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ACTIONS TAKEN AT SPRING MEETING

April 13-18, 1969

ELECTIONS - A. C. Barger was elected to the position of President-Elect. D. C. Tosteson was elected to a full four-year term on Council.

Ernst Knobil was elected to fill the unexpired term (three years) of A. C. Barger on Council.

All candidates nominated by Council were elected to membership (See Newly Elected Members).

ABSTRACTS FOR 1970 SPRING MEETING - The Council again proposed a system of reducing the number of abstracts by an appropriate method of selection on merit. The proposal was defeated by a fairly close vote at the Business Meeting. The lottery system of eliminating every n^{th} paper from oral presentation will again be in effect for 1970. If more than 850 abstracts are received every n^{th} paper will be excluded from oral presentation, but the abstracts will be published, if the author so chooses. No sponsored papers will be accepted. A person's name can appear only once on the program. An APS regular member, retired or honorary member must be one of the authors. In 1969 there were 75 abstracts eliminated from oral presentation by this method.

AIBS - The Society voted to discontinue its affiliation as an adherent society of the American Institute of Biological Sciences, but encouraged its members to become individual members of AIBS.

PUBLICATIONS - The Physiological Reviews Index will be available in June at \$10 per copy.

Handbooks under preparation are on Kidney; Endocrines; and Muscle. Mr. Stephen Geiger will join the APS staff as Executive Editor of the Handbooks on July 1.

Dr. Barger indicated that 18% of the Publication income was from page charges. He appealed to authors to continue paying page charges.

ANIMAL CARE LEGISLATION - Dr. Visscher introduced a resolution that further legislation at this time in the laboratory animal field is unnecessary and undesirable and that members of the APS oppose any legislation if it proposes to put any authority for the control of experimental design of studies in the hands of persons other than the investigator or his scientifically qualified peers. Resolution was passed.

LONG RANGE PLANNING - Dr. Prosser mentioned that several activities are in the planning stage. One is to develop a union of physiologically oriented societies. Another is to expand the Public Information Committee so that it can be active the year round.

Still another is the plan to establish an educational research office at APS headquarters. He asked members to send any comments or suggestions on these matters to Dr. Daggs.

APS ASSOCIATE MEMBERSHIP

There has been a misunderstanding in some quarters about Associate Membership in the American Physiological Society.

Associate Membership includes several categories of persons with a deep interest in physiology who do not qualify for Regular Membership. They are: 1) Advanced graduate students who have passed their preliminary examinations for the doctorate degree; 2) Teachers of physiology, particularly those in smaller colleges, who do little or no research but who teach physiological subjects and are in a position to influence students regarding future careers in physiology; and 3) Investigators who have not as yet had the opportunity or time to satisfy the requirements for Regular Membership.

Persons in the above mentioned categories may be proposed for Associate Membership by two Regular Members. They must be residents of North America at the time of election, not just at the time of nomination. They are elected to membership in the same manner as Regular Members. Associate Members may later be proposed for Regular Membership - if and when they satisfy the requirements, however there is no limitation on the duration of Associate Membership.

Associate Members pay a nominal membership fee (\$5 per year at present). They do not have voting privileges but may attend Business Meetings of the Society. They do not have the privilege of presenting a paper at the Federation meetings unless a Regular Member of APS is a coauthor. Beginning in 1970 they will pay only Regular Member registration fees at the Federation meetings and not be taxed non-member fees as is the Federation rule at present. Associate Members have the privilege of submitting a paper at the Fall meeting of the Society without Regular Member sponsorship. They receive *The Physiologist* gratis.

Proposal forms for Associate Membership may be secured from the Office of the Executive Secretary.

MEMBERSHIP STATUS

April 1, 1969

Active Members	3093
Retired Members	165
Honorary Members	17
Associate Members	253
	<u>3528</u>

SUSTAINING ASSOCIATES

Abbott Laboratories, Inc.	Hoffman-LaRoche Laboratories
Ayerst Laboratories	Lakeside Laboratories, Inc.
Burroughs Wellcome & Co., Inc.	Merck Sharp & Dohme Research
CIBA Pharmaceutical Products, Inc.	Laboratories
E & M Instrument Co., Inc.	The Norwich Pharmacal Co.
Eli Lilly & Co.	Chas. Pfizer & Co., Inc.
Gilford Instrument Laboratories	Riker Laboratories, Inc.
Gilson Medical Electronics	A. H. Robins Co., Inc.
Grass Instrument Company	Warner-Lambert Research
Harvard Apparatus Company	Institute
	Wyeth Laboratories

DEATHS SINCE FALL MEETING 1968

Theodore G. Bernthal - 9/1/68	Franklin C. McLean - 9/10/68
Lucien A. Brouha - 10/6/68	Zygmunt Menschik - 2/22/69
Sue Buckingham - 1/22/69	George T. Pack - 1/23/69
Janet Howell Clark - 2/11/69	Oscar Riddle - 11/29/68
Dwight Espe - 3/20/69	Donald Rosenbaum - 9/9/68
George Fahr - 12/3/68	Otto H. Scherbaum - 1/8/69
William J. Fry - 7/21/68	Robert M. Schlaer - 1/31/69
Edward L. Gray - 7/18/68	W. W. Tuttle - 1/3/69
W. D. Lotspeich - 11/28/68	

50-YEAR MEMBERS

Walter C. Alvarez	Paul E. Howe
Samuel Amberg	Andrew C. Ivy
Joseph C. Aub	Dennis E. Jackson
George A. Baitsell	Merkel H. Jacobs
Olaf Bergeim	Edward C. Kendall
Harold C. Bradley	Benjamin Kramer
Thorne M. Carpenter	Theophile K. Kruse
Percy M. Dawson	Henry Laurens
Herbert M. Evans	Edward Lodholz
Mable P. Fitzgerald	David Marine
Maurice H. Givens	Jesse F. McClendon
Charles M. Gruber	Frederick R. Miller
Addison Gulick	Sergius Morgulis
Frank A. Hartman	Eugene L. Opie
Harold L. Higgins	Alfred C. Redfield

Andrew H. Ryan
Benjamin H. Schlomovitz
Charles D. Snyder

George H. Whipple
Rosalind Wulzen

NEWLY ELECTED MEMBERS

The following, nominated by Council, were elected to membership in the Society at the Spring Meeting, 1969.

ADAMS, Walter C.: Asst. Prof. Biol. Sci., Kent State Univ.
BAINES, Andrew D.: Assoc. Prof. Pathol. Chem., Univ. of Toronto
BANCHERO, Natalio: Asst. Prof. Physiol., Univ. of Colorado Med. Ctr.
BARBOUR, Benjamin H.: Assoc. Prof. Med., Univ. Southern California
BENTLEY, Peter J.: Assoc. Prof. Pharmacol., City Univ. New York
BERTLES, John F.: Chief, Hematol. Unit, St. Luke's Hosp., N. Y.
BOSSOM, Joseph: Res. Assoc. Psychol., Brooklyn College
BRACHFELD, Norman: Asst. Prof. Med., Cornell Univ., N. Y.
BUNDY, Roy E.: Chmn, Dept. Physiol., Fairleigh Dickinson Univ.
CHRISTENSEN, James: Asst. Prof. Med., Univ. Hosps., Iowa City
DAW, John C.: Instructor Physiol., Univ. of Virginia
DeMartinis, Frederick D.: Asst. Prof. Physiol. & Biophys., Woman's Med. Coll. Pa.
EDER, Howard A.: Prof. Med., Albert Einstein Coll. Med.
EDMANDS, Robert E.: Asst. Prof. Med., Univ. of Indiana
ENROTH-CUGELL, Christina A.E.: Asst. Prof. Physiol., Northwestern Univ.
GANS, Joseph H.: Assoc. Prof. Pharmacol., Univ. of Vermont
GREEN, Daniel G.: Asst. Prof. Physiol. Optics, Univ. of Michigan
GREGOIRE, Adolphe T.: Asst. Prof. Physiol., Univ. of Michigan
GUTH, Paul H.: Dir. Med. Services, Orange County Med. Ctr., Calif.
HAZELWOOD, Robert L.: Assoc. Prof. Biol., Univ. of Houston
HOLEMANS, Rudolf: Asst. Member, Albert Einstein Med. Ctr.
HOUK, James C.: Instructor Physiol., Harvard Medical School
JAMISON, Rex L.: Asst. Prof. Med., Jewish Hosp. of St. Louis
KENNEY, Richard A.: Vis. Prof. Physiol., George Washington Univ.
KING, Theodore M.: Assoc. Prof. Physiol., Univ. of Missouri
KLAHR, Saulo: Asst. Prof. Med., Washington Univ. Sch. Med.
KOLLIAS, James: Asst. Prof. Appl. Physiol., Pennsylvania State Univ.
KOUSHANPOUR, Esmail: Asst. Prof. Physiol., Northwestern Univ.
LAWSON, Walter H., Jr.: Asst. Prof. Med., Downstate Med. Ctr.
LORBER, Mortimer: Asst. Prof. Physiol. & Biophys., Georgetown Univ.
MARGULES, David L.: Group Leader Psychopharmacol., Wyeth Labs.
MAYER, Steven E.: Prof. Pharmacol., Emory Univ.
MENA, Flavio: Assoc. Invest., Inst. Invest. Biomedicas, Mexico City
MENGEIER, William L.: Prof. Biol., Madison College
MIDGLEY, Alvin R.: Assoc. Prof. Pathol., Univ. of Michigan
MIZELL, Sherwin: Assoc. Prof. Anat. & Physiol., Indiana Univ.
PARMLEY, William W.: Res. Assoc. CV Inst., Harvard Med. Sch.
PIATNEK-LEUNISSEN, Dorothy A.: Res. Asst. Prof. Med., Hahnemann Med. Coll.
PORUSH, Jerome G.: Chief, Renal & Electrolyte Sect., Brookdale Hosp. Ctr., N. Y.
PRESHAW, Roy M.: Asst. Prof., Sect. Physiol., Mayo Cl. & Fndn.

