a few drugs (most supplied by industry or friends in research) I can get along well. Most members of my team are voluntary but not any less eager than any one of us. I remember the old days where we met at meetings and discussed problems of gastroenterology. I do not go to meetings often anymore in view of expenses. I have travelled around the world two or three times and I have seen many countries. After that I feel that I have done really enough travelling. I had to give up skiing and horseback riding, but I still enjoy swimming and diving.

S. A. Asdell to Hi Essex:

I read a lot, preferably books on travel or memoirs. Modern novels do not appeal to me. Also I travel as much as I can. Recent trips were to the Canaries and Madeira and to Iran, Greece and Turkey.

Edward Larsen to Hi Essex:

I have been a resident scientist at the Miami Seaquarium for the past two years and continuing my work on Sphoeroides, the puffer fish. I presented a paper "Source of the Toxin in Sphoeroides" at the Symposium on Physiological Compounds from the Sea at St. Petersburg, November 9, 1971. I had two papers at the Florida Academy of Sciences at Winter Park, April 9, 1972. At present I am in bad shape due to osteo-arthritis. If I do not get relief from my triumvirate of physicians I am going to go to a chiropractor, Christian Science practitioner, a geisha girl, or have acupuncture!

Louis Katz to Hi Essex:

I am still continuing to write (with Dr. Earl Silber), a textbook on Heart Disease, consisting of forty-one chapters, of which some thirty-five have been finished. The rest should be done within a year. It has been fascinating to write a textbook of all aspects of clinical heart disease based primarily, on the physiology of the heart and circulation. I spend one-half day on this. As you know, I am now Director Emeritus of the Cardiovascular Institute of Michael Reese Hospital and Medical Center. I am a consultant in this Institute, and the hospital provides me with a little office and a pretty secretary. I am now physically and mentally alert. The evidence is not only my own reaction, but the reaction of others. To be busy in some things that interest one is the best recipe

for meeting the aging process.

Robert Clarke to Bruce Dill:

I have continued to develop my primary hobby, handweaving, in which Mrs. Clarke joins me. Some editorial work at Wesleyan (my college) has been a diversion over a year or two. We are members of the Congregational Church, the oldest in town and one of the oldest in the State and I have been given responsibility for putting the archives into usable order and have done a bit of historical writing - nothing publishable as yet but a lot of fun.

Lee Wyman to Bruce Dill:

I am continuing my scholarly activities but not in physiology. I am busier than ever writing on what was a hobby and what turned into a professional activity, Navaho Indian cultural anthropology. Since retiring I have published five books and maybe a dozen papers on Navaho Indian ceremonialism, art, mythology, etc., and I have two more books in press right now. When you reach retirement age for goodness sake RETIRE. Do not take another paid position that ties you to hours and deadlines. God knows you have earned the privilege of working when, as and if you feel like it. I repeat WHEN, AS AND IF - (but if you are like me you will probably find yourself busier than ever). I turned down several offers of continued gainful employment when I retired and I have been having a ball ever since. I'm going on 75 and approve highly of miniskirts, detest maxis. Maxis are hard on girl-watchers. It's interesting to see what young people are doing and wearing. Young people are always fascinating.

Roberta Hafkesbring to Hy Mayerson:

I have many interests here at Leisure World, Laguna Hills, Calif.

O. M. Helff to Hy Mayerson:

I retired nine years ago from New York University, but have kept quite busy since then. During the summer and fall, I spend about six months in New Hampshire making extracts of amphibian tissues. These extracts are then used on the chemotherapy of mammary tumors of mice in Yonkers, where I stay for about two months. The remaining four months are spent wintering in Florida. I would not mind lecturing near Delray Beach, Florida during the winter or near Laconia, New Hampshire in the summer. Florida law, however, prevents salary payments to anyone over 70 years of age at a state college or university, so there remains only small private colleges. Although I have taught practically all the biological courses, my undergraduate specialties are histology and vertebrate embryology, while my graduate ones are experimental embryology and endocrinology. I am also quite well equipped to teach hygiene and human physiology.

Born in 1898Robert Anderson to Bruce Dill:

I am continuing my scientific activities here at Woods Hole. I had for many years planned on coming here when I retired and built a house for that purpose several years beforehand. As you probably remember, there are laboratories and excellent technical library facilities available from the MBL, under certain conditions and limitations, and that is the major reason for coming here. So far, I have used only the latter.

William Goldring to Hi Essex:

I have been "held over" as professor of medicine at NYU on a yearly reappointment basis with limited teaching duties for the second and third years. I am a member of the renal section of the department of medicine which meets weekly to review and discuss all renal and hypertension consultations in Bellevue and University Hospitals, requested by all services and performed by members of the renal section.

K. K. Chen to Hi Essex:

Please accept my thanks for your kind letter. I am glad to learn that you and Mrs. Essex are enjoying your good health, and had just returned from a trip to Mexico. I wish you many more years of happiness. Like yourself and Mrs. Essex, Amy and I are in good health, and just returned from the FASEB meeting in Atlantic City.