PREUSS, Harry G. : Asst. Prof. Med., Univ. of Pittsburgh Sch. Med.
 REMMERS, John E. : Res. Assoc. Physiol., Dartmouth Med. Sch.
 RIEDESEL, Marvin L. : Assoc. Prof. Biol., Univ. of New Mexico
 ROTHENBERG, Sheldon P. : Assoc. Prof. Med., New York Med. Coll.
 ROTHSCCHILD, Marcus A. : Chief, Rad. Service, N.Y. VA Hosp.
 SCHWARTZ, Arnold : Assoc. Prof. Pharmacol., Baylor Univ. Coll. Med.
 SENIOR, John R. : Asst. Prof. Med., Univ. Pennsylvania
 SHOFER, Robert J. : Asst. Prof. Anat., Albert Einstein Coll. Med.
 SOUTHERN, A. Louis : Assoc. Prof. Med., New York Med. Coll.
 STUBBS, Donald W. : Asst. Prof. Physiol., Univ. of Texas Med. Br.
 SUTHERS, Roderick A. : Asst. Prof. Physiol., Indiana Univ.
 TANNER, George A. : Asst. Prof. Physiol., Indiana Univ. Sch. Med.
 TAYLOR, Charles R. : Res. Assoc. Zool., Duke Univ.
 TRABER, Daniel L. : Asst. Prof. Physiol., Univ. of Texas Med. Br.
 URSCHER, Charles W. : Res. Assoc., Peter Bent Brigham Hosp.
 VERNON, Jack A. : Prof. Otolaryngology, Univ. of Oregon Med. Sch.
 WRIGHT, Ernest M. : Asst. Prof. Physiol., UCLA
 YOUSEF, Mohamed K. : Asst. Prof. Biol. Sci., Desert Res. Inst.
 YU, Byung P. : Asst. Prof. Physiol. Biophys., Woman's Med. Coll.
 of Pa.

ASSOCIATE MEMBERS

ALEXANDER, William C. : Grad Trainee - CV, Dept. Physiol.,
 Bowman Gray Univ.
 BAJPAI, Praphulla K. : Asst. Prof. Biol., Univ. of Dayton
 BANERJEE, Chandra M. : Staff Physiologist, Hazleton Labs., Inc.
 BREITMEYER, Michael O. : Asst. Prof. Biol. Engr., Rose Poly-
 technic Inst.
 CLAYTON, Judith A. : Res. Fellow Med., Harvard Med. Sch.
 DAVIS, Robert H. : Chief, Sect. Reprod. Endocr. Biol., Thos. M.
 Fitzgerald Mercy Hosp.
 DOWNEY, H. Fred : NIH Predoct. Fellow, Univ. of Illinois
 HAIGLER, Henry J. : Grad. Student Physiol., Bowman Gray Sch. Med.
 HEATH, Robert T. : Res. Fellow Biol., Calif. Inst. of Technology
 KANT, Kenneth J. : Instructor Physiol., SUNY, Buffalo
 KUTCHAI, Howard C. : Postdoct. Trainee, Biostatistics, Univ. Michigan
 STRAW, James A. : Asst. Prof. Pharmacol., George Washington Univ.
 TEN EICK, Robert E. : Guest Investigator Pharmacol., Columbia Univ.
 TRIMBLE, Mary Ellen : Grad. Student, Brown Univ.
 TRUONG, Xuan T. : Res. & Cl. Consult., Inst. Phys. Med. & Rehab.
 Peoria, Ill.
 ULANO, Harvey B. : Grad Student Physiol., Temple Univ. Sch. Med.
 WATKINS, Don W. : Postdoct. Trainee Physiol., Univ. Wisconsin
 WELCH, High G. : Asst. Prof. Phys. Ed., Univ. of Michigan
 WHITFIELD, Carol F. : Res. Assoc. Physiol., Pennsylvania State Univ.
 WIT, Andrew L. : Res. Assoc. Physiol., USPHS Hosp., Staten Island
 WYLIE, Richard M. : Res. Assoc., The Rockefeller Univ.

1968 FISCAL REPORTS
SOCIETY OPERATING FUND

INCOME

Regular Membership Dues	\$43,948
Associate Membership Dues	1,179
Sustaining Associates	6,600
Interest	4,572
Reimbursement from Federation Spring Meeting	14,553
Sale of Laboratory Experiments	622
Course for Physicians (net)	6,970
Insurance Dividend	107
Miscellaneous Income	752
Total Income	<u>\$79,303</u>

EXPENSES

Salaries and Benefits	\$29,218
Hotel and Travel	3,173
Addressing, Mailing & Shipping	1,838
Telephone	211
Printing	896
Supplies and Equipment	1,026
Rent	4,660
Dues to Federation	17,637
Dues and Assessments to Other Organizations	1,185
Education Committee	102
Bowditch Lecture	500
Miscellaneous Expenses	167
APS Business Office (SOF share)	13,368
Total Expenses	<u>\$73,981</u>

Excess of Income over Expenses	\$5,322
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PUBLICATION OPERATING FUND

INCOME

Subscriptions	\$427,290
Sale of Reprints, net	73,770
Sale of Back & Single Issues	12,769
Advertising, net	13,731
Page Charges	129,011
Author Alterations	719
Interest	15,264
Royalties	5,083
Insurance Dividend	1,906
Miscellaneous Income	159
Bad Debt Write Off	(1,203)
Total Income	<u>\$678,499</u>

EXPENSES

Salaries and Benefits	\$102,808
Section Editor Expenses	21,951
Professional Services	6,489
Printing and Engraving	327,197
Supplies and Equipment	1,677
Addressing, Mailing & Shipping	44,189
Telephone	1,349
Hotel and Travel	6,380
Repairs and Maintenance	153
Rent	17,137
Advertising Tax	2,500
Miscellaneous Expenses	165
APS Business Office (POF share)	53,474
	<hr/> \$585,469
Assigned to Special Publications	(25,113)
Advertising costs allocated to Journals	(5,664)
Total Expenses	<hr/> \$554,692
Excess of Income over Expenses	\$123,807

BUSINESS OFFICE EXPENSES

Salaries and Benefits	\$59,369
Supplies and Equipment	2,793
Mailing	335
Telephone	283
Hotel and Travel	655
Audit and Legal Fees	2,650
Rental of Equipment	330
Insurance	167
Federation Service Charge	2,646
Rent	9,566
Repairs and Maintenance	957
Dues and Assessments	70
Printing	294
Miscellaneous	85
Total Expenses	<hr/> \$80,200
Allocated to Advertising Expenses	(5,695)
Less Overhead Collected	(7,663)
	<hr/> \$66,842
Allocated to SOF	(13,368)
Allocated to POF	(53,474)

PUBLICATION CONTINGENCY AND RESERVE FUND

Balance Dec. 29, 1967 (market value)	\$1,033,032
Dividend and Interest paid to APS	\$33,052
Balance Dec. 31, 1968 (market value)	\$1,124,849
Increase in market value	\$91,817

CANNON'S THE WAY OF AN INVESTIGATOR

The Way of an Investigator originally published by Walter B. Cannon in 1945 was reproduced as a souvenir for the XXIV Congress in 1968 with the permission of the Cannon family. Many copies remain in the possession of the Society. These are available free of charge to department chairmen for graduate students upon request. Write to the Executive Secretary, American Physiological Society, 9650 Rockville Pike, Bethesda, Maryland 20014.

SUMMER COURSE - BIOLOGY OF AGING

A summer course in the biology of aging will be conducted from June 22 through July 11, 1969 in the Department of Biology, University of California, San Diego at La Jolla. The course is sponsored by the Adult Development and Aging Branch, National Institute of Child Health and Human Development, NIH in conjunction with several universities. The purpose of the course is to interest young scientists in research on the biology of aging. For detailed information write Dr. Gabe Maletta, National Institute of Child Health and Human Development, NIH, Bethesda, Maryland 20014.

REPORT OF TOUR BY COUNCILMAN

JOHN R. BROBECK

Some years ago when the American Physiological Society was in the midst of what the historical philosopher Arnold Toynbee might have recognized as a "time of trouble", the officers and Council of the Society began a visiting program for more effective communication with members of the Society and with members of departments of physiology. This year as a continuation of this effort it was my privilege to visit four schools with newly established programs for educating medical students. My visits included the following:

Brown University Program in Medical Sciences in Providence,
R.I.

Dr. Peter A. Stewart, Leader of the Physiology and
Biophysics Section;

Mount Sinai School of Medicine in New York, N. Y.

Dr. Irving L. Schwartz, Chairman of the Department
of Physiology, and also Dean of the Graduate School
of Biological Sciences;

Milton S. Hershey Medical Center of Pennsylvania State
University, Hershey, Pa.

Dr. Howard E. Morgan, Chairman of the Department of
Physiology;

University of Connecticut, School of Medicine and School of
Dental Medicine, Farmington, Conn.

Dr. John W. Patterson, Dean, formerly Head of the
Department of Physiology.

The program at Brown is unusual in that it is a specialization within the university's Division of Biological and Medical Sciences. It leads to a master's degree, and is intended to prepare students for completion of either the Ph.D. or M.D. degree or both, although students who wish to become medically qualified must finish their education at some other medical school. Until this year the total number of students has been small, but it will be increased some ten-fold next fall.

In spite of the unusual features of this particular program, the four schools I visited have certain qualities in common. Of these the most impressive is the spirit, morale, and enthusiasm of the several faculties. Being involved in something new, different, and potentially of great value to their regions or constituencies, and possibly to medical education generally, teachers and investigators have both a sense of excitement and also the satisfaction of bringing to pass what they themselves have had a share in planning. I know that these schools have had a bothersome number of visitors on missions such as mine; nevertheless, in every instance my reception was most gracious and reflected the enthusiasm of the staff for what they are doing.

A second notable quality is the quickness with which research programs have been established. No doubt this reflects foresight on the part of granting agencies in facilitating the moving or replacement of equipment, and in many instances the active transport of research programs without significant interruption. In fact, it was my impression that instead of interfering with research the move had in many cases served to enlarge and intensify the investigative effort.

Third, and one can see this even in pictures and drawings, is the striking character and imaginative architecture of the new buildings. After years of struggling with renovation of an old building, I was ready to appreciate how much easier it is to achieve convenient and attractive space for teaching, research and patient care in new construction. One of the most impressive features of all the plans is the magnificent (and no doubt very costly) facilities for animal care.

About design plans for teaching laboratories I have some misgivings. The classical "multipurpose" laboratory was invented before most schools of medicine embarked on new curricula. It is not clear that a curriculum where short, intensive courses are crowded into a "core", followed by rather generous time for elective work, it best fitted into one or two sets of multidiscipline laboratories. It may well turn out that plans for educational experimentation have once again outpaced the architecture of teaching facilities.

Finally, in our own "time of trouble", which is involving not so much the Society per se as the discipline as a whole, one can discern in the experience of the new schools the forces that are creating some of our problems. One of these forces is the opinion or judgment of faculty members and administrators outside the Department of Physiology. No longer can a department feel autonomous in deciding what shall be offered in the courses, in the utilization of time, nor even in the methods of presentation. Interest in "integrated" teaching plans modelled after the Western Reserve experiment is widespread, especially among professional medical educators and administrators. A prospective chairman, therefore, may be faced with the question, "Will you or will you not cooperate in integrated teaching?" In the case of a new school the major decisions about the nature of the curriculum may well have been settled before a given chairman is selected. Inasmuch as I was a student in one of the first so-called integrated courses in medical education (the physiology-biochemistry course at Yale before World War II), and because on occasion I have been given the responsibility for organizing and maintaining such courses, I was interested to see the very strong influence this idea has in the philosophy of new medical schools. One can even sense within the faculty as a whole, or at least among the believers in whatever system has been adopted, a sentiment that might be phrased, "Well, all right; if you don't want to do it our way, we'll make other arrangements and get along without you!" There are instances where this confrontation has led to proposals for teaching of physiology by clinicians. If a faculty decides that the physiology department, or the national community of physiologists, will not cooperate in the teaching of physiology according to some plan different from conventional courses, then that faculty is likely to decide to include

physiology "out".

Another major force at work in our troubles is the power of granting agencies. The federal agencies, mainly the National Institutes of Health in executing what is believed to be the intent of the Congress of the United States, have given to biochemistry the privilege of becoming almost independent of medical education. Research and even teaching of biochemistry are nearly ubiquitous - in departments of biochemistry in universities, veterinary and dental schools, schools of agriculture and nutrition; in programs in molecular biology; and in departments of microbiology, genetics, pharmacology, parasitology, and medicine, as well as in hospitals. Medicine needs biochemistry; but biochemistry no longer depends upon medicine for its financial or intellectual support. Many physiologists would now like to gain for our science this same privilege. Can physiology be defined in such a way, or structured in such a way, that it will have like biochemistry a broad appeal for funding in multiple environments? If so, will it remain identifiable as physiology; will it be called physiology, or something else? My own view is that physiology, i. e., the physiological sciences, are even more widely distributed than is biochemistry; but because of the diversity of techniques and requirements for training it has become impossible to insist upon the use of the preferred name, viz., physiology, for all of its ramifications. Nevertheless, the traditional relationship of physiology to medicine remains as one of our principle sources of strength, and our science would suffer if this tie were modified as it has been in the case of biochemistry. The elements of physiology essential to education in medicine cannot be permitted to leave the medical environment and influence, and medical faculties must continue to include someone able to teach physiology in its relevance to medicine. From my own modest survey of opinion, and from the experience of the newer schools of medicine, I believe that any given medical faculty will usually prefer to have this teaching done by professionally trained physiologists. But if as physiologists we decide that we cannot or will not fill this role in the education of physicians, someone else will be found to do it. This particular problem, however, may be moving already towards its solution. It is conceivable that through new curricula and combined M. D. - Ph. D. programs we may be in the process of training a new generation of teachers and investigators, whose commitment is neither to medicine nor to science so much as to medical science, whose interest will no doubt focus more and more upon human physiology, and who will preserve our very valuable ties with medical education.

INVITATION TO THE FALL MEETING UNIVERSITY OF CALIFORNIA, DAVIS

August 25-29, 1969

The physiologists of the Davis Campus, University of California, cordially invite all members of the Society to attend the 1969 fall meeting. Davis is located in the Sacramento Valley, a rich agricultural area, with an August climate characterized by warm (but dry) days, and quite cool nights. It is a town of 22,000, largely residential and oriented towards the University. It is readily accessible by air, via Sacramento Metropolitan Airport, and by road (I. S. highway 80 passes through the campus). Special transportation will be provided between the airport and the campus.

Physiology has a 40-year history of development at Davis. From the initial appointments in the College of Agriculture in 1929, the number of physiologists has increased to 63 (including 32 APS members) representing 17 departments in four schools and colleges (Agriculture and Environmental Science, Letters and Sciences, Medicine, and Veterinary Medicine). Consequently, physiology on this campus comprises an unusual breadth of interests and activities. All of the physiology faculty participate in the Graduate Group in Physiology, which manages all graduate instruction in Physiology. This group also serves as a forum for all other matters of mutual interest, providing regular communication among the physiologists.

The Refresher Course will be concerned with "Bioenergetics and Cell Organelles" and arranged by Dr. James Green of Rutgers University. It will commence at 9 AM, Monday, August 25.

The Bowditch Lecture will be delivered by Dr. John Urquhart, of the University of Pittsburgh, at 4 PM, Thursday, August 28. He will speak on "Blood Borne Signals, the Measuring and Modeling of Hormonal Control and Communication."

Two Symposia will be held on Friday morning, August 29. One, honoring Professor Max Kleiber, will deal with "Energy Metabolism." The other, "Avian Physiology," will be oriented towards acquainting mammalian physiologists with the functional properties of birds, including their usefulness as experimental subjects.

Dr. Loren Carlson will address the Society at the Annual Banquet, which will be held in Freeborn Hall on the campus, Thursday evening, August 28. This will be preceded, at 6:30, by a champagne reception.

Scientific Sessions will be held on the campus, Tuesday through Thursday, August 26-28. Special Lounges, with refreshments, will be maintained throughout the week for informal discussions among attendees. "Open House" also will be held in several laboratories on the campus. Wednesday and Friday afternoons will be left unscheduled so that attendees may view the campus at leisure.

A variety of recreational facilities will be available, and social activities will be arranged during the meeting. These will include tours of the "Gold Country," "Wine Country," etc.

Air conditioned Housing will be available on and adjacent to the campus, and at nearby hotels and motels. Meals also will be available on or near the campus.

Registration will begin Sunday, August 24.

H. H. Cole, Chairman of Organizing Committee

SECOND INTERNATIONAL SYMPOSIUM ON ATHEROSCLEROSIS

The Second International Symposium on Atherosclerosis will be held at the Conrad Hilton Hotel, Chicago, Illinois, November 2-5, 1969. In addition to a number of invited papers dealing with various aspects of atherosclerosis and arteriosclerosis there will be selected 10-minute submitted papers. For a program and further information write to Chicago Heart Association, 22 West Madison Street, Chicago, Illinois 60602.

SYMPOSIUM ON PHYSIOLOGY AND BIOCHEMISTRY OF MUSCLE AS A FOOD

A Symposium on Physiology and Biochemistry of Muscle as a Food will be held at the University of Wisconsin, Madison, Wisconsin, July 14-16, 1969. The Symposium will feature leading international authorities on the physiology and/or biochemistry of muscle. Discussion sessions will subsequently be held to direct these basic presentations toward the use of muscle as a food. For further information write E. J. Briskay, College of Agriculture and Life Sciences, University of Wisconsin, Madison, Wisconsin 53706.

SYMPOSIUM ON CHALLENGES IN LIVING SYSTEMS

A Symposium on Challenges in Living Systems will be held Wednesday August 20, 1969 during the AIBS annual meeting at Burlington, Vermont August 17-22, 1969. The Symposium will cover such topics as sex steroids; antibody formation; biochemistry of embryonic development; endocrine aspects of the nervous system; and, behavior genetics. For further information write H. W. Norton, Dept. of Animal Science, College of Agriculture, University of Illinois, Urbana, Illinois 61801.

THIRTEENTH BOWDITCH LECTURE

The Determinants of Myocardial Oxygen Consumption*

EUGENE BRAUNWALD

Elucidation of the determinants of myocardial oxygen consumption has been the object of extensive research for more than one-half century. The heart is an aerobic organ and can develop only a small oxygen debt. Therefore, in a steady state, determination of the heart's oxygen consumption provides a precise measurement of this organ's total metabolism. It has been known for many years that the total metabolism of the arrested, quiescent heart is only a small fraction of that of the working organ. Thus, while the oxygen consumption of the beating heart ranges from 3 to 15 ml/min/100 Gm. of left ventricle, the oxygen consumption of the heart arrested with excess potassium is only 1.2 to 1.4 ml/min/100 Gm. The major purpose of the investigative efforts, to be reviewed herein, has involved the identification of those aspects of cardiac activity which are responsible for the difference between these basal levels and those occurring during activity.