Philip B. Armstrong to Hi Essex:

I retired from the department of anatomy here at Upstate in 1968. However I am continuing in the department as a voluntary worker. The center furnishes me with laboratory space and some research support. I continue to teach as in the past (gross anatomy). Mrs. Armstrong says the only difference is that I am not paid for it. But I am having a most enjoyable time. This summer as in the past I will be at the Marine Biological Laboratory in Woods Hole on a grant from the New York State Research Foundation which will pay for my laboratory fees with some additional funds for incidental supplies.

E. J. Baldes to Hi Essex:

I retired from the Clinic in September 1963. Since then I have spent four years in government service with the Army Research Office in Life Sciences Division, Scientific Analysis Branch as a biophysicist. This assignment was in Arlington, Virginia. During the past five years I have been scientific advisor to the US Army Aeromedical Research Laboratory at Fort Rucker, Alabama. I am planning to retire in July 1972 to 1415 Alto Vista Drive, Vista, California 92088. I have no plans whatsoever for the future.

Eleanor Mason to Bruce Dill:

What a happy service this is, keeping in touch with us as still belonging! I have a final paper in Human Biology on "Variations in Basal Metabolic Rate Responses to Changes between Tropical and Temperate Climates." It presents previously unpublished data from Bombay together with earlier climatic-change studies from Madras on a good number of individuals, men and women, "European" and Indian, and on some individuals over long periods of tropical residence. It was a rather a thrill to read in Professor Eugène Schreider's article in the Janvier 1972 issue of *La Recherche* on "Les Limites d'Adaptabilité Humaine," in his discussion of the importance of individual differences in adaptation to hot environments: "Le problème a été bien saisi par quelqu'un qui l'a étudié avec plus de persévérance que tout autre physiologiste, grâce à l'observation d'un nombre appréciable d'individus, suivis pendant des périodes de temps assez longues, tantôt dans un climat, tantôt dans un autre." And the reference is to yours truly! I think a retired senior physiologist may be pardoned for a touch of delight over appreciation of long years of quiet work. I look forward to meeting other environmental physiologists and perhaps some anthropological ones at the Regional meeting of the International Union of Physiological Scientists in Sydney in August, when there will be a special Environmental Physiology Symposium on Physiological Responses to Hot Environments. Here in the Cambridge-Boston area I am happily in touch with a good number of friends and former students from India and their families.

Joseph Still to Bruce Dill:

Though I had to abandon physiological research on aging a number of years ago, I'm fortunate in being able to apply my theories of aging in my medical practice. You may recall that I developed the Cybernetic Theory of Aging which suggested that changes in the vegetative control panel (hypothalamus and brain stem) are the cause of the physiological changes that occur with aging. I did not then realize the extent to which the endocrine system tends to break down with increasing age and the fact that the occurrence of most if not all degenerative disease have now been shown to have at least some relationship to endocrine abnormalities. In my practice I treat a great many patients who are hypothyroid and/or hypoglycemic and/or diabetic. Many of the women relate the development of the problems that bring them to me either to the onset of menses, to a pregnancy or to the menopause - all endocrine crises. Through the use of thyroid, estrogen and education, I have found that some really remarkable age rollbacks can be achieved. Though I have no intention of ever retiring in the full sense of the word, I would like to find a physician to help me so I could devote more time in future to researching and writing about some of the results of what I call preventive endocrinology. Are there any candidates on your list?

Alex Hollaender to Bruce Dill:

I have an office and laboratory here in Oak Ridge, and am still a consultant to the biology division. I spend 60% of my time at the University of Tennessee as special assistant to the Vice Chancellor for

Research. I am also continuing the organization of the Latin American symposia. The twelfth of the series was just held at La Plata University and was quite successful. This year's will be in Cali, Columbia on Plant and Animal Improvement and Molecular Biology. In 1973 it will be held at Salvador da Bahia, Brazil and will deal with Reproductive Physiology and Genetics, and finally, we hope to hold the 1974 symposium in Lima, Peru on the subject of Basic Aspects of Nutrition. These Symposia have been supported the last five years through a grant from the Ford Foundation to the National Academy, with additional funds from the AEC and NSF, and helpful support from the OAS. I have just completed my term as President of the Environmental Mutagen Society which we started about two years ago in an attempt to bring the importance of testing for mutagenesis to pharmacologists, industrial people, chemists, etc. who should really do the testing. We are emphasizing the basic aspects, and publish a checklist of chemicals that have been tested for mutagenesis as well as a Newsletter. The incoming President of the Society is Dr. Ernst Freese of the NIH. I am also involved in several other international activities in connection with the environment, mostly from the genetic or radiation point of view. My recommendation for those approaching retirement who are well enough to remain active is to plan far enough ahead so that when the time comes one has several projects going, some of which may turn out very successfully. In my case, I just edited a couple of volumes on Chemical Mutagens: Principles and Methods for Their Detection. This is a quickly developing area that is turning out to be quite important.