The contractile process is a complex one and is initiated by electrical depolarization of the myocardial cell. Little, if any, quantitative data have been available defining the O_2 requirements of electrical activation of the heart. In order to investigate this problem we utilized an isolated canine heart preparation (Fig. 1) in which the coronary bed was perfused at a constant rate and the PO_2 of coronary venous blood was recorded continuously with an O_2 electrode inserted into the coronary venous line. Electromechanical dissociation was produced by perfusing the heart with whole blood from which almost all of the ionic calcium had been removed with an exchange resin, and propagated depolarizations were induced at controlled frequencies by stimulating the heart electrically. The changes of myocardial oxygen consumption associated with increases in the frequency of depolarization were determined by measuring changes of venous PO_2 , calculating venous O_2 content, while arterial O_2 content and coronary blood flow were held constant (18). Increases in the frequency of depolarization were uniformly accompanied by only very small increases of myocardial oxygen consumption, averaging 0.40 μ liter/activation/100 G. A 100 G heart contracting at a frequency of 100/min. would then consume only about .04 ml/ O_2 /min. as a direct consequence of the depolarization process. Thus, the quantity of oxygen required for electrical activation of the heart is approximately 0.5% of the total oxygen consumed by the normally contracting heart. Since the oxygen cost of electrical depolarization is trivial in relation to the cost of contractile activity, attention was directed to the delineation of the aspects of contraction that do require substantial quantities of oxygen.

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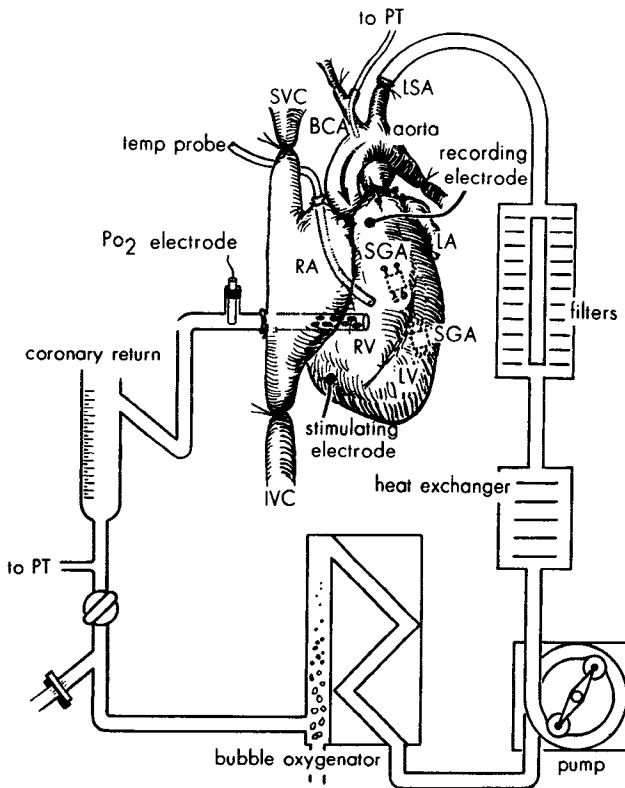


Fig.1. Isolated canine heart preparation for studying O₂ requirements of electrical activation of the myocardium. SVC: superior vena cava, IVC: inferior vena cava, RA: right atrium, RV: right ventricle, LA: left atrium, LV: left ventricle, BCA: brachiocephalic artery, LSA: left subclavian artery, PT: pressure transducer, SGA: strain gauge arch. (Reproduced by permission from Klocke, F.J., E. Braunwald, and J. Ross., Jr. Oxygen cost of electrical activation of the heart. *Circulation Res.* 18: 357, 1966).

It was demonstrated by Rohde in 1912 that myocardial oxygen consumption varies directly as a function of the product of developed pressure and heart rate in the cat isovolumetric left ventricular preparation (30). Shortly thereafter, Evans and Matsuoka concluded from studies on the Starling heart-lung preparation that "there is a relation between the tension set up on contraction and the metabolism of the contractile tissue"(9).

The relative effects of aortic pressure, stroke volume and heart rate on oxygen consumption were compared (3, 32) in an isolated supported canine heart. In this preparation (33) the coronary venous return is directed to the jugular veins of the support dog, which continuously renews the isolated heart circuit with fresh arterialized blood, thereby permitting stable performance characteristics. The results of a typical experiment are illustrated in figure 2.

The effects of progressively raising mean arterial pressure at various levels of cardiac output were determined at a constant cardiac frequency. In run A, (Fig. 2A, top) arterial pressure was increased from 75 to 125 to 175 mm/Hg at a cardiac output of 1 liter/minute while in run B, pressures were increased over this range at an output of 2.6 liters/minute and in run C at a cardiac output of 4.2 liters/minute. It is evident on the rear panel of Fig. 2A, top, that there is no simple linear relationship between minute work and myocardial oxygen consumption. For example, at an oxygen consumption of 15 cc per minute, the minute work varied from 4.5 to 15 kilogram meters, depending on the level of the cardiac output. The panel on the right shows the relationship between myocardial oxygen consumption and the so-called tension-time index, i. e., the area beneath the left ventricular pressure pulse per minute. These two variables changed in the same direction at all levels of aortic pressure and cardiac output. Similar relations between the tension-time index and myocardial oxygen consumption were observed when cardiac output was progressively increased at a constant arterial pressure and cardiac frequency (Fig. 2B, bottom) and when the latter was varied at a constant arterial pressure and cardiac output.

These results were consistent with and extended the work of Rohde (30) and of Evans and Matsuoka (9) and it was suggested from this investigation that the tension-time index is a fundamental determinant of the oxygen consumption of the contracting heart. More recently, it has been emphasized that the tension in the wall of the ventricle is a direct function of the radius and the intraventricular pressure and is inversely related to ventricular wall thickness, and that tension in the myocardial wall is a more definitive determinant of myocardial energy utilization than is developed pressure (29).

Despite these, and other studies demonstrating the close relation between developed intraventricular pressure or myocardial wall tension and myocardial oxygen consumption, it has become apparent that tension cannot be the sole important determinant of the heart's metabolic requirements. Thus, it was observed in the conscious dog, by Gregg that myocardial oxygen consumption correlates poorly with the tension-time index during exercise or sympathetic nerve stimulation (14), while Krasnow and his associates observed a discrepancy in the relation between the tension-time index and myocardial oxygen consumption when isoproterenol was administered to humans (20).

We then examined the possibility that velocity of contraction, a reflection of the heart's contractile state, might be an additional important determinant of myocardial oxygen consumption. This hypothesis

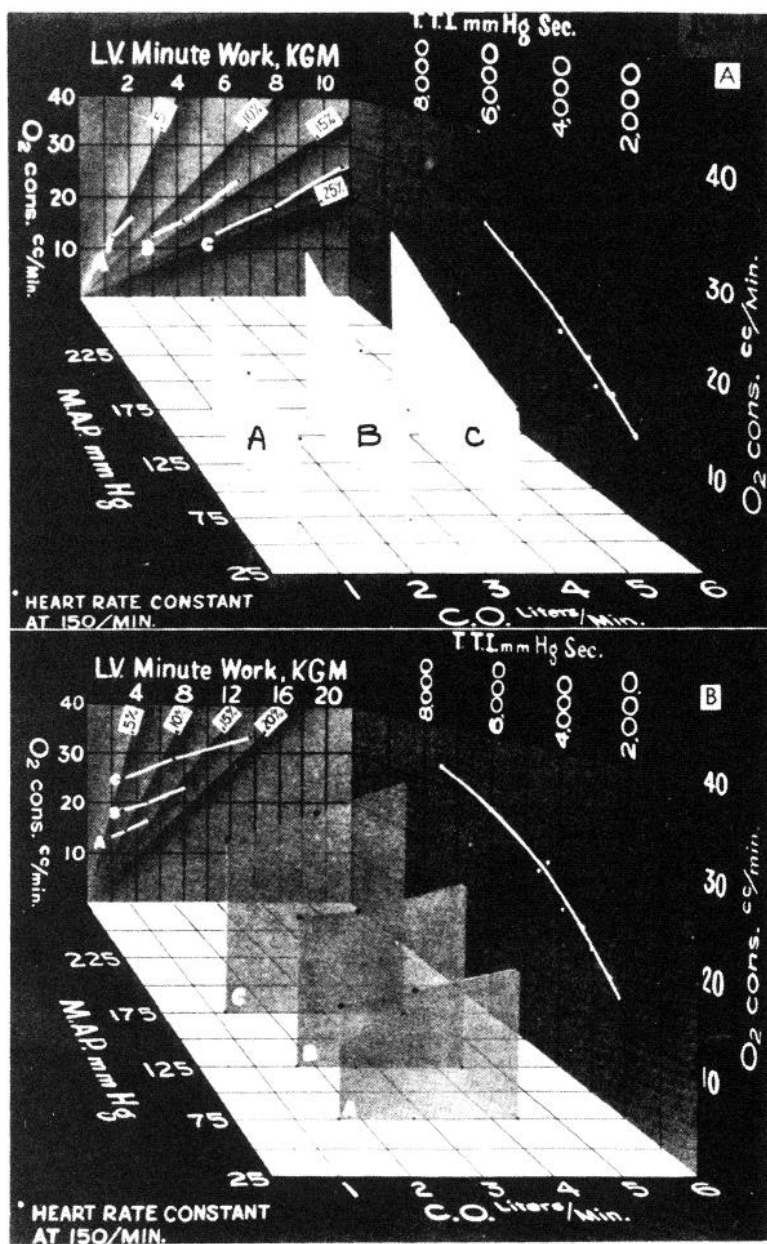


Fig.2. Base panel shows the experimental conditions (cardiac output and aortic pressure) when each determination of O_2 consumption was made. The height above the base panel of each experimental point represents its O_2 consumption. The rear panel shows the plot of left ventricular minute work in kgm. against myocardial O_2 consumption. The shaded lines on the rear panel labeled with % figures are iso-efficiency lines. The right hand panel shows the relationship between the Tension-Time Index (T.T.I.) in mm Hg seconds and myocardial O_2 consumption in cc/min. A, Three pressure runs at low, medium and high cardiac outputs. Note the negligible change in external efficiency as aortic pressure is increased within any given run. B, Three flow runs at low, medium and high mean aortic pressures. Note the increase in external efficiency within the course of any given flow run. (Reproduced by permission from Sarnoff, S.J., E. Braunwald, G.H. Welch, Jr., R. B. Case, W. N. Stainsby, and R. Marcruz. Hemodynamic determinants of oxygen consumption of the heart with special reference to the tension-time index. *Am. J. Physiol.* 192: 148, 1958).

was examined in a right heart by-pass preparation in which blood was pumped at a constant rate into the pulmonary artery and in which, therefore, left ventricular output was maintained constant. Aortic pressure and cardiac frequency were also controlled and maintained constant (31). The coronary venous effluent was drained through a cannula in the right atrium and right ventricle and myocardial oxygen consumption was calculated as the product of coronary blood flow and the coronary arterio-venous oxygen difference.