Ernst Simonson to Bruce Dill:

I suffered a stroke last June, but my recovery has been quite satisfactory, so I resumed my work already in September on a somewhat reduced scale. Karl Smith (Madison, Wisconsin) has taken the major responsibility for the second volume "Psychology of Fatigue." The manuscript of volume II should be ready early Fall. It will be a novel approach based on cybernetic feedback from the molecular behavioral level.

John Sampson to Hy Mayerson:

I have been fortunate to remain active under the University of California's regulations that permit active teaching appointments for those that departmental chairmen desire. I had a routine "coronary" three years ago but recovered almost perfectly without limitations.

Bill Windle to Hy Mayerson:

I am keeping busy after finally retiring from the Institute of Rehabilitation Medicine of NYU in February 1971. Ella and I at that time moved to Granville, Ohio, where we both graduated from Denison University (1921 and 1922). I have been assigned a laboratory at the University in which to carry on microscopical studies, and have received grant support from UCP and NIH for two years. I am also continuing to edit "Experimental Neurology." We spent the first three months of this year at UCLA where I have some lectures and seminars under

auspices of the anatomy department. There have been several other noteworthy events since I last responded to inquiries by the Committee on Senior Physiologists: My book "Physiology of the Fetus" was published by Thomas last November. I received the 1971 award of the Association for Research in Nervous and Mental Disease last December. And last week in Florida at the Conference on Central Nervous Regeneration, the National Paraplegia Foundation announced that Roger Sperry (Cal. Tech.) and I will share the first William T. Wakeman Basic Research Award, to be presented at a meeting in Milwaukee on June 28 of this year. I believe I am every bit as active in retirement as I was before, but at somewhat different tasks. Although I no longer engage in animal experiments, my laboratory is next to the rat room and I am reminded by the aroma of earlier although not necessarily happier times.

Leonard Carmichael to Hal Davis:

I have a full time job; my title is Vice President for Research and Exploration of the National Geographic Society. My office is primarily concerned with the staff work that assists our Committee for Research and Exploration in deciding about the funding of research grants. I find this work very interesting and rewarding. My life-long interest in animal behavior continues unabated, and I find that our Research Committee is often able to assist in the support of field investigations in this area of study. I also continue editorial work in my academic field.

Eugene Still to Bruce Dill:

I have just about given up my scientific activities except for attending meetings. Some years ago I came into possession of a book containing a full description of a British battleship of circa 1800. I redesigned this vessel, with the fewest changes into a cruising yacht. We are now not too far from launching. She will be a brigantine of 150 tons. This little chore has kept me busy, in good health and has provided a great deal of pleasure.

Walter Redisch to Hal Davis:

I am continuing my scientific activities. I intend to retire officially on January 1, 1973. Then it will be my outspoken desire to move to another area. My advice is, stick to the eternal principles of honest, pure research, with practical applications remaining incidental; only then can they be valuable.

Born in 1899

Arthur DeGraff to Hi Essex:

I am still actively teaching at New York University School of Medicine. I no longer have tenure, but I am reappointed year by year, and so far I have been lucky in getting reappointed each year. I hope that this will continue for a few years more anyhow. At the present time I am not directly involved in any research problems, but I am still teaching, both in pharmacology and in medicine. As you probably know,

for some time my activities have been more in the field of pharmacology than in physiology, although I am still interested in cardiac physiology. I do have a word of advice for those who are approaching retirement; that is, do not retire unless you are forced to because of health or other reasons.

Robert Lackey to Hi Essex:

I am in good health and enjoying retirement very much. I am no longer engaged in research but am still devoting considerable time to teaching which is a source of much satisfaction to me. I enjoy the leisure to read in fields for which I had little time before retirement and also the opportunity for travel.

Hudson Hoagland to Hi Essex:

I still have my office and secretary and I am doing some writing and am active on several committees, including two editorial boards. I am consulted on various administrative policies of several scientific institutions of which I am a trustee or honorary trustee. My days seem to be quite busy although I am appalled at how rapidly I have lost contact with experimental work in physiology and biochemistry. To those who are approaching retirement, I can only say that it is essential in my opinion to have some intellectual interests or hobby to develop on retirement. Without this I think life would be awful.

Charley Best to Hi Essex:

I am continuing with my scientific activities and have rarely been busier than during 1971 and 1972. I have been lecturing in many parts of the world (England, Holland, Denmark, Brazil, Israel, Rome, as well as in a great number of places in the U.S. and Canada) usually on The History of Insulin and the Present Position. I have a position which enables me to continue with my scientific activities. I am a Graduate Lecturer in Physiology and usually give some twenty lectures a year outside Toronto. I am helping my wife write a book on our lives. She has completed some 12 chapters. In addition I am interested in having plenty of exercise - walking, riding horseback, swimming and playing golf. Since January 1 of this year we have been two weeks in Florida, attending the American Diabetes Association meetings, lecturing, and having a short holiday. In February we went out to California to the City of Hope Hospital where I dedicated a new department of endocrinology of which my friend Rachmiel Levine is Director. We met a lot of old friends and I was greatly impressed by the facilities for research and treatment of patients there at Duarte.

Maurice Tainter to Bruce Dill:

I am still working as a consultant to Sterling Drug Inc. in much the same way as when I wrote you in January 1970. However, as of last fall, my time is theoretically restricted to a half-time than a full-time basis. Aside from this, there is no startling news except that I have maintained my interest in legislative and regulatory problems in Washington.

F. D. W. Lukens to Hy Mayerson:

Like you I "retired" from the laboratory in 1966 to the VA Hospital and spent five years trying to resolve people problems as Chief of Staff. Now I have moved farther along the retirement road as staff physician to extended care patients. They have a need and afford the satisfaction of trying to meet that need. I am not on a single committee (does that evoke scorn or envy?) but just try to give patient care at the ward level. I continue to read a few journals related to my research interests and time adds a little clarity to one's ideas. To your third question, I would not like to move again, and, finally, I join the majority of you who want to keep going as long as possible.

Evelyn Anderson (Haymaker) to Bruce Dill:

I have reduced my scientific activities to trips to the Lane Medical Library - I have a chapter on the Pituitary and Hypothalamus which I must keep up to date. Being retired has given me a new lease on life - attempting to capture many of the activities I couldn't participate in during my career years - gardening, politics, general education, and world affairs (through reading). We have three children and six grandchildren, which could make an interesting career in itself. I am on the Board of Trustees of Carleton College (Minnesota) which could also be a career if there was more time available. So I'm as busy as ever. Look forward to retirement as the happiest and busiest time of life.

Anna Baetjer to Hal Davis:

Thanks to Dick Riley, Chairman of this department, I am continuing my research and teaching (but of course without salary) as Emeritus Professor of Environmental Medicine.

Born in 1900

Julius Sendroy to Bruce Dill:

I am the Consultant Chemist at the Navy Medical Neuropsychiatric Research Unit at San Diego, carry out some work for the Bureau of Medicine and Surgery in Washington, am a member of the Board of Directors of the National Registry in Clinical Chemistry and other committees, and attend meetings from coast to coast and in Europe (this summer). I might be interested in a part-time advisory, administrative or research position in Southern California. However we are delighted with our home in Rancho Bernardo - a home on which we are still exercising our artistic and manual talents. We would not consider moving anywhere else.

David Rioch to Bruce Dill:

I retired in July of 1970 and have been at the Institute for Behavioral Research with the flattering title Coordinator, Adult Learning Center, half-time since then. I have also been trying to write some things. Writing was never easy, but as I get older I find it increasingly difficult.

E. S. Nasset to Hi Essex:

I continue to investigate problems in GI physiology and have a post-doctoral and a predoctoral fellow, plus a couple of technicians to help me. I gave a paper last week at Atlantic City. I am still a lecturer at the University of California at Berkeley but my research is done here at Children's Hospital. My present seminar at Berkeley is on Alimentation.

John C. Scott to Hy Mayerson:

I am very happy to know that you are enjoying your new job in the teaching hospital in New Orleans. I think most of us would be quite unhappy if we did not have a chance to continue some of our life-time professional habits.

I am still at Hahnemann, where I have been continuously since 1924. Thanks to the kindness of my successor, Dr. Angelakos, I have remained as a professor of physiology and continue to teach, serve on faculty committees and maintain a small research laboratory. I believe that I am working as hard as I did in former years and I'm quite sure that I enjoy my activities even more than I did a few years back. I note that the Committee on Senior Physiologists includes Drs. Dill, Essex and Davis, as well as yourself. I consider each of these men old friends of mine and hope that you will send my greetings to them in lieu of a separate letter. I was in New Orleans a couple of years ago, at the American Heart Association meetings and stayed in a hotel where I could look across to the University. It reminded me of my old friend Dr. Ashman, who was interested in cardiac physiology and as you may recall, had written a monograph on the electrocardiography some years back. I intended to stop in and see if he was still about, but neglected to do so. Within the year, I was saddened to read of his death. It seems that we should not neglect to look up old acquaintances and say hello whenever the opportunity arrives.

Herbert Wells to Hy Mayerson:

Many thanks to you and the others of the Committee on Seniors on what you are doing for our group. I keep busy with problems of house and yard, projects in woodworking. Studies in elements of electronics, and cryptograms provide much of the fun to keep me happy. Perhaps prospective Seniors can get the best reassurance from accounts, such as yours that can give them confidence that they too "can still perform satisfactorily in an entirely new setting," and that this satisfaction can involve fun of solving problems that are not necessarily physiological. May I urge that (if you have not already done so) you publish in "The Physiologist" that message you so kindly wrote to me, A votre sante.

Gerry Evans to Hy Mayerson:

I spend one month a year as a consultant and most of the remaining time gardening. It's hard to tell an old man anything. Retire in good time to a planned retirement that gets you up every morning interested

and preferably physically active. It doesn't have to be important. Keep in touch with youth.