Figure 3 shows the effects on myocardial oxygen consumption of a variety of interventions which alter the velocity of contraction, reflected in the peak left ventricular ejection rate (37). It is of interest that the administration of calcium, paired electrical stimulation, (sustained post-extrasystolic potentiation) and the administration of norepinephrine, exerted similar effects on the velocity of contraction and on oxygen consumption. The combinations of paired stimulation and norepinephrine, and of paired stimulation and calcium augmented both velocity and oxygen consumption, to a greater extent than did the single interventions. The bottom panel of figure 3 shows the relationship between the alterations in oxygen consumption and the changes in the tension-time index. In all instances oxygen consumption rose, while the tension-time index actually declined, as a consequence of the shortening of the duration of ejection. On the basis of these observations, it was proposed that the velocity of contraction of the myocardium, reflecting the contractile state of the heart, is also a major determinant of myocardial oxygen consumption (31, 37).

Initially, this proposition did not appear to be consonant with many previous studies showing that digitalis glycosides do not increase myocardial oxygen consumption (1, 15, 34), although it is well known that substantial increments in the velocity of contraction and contractility of the heart result from the administration of these drugs (38, 40). The right heart by-pass preparation in the dog in which heart rate, stroke volume and mean aortic pressure were held constant, was again employed to this problem (8).

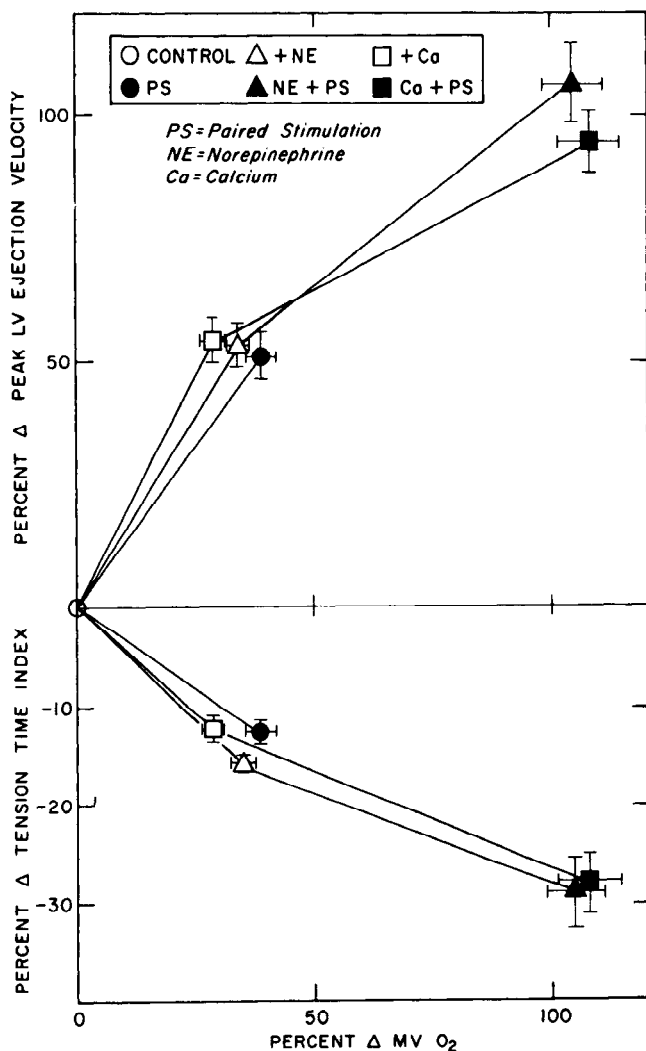


Fig.3. Relation of percent change in peak velocity of left ventricular (LV) ejection and of left ventricular tension-time index with the percent increase in myocardial oxygen consumption (MVO_2) in a variety of inotropic interventions in eight dogs. Cross bars = 1 SE of mean. (Reproduced by permission from Sonnenblick, E. H., J. Ross, Jr., J.W. Covell, G.A. Kaiser, and E. Braunwald. Velocity of contraction as a determinant of myocardial oxygen consumption. *Am. J. Physiol.* 209:919, 1965.)

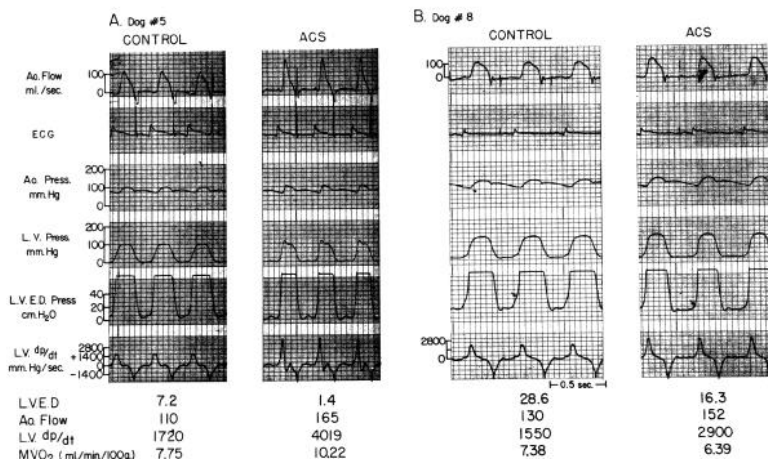


Fig. 4. Representative tracings obtained from two experiments before (control) and after acetylcholine (ACS). A = normally functioning heart, B = acutely failing heart. LV = left ventricle. E.D.P. = end-diastolic pressure, MVO_2 = myocardial oxygen consumption. (Reproduced by permission from Covell, J.W., E. Braunwald, J. Ross, Jr., and E.H. Sonnenblick. Studies on digitalis, XVI. Effects on myocardial oxygen consumption. *J. Clin. Invest.* 45: 1535, 1966.)

Figure 4 are tracings from two experiments which show the effects of acetylcholine in a relatively normal heart on the left, and in a failing heart on the right. In both hearts acetylcholine increased the velocity of contraction, as reflected in the peak aortic flow velocity and in the rate of change of intraventricular pressure; however, myocardial oxygen consumption increased in the normal heart, while it diminished in the failing heart. In the nonfailing heart, ventricular end-diastolic pressure, and therefore end-diastolic volume, which were normal initially did not decline strikingly, while in the failing heart, in which these variables were elevated, a substantial reduction in left ventricular end-diastolic pressure and volume occurred.

From these and similar experiments with norepinephrine we concluded that the change in myocardial oxygen consumption that is observed following the administration of inotropic drugs, such as cardiac glycosides or catecholamines, to the nonfailing heart is the end result of the effects of two major determinants of myocardial oxygen consumption which change in opposite directions, i.e., tension, which is reduced and myocardial contractile state, which is augmented. In the dilated ventricle, both the catecholamines and glycosides increase contractility, so that the left ventricular end-diastolic pressure and volume fall substantially. This decrease in ventricular volume leads, on the basis of the Laplace relation, to a decline in intramyocardial tension, which tends to reduce myocardial oxygen consumption. However, the

decrease in myocardial oxygen consumption which might be expected to result from falling tension in the ventricular wall is offset by the increase in contractility, which tends to augment the myocardial oxygen consumption. The net result of these opposing effects is to produce either no change, a small increase or a small decrease in myocardial oxygen consumption (36). Thus, the change in myocardial oxygen consumption which follows an inotropic stimulus depends on the degree to which intramyocardial tension is reduced in relation to the extent to which the contractile state is augmented. In heart failure with ventricular dilatation, digitalis glycosides may reduce myocardial oxygen consumption, or leave it unchanged, while in the normal heart digitalis increases myocardial oxygen consumption. Clinically, this fact may be of importance, since it helps to explain the relief of angina pectoris which digitalis occasionally produces when it is administered in the presence of ventricular failure. However, in the well compensated patient without cardiac enlargement or failure who also has angina pectoris, digitalis glycosides have been observed at times actually to intensify the latter symptom, presumably by increasing the contractility of the heart, and, hence, its oxygen requirements, without substantially decreasing heart size and hence wall tension, which might have offset this effect.

The conclusion that myocardial contractility is an important determinant of myocardial oxygen consumption is also supported by observations on the effects of reducing contractility. Thus, a decline in contractility and in the velocity of contraction, produced by cardiac depressant drugs, including propranolol, procaine amide and pronethalol, were shown by Graham et al. to reduce myocardial oxygen consumption when wall tension was held constant, or almost so (13).

Figure 5 illustrates the data summarized above and shows the relation between a variety of stimuli which alter the velocity of cardiac contraction and myocardial oxygen consumption. Positive inotropic interventions included acetylstrophanthidin, MJ, an aminophyllin-like drug, calcium, norepinephrine, post-extrasystolic potentiation, and the combination of norepinephrine and post-extrasystolic potentiation. The negative inotropic interventions included pronethalol, propranolol and procaine amide. Within broad limits, the extent of the change in myocardial oxygen consumption was related to the change in dp/dt , which in these experiments was used to reflect alterations in the velocity of contraction.