Kacy Cole to Hy Mayerson:

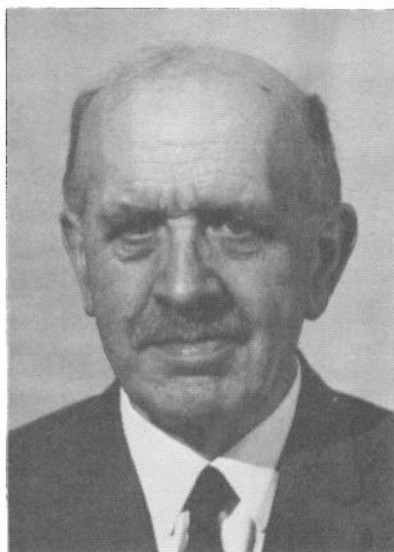
I've resigned all and sundry, been retired and, so far, rehired a year at a time. My book had amazingly flattering reviews and the second printing has just come out. Even more incredible is my brand new election as Foreign Member of the Royal Society. How lucky can you get? Except that I still want to know how an ion gets through a membrane.

James Bordley to Hal Davis:

I am a consultant in hospital and regional health planning.

F. J. W. ROUGHTON, F. R. S.

1899-1972



On April 29, 1972 at the age of 72 years, Francis John Worsley Roughton, emeritus Plummer Professor of Colloid Science at Cambridge University died in Cambridge, England. Although the mainstream of his life and focus of his loyalties were in his beloved Cambridge and Trinity College, he nevertheless maintained exceptionally strong ties with students and colleagues in the United States. Indeed it may be said that his work had more influence in this country and that many of the ideas stemming from his laboratory in Cambridge came to full scientific development and clinical application here. He was a familiar figure at meetings of the American Physiological Society and an Honorary Member since 1957.

The Roughton family came from the town of Kettering, Northamptonshire, where Roughtons had been physicians since about 1735 in unbroken line and where F. J. W. Roughton was born on June 6, 1899. His early intentions were to follow his father, John Paul Roughton, into the practice of medicine. He entered Winchester College, from whence he won a scholarship in mathematics and the natural sciences to Trinity College, Cambridge, which he was able to take up in 1918 because a cardiac anomaly rendered him ineligible for military service. His accomplishments in his studies in the sciences and his creative ability gave early indication of his potential in research and his Ph.D. Thesis on the Kinetics of Oxygen and Carbon Monoxide in Blood won his election as a Fellow of Trinity in 1923. However, the duties and opportunities of this Fellowship were not consistent with the completion of his medical qualification, to which he never returned.

Roughton started his faculty career at Cambridge as a University Lecturer in Biochemistry in 1923, but moved into physiology by 1927. Once elected a Fellow of Trinity College he remained connected with it all his life. During World War II, F. J. W. Roughton was a Visiting Research Fellow in War Science and Medicine at Harvard and

Written by Robert E. Forster

Columbia Universities and he spent much of his time at the Harvard Fatigue Laboratory working on such service related problems as CO poisoning and high altitude physiology. He was appointed Plummer Professor of Colloid Science at Cambridge University in 1947, retiring in 1965. He received many honors among which he prized most his election to the Royal Society in 1936 and his Hopkins Lectureship in 1970.

He married Alice Hopkinson, daughter of Professor B. Hopkinson of Cambridge in 1925. Mrs. (Dr.) Roughton is a general practitioner and psychiatrist practicing in Cambridge and their large home on 9 Adams Road is famous for hospitality and particularly as a haven for young foreign students. The Roughton's have two children, a daughter Rosemary, a son Geoffrey and several grandchildren.

Roughton's research sprang from his interest in respiratory physiology and although it led him far afield he never lost his fascination with the mechanisms of gas exchange. Two main themes are identifiable which he followed continuously throughout his professional career. The first was the physical chemistry and particularly the rapid chemical reactions of O_2 , CO and other ligands with hemoglobin and the second the reactions of CO_2 in the blood. He published about 100 papers, all of which are remarkable for their content and style.

As a student in Trinity College he was inspired and initiated into biochemistry by Sir Frederick Gowland Hopkins, the Father of English Biochemistry, who was a Fellow of Trinity and who had been called back to direct medical studies because so many of the younger faculty were away in the World War. By the summer of 1919, Joseph Barcroft, A. V. Hill and Hamilton Hartridge had returned to Kings College and provided catalytic stimulation in physiology and biophysics. According to his own story, Roughton introduced himself to Joseph Barcroft on the stairs of the physiological laboratories in order to proffer criticism of the latter's paper describing his adaption to high altitudes in the famous Glass Box. This was in May, 1920, only several days after the article had first appeared in print. Barcroft responded in his famous good humor, admitted the validity of the criticism and asked Roughton to work with him on the problem. This led in 1921 to Hartridge inviting young Roughton to join him in experiments on the rate of the reactions of CO and O_2 with hemoglobin, a question which Barcroft had attempted to answer, unsuccessfully. Hartridge had conceived of using intense light to dissociate a flowing solution of HbCO, which also contained dissolved O_2 , and observing the time course of recombination downstream with a "reversion spectroscope." This last was an ingenious instrument invented and constructed by Hartridge, with which an observer could rapidly determine the mean wavelength of the absorption bands of hemoglobin compounds. Roughton supplied the knowledge of physical chemistry and respiratory physiology. This partnership produced a series of 8 papers between 1923 and 1928 which reported the first measurements of rapid (in the millisecond range) chemical reactions in solutions and described the rapid mixing technique in both continuous flow and stopped-flow instruments. Roughton's Ph.D. Thesis was a synthesis of these new measurements of the speed of O_2 and CO reactions in blood with

existing knowledge of O_2 exchange in the lungs, particularly in reference to the controversy of "secretion versus diffusion" which was still raging at the time. As important as this was and is to respiratory physiology, the papers with Hartridge (1,2) also represent the beginnings of the field of modern rapid chemical reaction kinetics which has contributed so much to biochemistry and chemistry. It is to be regretted that these pioneering investigations have not received the recognition they deserve.

Roughton went on in the 1930's to develop techniques for the measurement of rapid changes in temperature and apply them to a wide range of chemical reactions, such as those of acid, alkali and CO_2 , and the buffering of amino acids and proteins.

In 1955 he started a fruitful collaboration with Quentin Gibson, then at the University of Sheffield, applying the stopped-flow reaction apparatus to a variety of old and new problems related to the physical chemistry of hemoglobin. This partnership was active until the mid 1960's.

For all his application of physical chemistry and mathematics to physiological problems, Roughton always remained fundamentally a physiologist. His chapter in the American Physiological Society Handbook on the transport of O_2 and CO_2 covers this topic, including recent advances, with clarity and precision, for the student of physiology. Whenever his researches into reaction kinetics made it possible to grasp a significant physiological measurement he did not fail to take advantage of the opportunity. Of such was his calculation of the capillary blood volume of the lung and of the average length of time a corpuscle takes to pass through the lung capillaries (5).

At the Harvard Fatigue Laboratory in 1941 Forbes, Sargent and Roughton measured the uptake of CO by men exercising at different work loads and different alveolar PO_2 . Appreciating the uses to which the data could be put, Roughton went on himself and measured the rate of CO uptake by human red cells at $37^\circ C$ in a crude continuous-flow rapid-reaction apparatus using a Hartridge reversion spectroscope which turned up in New York. With the two sets of data, several judicious estimates and an intricate series of maxima-minima arguments he arrived at a limiting value of 60 ml for the average pulmonary capillary blood volume in 1945, not significantly different from the values he, Briscoe, Krauzer, Cander and I obtained in Philadelphia in 1953 using more sophisticated apparatus and a complete mathematical analysis.

As a student he acquired from Barcroft, and never lost, a curiosity about the mechanisms of gas diffusion in the lung. During World War II in his consultant capacity at Harvard and Columbia, and in Washington, he stimulated thought and research on this topic. Thus he was in considerable part responsible for the renaissance of investigation into the diffusion of gases in the lung that followed the war. He was never far from laboratories working on these problems in this country and the present widespread measurement of pulmonary diffusing capacity in the clinic is a direct result of his interest.

In vivo, O_2 and CO_2 exchange with red cells, not with a hemoglobin solution, and comparative measurements of the rate of gas uptake by cell suspensions and homogenous solutions of hemoglobin in 1927 demonstrated that the process was much slower in the former, although it was more convenient and accurate to make experimental observations in solutions. Diffusion plus chemical reaction within the substances of the red cell, plus the additional possibility of diffusion resistance through the cell membrane, slow the overall process many-fold and complicate the physiological interpretation of kinetic data on cell suspensions. Roughton developed a theoretical mathematical treatment of the process in 1931, but an analytical solution was not possible. He did manage to solve the differential equations for limited cases. He returned to the problem with Mrs. Nicolson about 20 years later using numerical solutions and endeavoured to separate the resistance to diffusion of the membrane from that within the cell, towards which goal he made progress but did not reach a final conclusion.

Roughton maintained an interest in the diffusion of gases, which was so basic to much of his work. He and associates determined the diffusion coefficient of CO , N_2 and O_2 in concentrated hemoglobin solutions in 1952 to 1956 and studied special cases of diffusion plus chemical reaction; "advancing front" diffusion of O_2 in hemoglobin solution; diffusion of gases through a membrane and thence into a medium where a rapid irreversible reaction takes place; and the permeability of molecular monolayers to CO_2 .