With the evidence for the importance of both tension and contractility as determinants of myocardial oxygen consumption it was felt that it would be of importance to make a direct comparison of the relative quantitative influences of each of these factors on myocardial oxygen consumption independently. Therefore, the relative effects on myocardial oxygen consumption of changes in tension development and in the contractile state of the myocardium were assessed in the same heart. This was accomplished by utilizing an isovolumetric, left ventricular preparation in which wall tension could be altered at a constant contractility, and, conversely in which the contractile state of the myocardium could be increased at any desired level of developed tension (12).

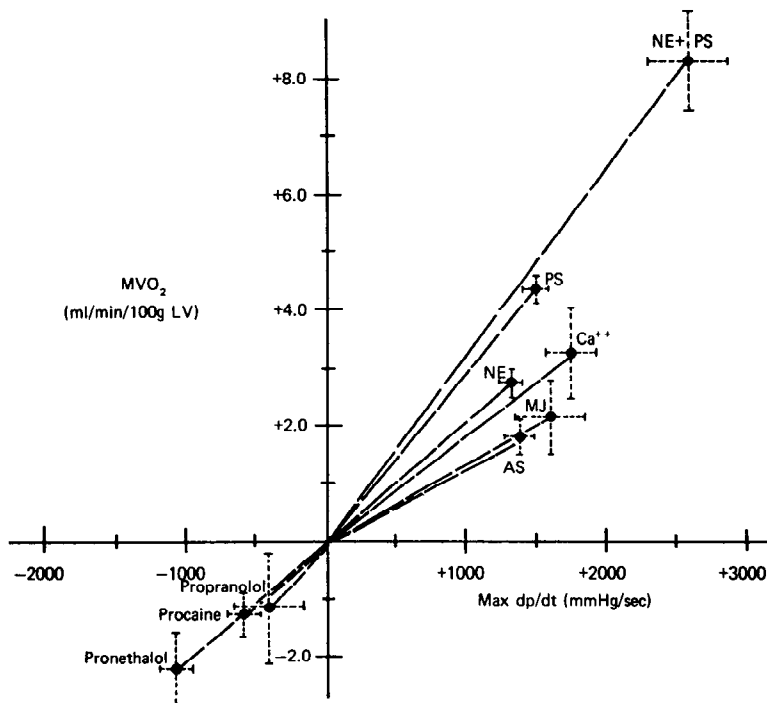


Fig.5. Relation between changes in maximum intraventricular dp/dt and myocardial oxygen consumption ($\dot{M}V\dot{O}_2$). Each point represents the average of a series of experiments \pm SE. NE = norepinephrine, PS = paired electrical stimulation, Ca^{++} = calcium, AS = acetylcholinesterase inhibitor.

The preparation employed is shown in Figure 6. The dog was on total cardiopulmonary bypass; in order to control ventricular volume and to achieve isovolumetric contractions of the left ventricle, a latex balloon was inserted into the left ventricle. The balloon was filled with varying volumes of saline and myocardial oxygen consumption was first measured at varying levels of peak tension, achieved by varying the ventricular volume at the same contractile state. Then, norepinephrine was infused at a constant rate into the ascending aorta just above the aortic valve. When a steady state of increased contractility was obtained, the volume of the left ventricular balloon was reduced in order to match the peak tension during the pre-norepinephrine control values, and myocardial oxygen consumption was re-determined.

The results from one experiment are shown in Figure 7 in the form of left ventricular force-velocity curves. The three curves designated by the solid symbols are force-velocity curves in the control state, in

which peak developed tension was progressively increased by augmenting ventricular volume. The extrapolated velocity intercept of these curves at zero tension, V_{\max} , remained constant at 44 cm/sec with this intervention, indicating that the contractile state was unchanged. The intercept on the abscissa, i.e., peak tension, however, rose as ventricular volume was increased and myocardial oxygen consumption was found to be a function of this variable. In contrast, during norepinephrine infusion, V_{\max} was increased from 44 to 58 cm/sec., as signified by the open triangles, indicating that an augmentation of contractility had taken place. With this increase in V_{\max} myocardial oxygen consumption rose substantially above the level associated with the same peak tension, but at the control level of contractility.

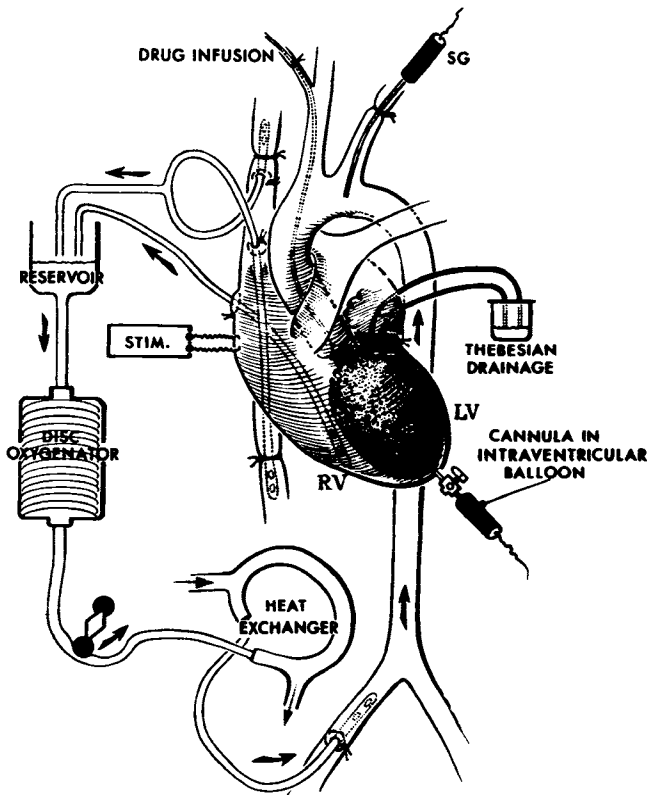


Fig.6. Isovolumetric left ventricular preparation with right heart bypass and retrograde systemic perfusion. Stim., stimulator with electrodes on the right atrium; SG, strain gauge. (Reproduced by permission from Graham, T.P., J.W. Covell, E.H. Sonnenblick, J. Ross, Jr., and E. Braunwald. Control of myocardial oxygen consumption: Relative influence of contractile state and tension development. *J. Clin. Invest.* 47: 375, 1968.)

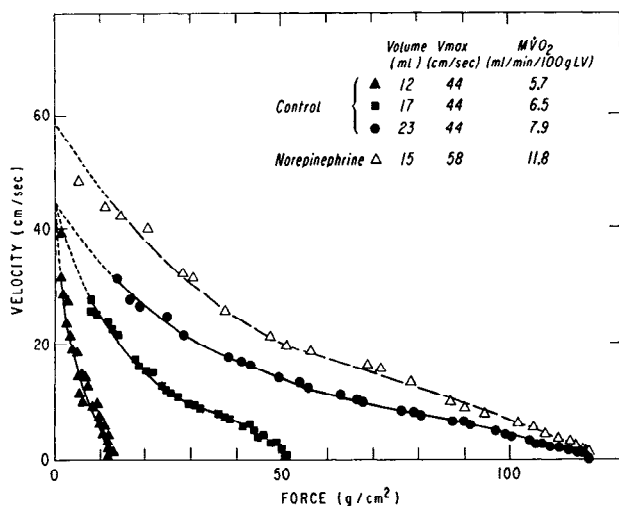


Fig. 7. Left ventricular contractile element force-velocity relationships. Velocity = contractile element velocity; force = force/unit area (Pr/2h). V_{max} = intercept on the ordinate; closed symbols = effects of varying ventricular volume at a constant V_{max} ; open symbols = effect of increasing V_{max} with norepinephrine. Values of V_{max} are estimates and not absolute values. (Reproduced by permission from Graham, T.P., J.W. Covell, E.H. Sonnenblick, J. Ross, Jr., and E. Braunwald. Control of myocardial oxygen consumption: Relative influence of contractile state and tension development. *J. Clin. Invest.* 47: 380, 1968).

The effects of varying tension and contractility on myocardial oxygen consumption are shown in Figure 8. The closed circles and solid line illustrate the effects of progressively increasing tension at a V_{max} of 47 cm/sec., while the open triangles and broken line show the upward shift of the tension-myocardial oxygen consumption relation when contractility was increased with the infusion of norepinephrine, when V_{max} rose to 63 cm/sec. The effects on myocardial oxygen consumption of a higher concentration of norepinephrine and a further augmentation of V_{max} to 76 cm/sec. are also demonstrated.

The data from this entire group of experiments are summarized on Figure 9, both graphically and numerically. The three diagonal parallel lines are myocardial oxygen consumption isopleths, showing the levels of tension and V_{max} associated with 20, 40 and 60 microliters per beat/100 G respectively. The reciprocal relation between tension and velocity is evident. Any given level of myocardial oxygen consumption can be achieved with a relatively high level of V_{max} and low peak developed tension, or a low level of V_{max} and a relatively high level of peak developed tension. The broken lines near the center of the figure illustrate the increases in peak developed tension and V_{max} required to

increase myocardial oxygen consumption by 50% from 40 to 60 micro-liters/beat/100G. Such an increase could be achieved either by increasing V_{\max} by 42% at a constant developed tension, as shown by the vertical arrow, or by increasing peak developed tension by 83% at a constant level of V_{\max} , as shown by the horizontal arrow. From these studies it was concluded that the quantitative effect on oxygen utilization of changes in contractility is substantial and is similar in magnitude to the effect of altering tension development.