The first of a series of publications appeared in 1932 representing the second main theme of Roughton's work dealing with the kinetics of the reactions of CO_2 with body fluids. Trained in physiology and surrounded by Barcroft's students and associates interested in O_2 and CO_2 transport by the blood, it seems inevitable in hindsight that Roughton would have applied his experience and techniques to the study of the kinetics of CO_2 . Brinkman, Margaria and Roughton published in 1933 what is still the definitive paper on the theoretical kinetics of CO_2 reactions. Following up the observations of Henriques that the uncatalyzed hydration-dehydration of CO_2 was speeded up by hemolyzed blood, Mel-drum and Roughton in 1933 (3) reported the discovery, purification and baptism of carbonic anhydrase, only a matter of months ahead of Stadie and O'Brien at the University of Pennsylvania. They also found several simple compounds that inhibited carbonic anhydrase, such as cyanide. Roughton was at this point able to synthesize the known facts into a schema of O_2 and CO_2 exchanges of blood which he presented in a review in 1935 (4). His diagram illustrating gas exchange in the lungs, including the diffusion of HCO_3^- into the red cells in exchange for Cl^- ; its catalyzed dehydration there to CO_2 which then diffuses rapidly into the alveolar gas; the release of CO_2 from hemoglobin carbamate; and; the intricate interactions of CO_2 and O_2 is in almost every text book of physiology published today.

The importance of the discovery of carbonic anhydrase to physiology and to clinical medicine is hard to overestimate. It is vital to the secretion of acid by the kidney and stomach and of alkali by the pancreas. Its inhibition is important in the treatment of glaucoma and formerly of

heart failure. Roughton kept up an interest in the physiological applications of his work and consulted in many particulars, for example with brewers on the influence of the enzyme in preserving the head of beer.

He continued his research into CO_2 chemistry with further investigations into the catalytic effects of buffers on CO_2 hydration-dehydration in 1938; the thermochemistry and kinetics of heat changes in the early 1940's, and; the reactions of CO_2 with OH^- in the early 1950's. He reviewed existing knowledge of the enzyme in 1934 and again in 1951. His last published work in this field was with the Hemingway's on the speed of the Hamburger Shift in 1970.

Christian Bohr originally suggested that CO_2 formed a compound with hemoglobin in blood and gave it the name "carbhaemoglobin." However, investigators were unable to verify its existence in the presence of HCO_3^- . Once carbonic anhydrase was recognized, it could be easily inhibited and in 1933 Meldrum and Roughton were able to separate a compound of CO_2 with hemoglobin, which they considered hemoglobin carbamate, from HCO_3^- because the uncatalyzed dehydration-hydration reaction is so much slower. They also found that the oxygenation of hemoglobin caused a marked fall in hemoglobin carbamate concentration. Roughton ascribed this to an allosteric effect within the protein molecule and incorporated it into his overall scheme of O_2 - CO_2 exchanges. He computed that about one third of the total arteriovenous CO_2 content difference across the lungs derives from carbamate. However, many investigators were unsatisfied by the techniques he used to analyze carbamate, particularly the barium hydroxide method which was supposed to precipitate HCO_3^- while leaving carbamate in solution. At this time it was technically difficult to make reliable measurements of small differences in pH. In 1948 Jeffries Wyman calculated that the well known increase in acidity accompanying oxygenation of hemoglobin (Bohr effect) could explain the supposed "allosteric" decrease in CO_2 content of blood. This initiated a controversy that was only recently resolved. Roughton, Rossi-Bernardi and others found experimentally that hemoglobin carbamate decreased on oxygenating blood or hemoglobin solution at constant pH and constant Pco_2 . They also recognized that the buffer capacity of hemoglobin carbamate itself could reconcile the calculations of Wyman and the more recent experimental data.

CO_2 is only one of several chemical entities that react with hemoglobin to lower its affinity for O_2 . These include hydrogen ion, 2,3, diphosphoglycerate and some other organo-phosphates as well as certain common anions. F. J. W. Roughton's final scientific publication is on the subject of oxygen-linked ligands with Rossi-Bernardi and the Milan group.

The O_2 and CO equilibrium curves with hemoglobin always intrigued Roughton. The possibility of obtaining all 8 reaction velocity constants required by the Adair theory was a goal that was always in front of him. Forbes and he obtained very precise equilibrium curves in 1931 using gasometric techniques, for which Roughton always had a firm respect, in contrast to his suspicions of the reliability of spectrophotometric methods. At the Harvard Fatigue Laboratory in 1942 he investigated

with Darling the influence of HbCO and methemoglobin on the O₂-hemoglobin equilibrium curve, a matter of great interest and importance today in connection with environmental CO toxicity. From 1951 to 1955 he, Paul, Otis and Lyster attacked the extremes of the sheep equilibrium curves because of the critical nature of these regions in defining the numerical value of Adair's equilibrium constants, particularly for the 1st and 4th ligand molecules. About the same time he and Gibson, using the latter's stopped-flow reaction apparatus, measured the reaction velocity constants for the 1st and 4th ligand molecules, providing an alternative approach to the Adair equilibrium constants. Most recently he has been collaborating with John Severinghaus using an extremely sensitive O₂ electrode method to define the top of the O₂ equilibrium curve to a new order or precision, but this work has not yet been published to my knowledge.

Most of Roughton's work required determination of gases, particularly O₂, CO and CO₂. Thus he was involved in the development of new analytical apparatus and techniques throughout his career. He was a virtuoso on the Van Slyke apparatus and developed several new techniques for its use in blood gas analysis. While he and P. F. Scholander were at the Fatigue Laboratory during World War II they developed a series of rapid methods for analyzing blood gases which were based on a modified glass tuberculin syringe, known now as the Roughton-Scholander syringe, or vice versa, and which could be used in the field.

Professor Roughton had a real working relationship with colleagues from San Francisco and Los Angeles to Milan and his periods of residence were models of efficiency. In contrast to many modern investigators, particularly American, who, blessed or perhaps cursed, with a surfeit of sophisticated apparatus, expect initial measurements to fail and therefore almost automatically discard them, Roughton planned each experiment carefully and all the data he collected appeared in a resulting publication. He was probably a shy individual and had a not-so-secret interest in ball room dancing and a vast store of remembered poetry particularly Gilbert and Sullivan. He had many delightful idiosyncracies, such as rising on his toes while lecturing, chewing his necktie in contemplation, and wearing a Panama hat in the tropical Philadelphia summer. For some reason he was appreciated most in the United States. Many of his students are here and most of his collaborators, all of whom will miss him. His published works are an indestructible memorial, an evidence of his great contributions to science and particularly physiology. Students unborn will enjoy a vicarious thrill of discovery in reading his papers.

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ALLAN HEMINGWAY

1902-1972

Allan Hemingway, Emeritus Professor of Physiology at the University of California, Los Angeles, died in his sleep on April 22, 1972 at his home. He is survived by his wife Claire Conklin Hemingway and by his daughters, Mrs. James Spicola and Mrs. William Kelley, and grandchildren, Ann, John, and Thomas Spicola and Claire, Susan, and Shawn Kelley, all of Minneapolis, Minnesota.

Allan had his school and academic education in his native British Columbia, followed by his Ph.D. in physics at the University of Minnesota, his studies there in the preclinical medical sciences, and his career at that institution where he reached the professorship in physiology in 1947. In 1951, he came to UCLA as the first faculty member to arrive in the physiology department of the new School of Medicine.

His investigative work, which gave rise to some 120 papers, covered a wide range of subjects, and was characterized by a balanced mastery of neural and vegetative physiology and a fine attention to methodological perfection. Technical researches on diathermia were the first wave of his activities, whereupon, via early research on glass electrodes, he made several inquiries into the physiology of body fluids. This led to the fields of his major life-long interest; respiration and metabolism, and the control of body temperature.

One major phase of this, around 1940, was his collaboration with A. O. Nier on the development of workable mass-spectrometers for the use of stable isotopes for metabolic tracer work, and their performance of a number of pioneering investigations on metabolic pathways with workers like Wood and Werkman and others who were to become leaders in the field of both microbial and mammalian metabolism. This also included, in 1950, a paper on the use of mass-spectrometry in the assessment of alveolar ventilation.

In the main body of his researches, he investigated respiratory and thermoregulatory functions, and related circulatory adjustments, both at the basic level and in relation to clinical and environmental problems. He influenced many postdoctoral students, among whom E. B. Brown, Walter Freeman, Y. Kawamura, John Murray, Gabriel Nahas, Alvin Sellers, Daniel Simmons, Douglas Stuart and Marian Swendseid reached Professorships in Physiology, Medicine, or Nutrition, and he kept in touch with other major investigators, as evidenced last in a 1970 study by the Hemingways with Roughton on the velocity of the chloride shift, for which the basis was laid during his sabbatical at Cambridge in 1958.

It was in his research on thermoregulation - one phase of which he pursued during his 1963-1964 sabbatical in New Zealand - that his ability to bridge somatic and neurophysiology was particularly impressive. In the course of his work with Lucy Birzis on the hypothalamic control of shivering, we encounter what I believe were the first unit recordings in that region. The authors were characteristically modest on this point, but in their 1957 paper made the prophetic remark that "This type of

recording should be useful for anatomical localizations of other hypothalamic functions, where a change in total discharge can be correlated with a change in some parameter of the function under investigation."

In addition to his active research pursuits, he was a devoted and conscientious teacher, who set an example in the exceptional care he lavished on the instruction of laboratory experiments and the procedures followed in those.

He served in a number of consultative and public functions, among which an NIH committee on the selection of both predoctoral and postdoctoral fellows was closest to his heart. His work as the Chief of the Laboratory of Biophysics at Randolph Field involved important work on motion sickness and other aspects of aviation physiology. His service as a VA consultant led to his full-time work at the San Fernando VA Hospital, where he and his wife continued vigorous research activity. His laboratory was completely destroyed in the 1971 earthquake, but undauntedly he was establishing a new one at Sepulveda.

With his unflagging dedication to his work, his high personal integrity, and his youthful attitude, his memory should remain an example for all of us. The department honored Dr. Hemingway upon his retirement with an annual seminar, at which Severinghaus and Yamamoto were the first speakers so far, and which now will be continued, unfortunately, in his memory.