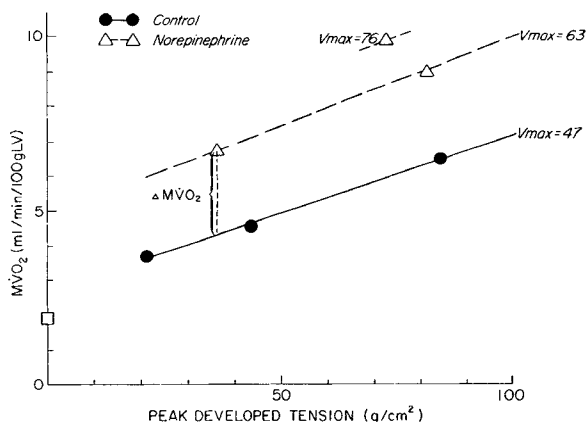


Fig.8. $\dot{M}\dot{V}O_2$ as a function of peak developed tension. Closed circles = effects of various levels of tension at a constant V_{\max} ; open triangles = observations during norepinephrine infusion; open square = $\dot{M}\dot{V}O_2$ with potassium chloride arrest. The change in $\dot{M}\dot{V}O_2$ ($\Delta\dot{M}\dot{V}O_2$) with norepinephrine at a constant tension was obtained by interpolation when tension was not precisely matched, as illustrated here by the dotted vertical line. (Reproduced by permission from Graham, T.P., J.W. Covell, E.H. Sonnenblick, J. Ross, Jr., and E. Braunwald. Control of myocardial oxygen consumption: Relative influence of contractile state and tension development. *J. Clin. Invest.* 47: 380, 1968.)

In many of the experiments reviewed thus far norepinephrine was utilized to increase V_{\max} or myocardial contractility, but, it is justifiable to ask whether or not the catecholamines alter myocardial oxygen consumption by a direct action, i.e., one that is independent of their cardiodynamic effects. If such direct stimulation of oxidative metabolism existed it might be considered to be responsible for the so-called oxygen wasting effect of the catecholamines. The isolated canine heart preparation shown in figure 1 was utilized to study this problem (19). The manner in which catecholamines affect oxygen consumption was determined at first when the heart was beating spontaneously and therefore altered its contractile activity under the influence of catecholamines, and then it was remeasured when the same heart was arrested by perfusing it with excess potassium and the changes in contractile activity which ordinarily occur in response to catecholamines

could be prevented.

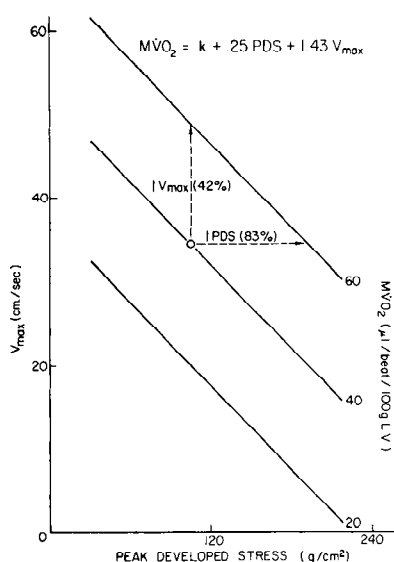


Fig.9. $\dot{M}\dot{V}O_2$ isopleths as a function of V_{max} and peak developed tension. Isopleths were calculated from the equation at the top of the figure which was derived by multiple regression analysis. Broken lines indicate effect on $\dot{M}\dot{V}O_2$ of hypothetical increases in PDT at a constant V_{max} (horizontal lines) and in V_{max} at a constant PDT (vertical line). (Reproduced by permission from Graham, T.P., J.W. Covell, E.H. Sonnenblick, J. Ross, Jr., and E. Braunwald. Control of myocardial oxygen consumption: Relative influence of contractile state and tension development. *J. Clin. Invest.* 47: 381, 1968.)

Figure 10 illustrates the increases in myocardial oxygen consumption produced by varying doses of isoproterenol. Qualitatively similar results were obtained with epinephrine and norepinephrine. In the contracting heart (fig. 10, open symbols) catecholamines produced large increases in myocardial oxygen consumption. However, a comparison of the effects of the same doses of amines revealed that the increase of myocardial oxygen consumption observed in the arrested hearts were only 5 to 10% of those occurring when the same hearts were contracting. From this investigation it was concluded that although large doses of catecholamines can increase oxygen consumption slightly in the arrested heart, the increases of oxygen consumption which the catecholamines produce in the beating heart can be attributed primarily to the augmentation of myocardial contractile activity which they induce.

Up to this point, five separate determinants of myocardial oxygen consumption shown in Table 1 have been discussed. No.3, the basal cost, i.e., the oxygen consumption of the nonbeating, non-depolarized heart; No.4, the oxygen cost of depolarization, and No.8, the direct metabolic effect of agents such as catecholamines, which may stimulate myocardial oxygen consumption slightly, independently of their actions on cardiac contraction, are all relatively minor. The two major determinants, discussed thus far, are No.1, myocardial tension development and No.2, the contractile state of the myocardium. Determinant No.5, the activation of the contractile machinery of muscle is, according to current concepts, carried out by ionic calcium, which is stored in the

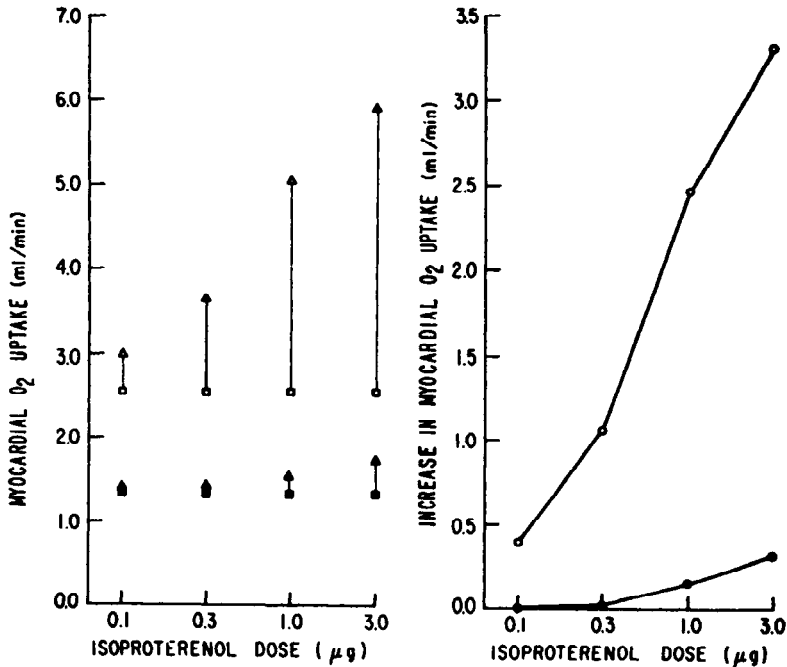


Fig.10. Responses of myocardial O_2 uptake to graded doses of isoproterenol. Open symbols depict values when the heart was beating and solid symbols values when the heart was arrested. On the left, control values are shown by squares and maximum values of myocardial O_2 uptake after isoproterenol by triangles. On the right, increases in myocardial O_2 uptake induced by isoproterenol above control levels are shown by open circles when the heart was contracting and solid circles when the heart was arrested. (Reproduced by permission from Klocke, F.J., G.A. Kaiser, J. Ross, Jr., and E. Braunwald. Mechanism of increase of myocardial oxygen uptake produced by catecholamines. *Am. J. Physiol.* 209: 913, 1965.)

sarcoplasmic reticulum of resting muscle and which is released following activation, so that it diffuses to the myofilaments. Subsequently this calcium is actively removed by the sarcoplasmic reticulum. The latter process has been shown to require energy and leads to relaxation of the muscle. In isolated preparations of sarcoplasmic reticulum from skeletal muscle, one molecule of ATP has been shown to be required for the binding of two calcium ions (16). The relative magnitude of the energy costs of activation, however, remains a matter of dispute. In direct measurements on cardiac muscle, carried out by Ricchiuti and Gibbs, heat release associated with activation was found to be about one-third of the total heat associated with isometric contraction (28). However, in that investigation the tension produced by the muscle was

relatively low and it would have been anticipated that activation heat would have constituted a smaller fraction of total heat had these muscles developed greater force. Furthermore, in the study by Pool and Sonnenblick, in which the chemical energy associated with contraction in isolated cardiac muscle was analyzed, the activation energy was found to be very small (26).

As far as the energy costs of maintenance of the active state are concerned, (Table 1 No. 6) again we are on uncertain ground. It has recently been found by Gibbs and his collaborators that energy turnover is increased in the frog sartorius muscle by agents which prolong the duration of the active state (11). However, since cardiac muscle cannot be tetanized, the energy cost of continued activation, that is, the maintenance energy, has not been clearly defined. However, Monroe has demonstrated that the release of all pressure in an isovolumetrically contracting ventricle midway through the course of contraction reduces myocardial oxygen consumption by less than 10% of control (21). This observation suggests that the maintenance of tension is a relatively minor determinant of myocardial oxygen consumption.

Finally, then, what about determinant No. 7 in Table 1, i. e., shortening against a load? In order to define the effects of myocardial fiber shortening and of contractile element work on myocardial oxygen consumption, a system was required in which the mechanical behavior of muscle could be defined with greater precision than is possible in the intact ventricle. Accordingly, studies were carried out by Coleman et al. on isolated cat right ventricular papillary muscles in vitro. The muscle was fixed at its base to a rod entering the bottom of the bath, while its upper end was attached to an isotonic transducer or a force transducer. This made it possible to vary the preload and afterload independently and permitted the muscle either to shorten, to develop tension or to contract in an afterloaded manner. Oxygen consumption was determined by circulating oxygenated Krebs's solution through the bath and recording the PO_2 of the effluent by means of a Clark-type electrode (4).

The effects of drugs such as norepinephrine and acetylcholinesterase inhibitors, which augment myocardial contractility on the isolated papillary muscles' oxygen consumption were identical to the effects observed in the intact canine heart (5, 6), i. e., as in the intact ventricle, myocardial oxygen consumption was related to tension in a linear manner and this relationship was displaced upwards by the positive inotropic agents.

From these observations we gained confidence in the relevance of these studies on the oxygen consumption of the isolated papillary muscle to the intact ventricle and considered that this system should allow a clarification of the oxygen cost of shortening and of work performance.

The effects of progressive increments in afterload at a constant preload are illustrated in figure 11 (7). On each panel, load or force is plotted along the abscissa. The circles in panels A and B show that at any given initial muscle length the velocity and extent of shortening diminish as afterload is increased. This reciprocal relation between

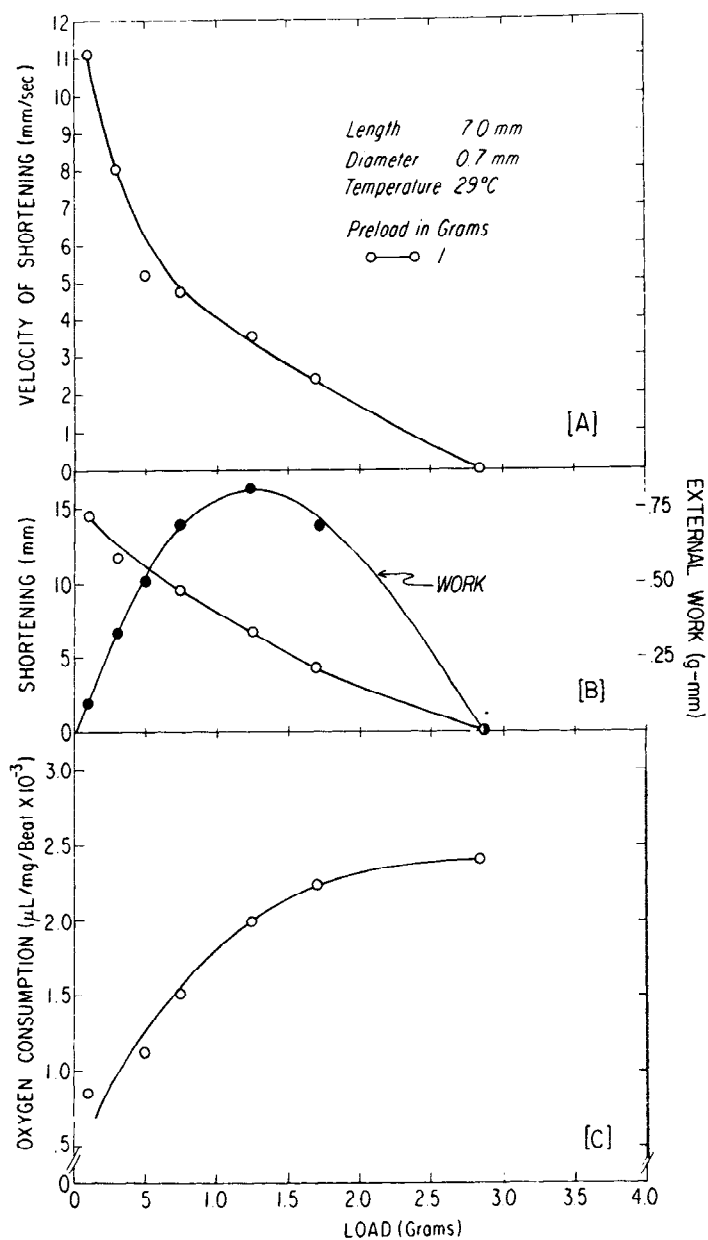


Fig. 11. Effect of varying afterload at a constant preload on myocardial mechanics and myocardial oxygen consumption. Ordinates are velocity of shortening (upper panel) shortening and external work (middle panel), and myocardial oxygen consumption (lower panel). Abscissa is total load (preload and afterload). (Reproduced by permission from Coleman, H.N., E.H. Sonnenblick, and E. Braunwald. Myocardial oxygen consumption associated with external work. The Fenn effect. *Am. J. Physiol.* In press.)

force and velocity in panel A is the classical force-velocity curve. The external work, i.e., the product of afterload and displacement, shown as the solid circles in panel B, is zero at zero load. With progressive increments in afterload, external work increases, to reach a maximal value at approximately 50% of isometric load, and declines thereafter to zero when contraction is isometric, i.e., when there is no displacement. As shown in the bottom panel, the papillary muscle's oxygen consumption increases in an almost linear fashion with increments in afterload up to approximately 50% of isometric force; thereafter, further additions of afterload are associated with only small increases in oxygen consumption. From this observation it may be concluded that: 1) at any given level of contractile state and initial muscle length, oxygen consumption does not simply correlate directly with the external work performed by the muscle and 2) even at a level of constant contractility, myocardial oxygen consumption is not a simple linear function of tension development. The relative contributions of shortening and of external work on myocardial oxygen consumption were evaluated by comparing the oxygen consumption of isometric contractions to the oxygen consumption of afterloaded contractions in which shortening and external work occurred at the same level of tension development. The results of one such experiment are illustrated in figure 12. The relationship between load and oxygen consumption for a series of isometric contractions in which various levels of force were developed is shown as the open circles, while the relationship between load and oxygen consumption for the afterloaded contractions, in which shortening and external work occurred, is shown by the solid circles. The stippled area represents the increment in oxygen consumption at any given load which may be attributed to fiber shortening.

These experiments demonstrate that in addition to contractility and tension development, myocardial oxygen consumption is influenced by external shortening against a load. Thus these studies serve to extend to the myocardium the observations which Dr. Wallace Fenn, the distinguished President of this XXIV International Congress of Physiological Sciences, made on skeletal muscle 45 years ago (10). Fenn showed that shortening of skeletal muscle against a load results in an additional release of heat which is proportional to the work which the muscle performed. The results illustrated in Figure 12 thus indicate a Fenn effect in the myocardium. In addition to the qualitative similarities between the effects of external work on the energetics of cardiac and skeletal muscle, these findings also indicate a general quantitative similarity for the Fenn effect on the energetics of these two forms of striated muscle.

From the model of muscle proposed by A. V. Hill (17) muscular

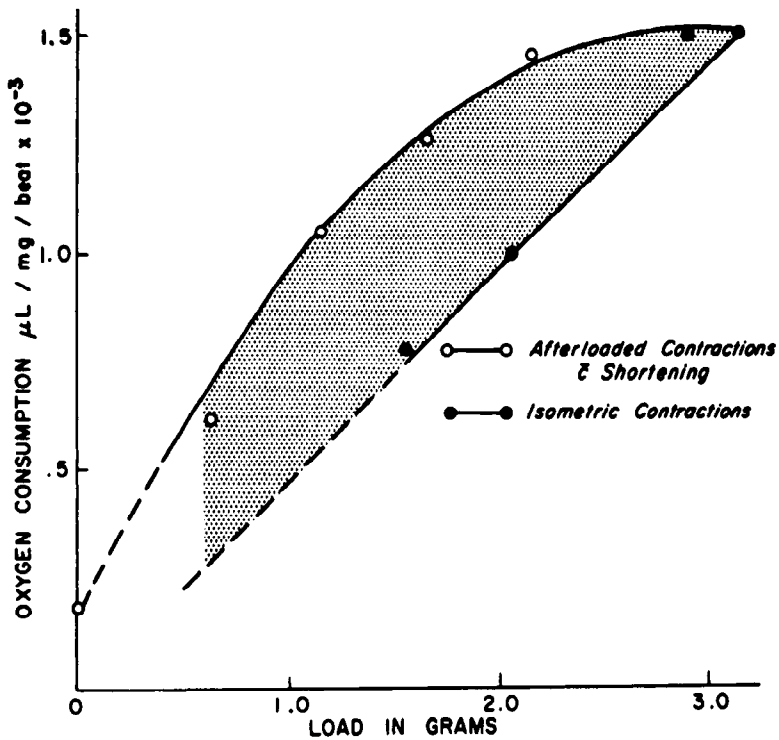


Fig.12. Comparison of the oxygen consumption of isometric contractions (closed circles) with oxygen consumption of afterloaded isotonic contractions at equal levels of tension development (open circles). The stippled area is the increment oxygen consumption associated with shortening and external work in afterloaded contractions. The point on the ordinate at $0.23 \mu\text{L}/\text{mg} \text{ beat} \times 10^{-3}$ represents an average intercept as determined in eight experiments. (Reproduced by permission from Coleman, H.N., E.H. Sonnenblick, and E. Braunwald. Myocardial oxygen consumption associated with external work. The Fenn effect. *Am. J. Physiol.* In press.)

activity can be analyzed in terms of a contractile element in series with a passive elastic component, the series elastic component, and tension developed can be considered in terms of the work performed by the contractile elements in stretching this series elastic component. This form of work may be termed "internal contractile element work." On the other hand, the work which the contractile elements perform in moving a load comprises the external work. During isometric contraction, when the external work of the muscle is zero, the contractile elements do shorten, and the extent of this shortening can be calculated

from the stiffness of the series elastic component. In this manner the work performed by the contractile elements during isometric contraction can be calculated as the product of load and the extent of shortening of the contractile elements.

In experiments in which the oxygen costs of contractile element work expended in the development of tension, that is, in simply lengthening the series elastic component (internal contractile element work) were compared with the oxygen costs resulting from contractile element work associated with the performance of external work, it became quite clear that the work performed in stretching the series elastic component is much more costly in terms of oxygen than is the work performed in shortening the muscle. Phrased in another way, these data suggest that the performance of external work by the muscle is associated with a substantially smaller unit energy cost than is the performance of internal contractile element work during tension development. The sum of the relative energy costs of the two types of work produces the non-linear relation between oxygen consumption and total contractile element work (Figs. 11 and 12). It is evident, then, that myocardial oxygen consumption is linearly related to both the external and internal work performed by the muscle; however, the performance of internal work by series elastic extension during tension development has approximately twice the unit energy cost of external fiber shortening work.

These findings, quantifying the difference between the energetic cost of tension development and of external work, are in agreement with the observations of Evans and Matsuoka (9) and our own (32) on the isolated heart, in which it was observed that external work performed against high pressure loads resulted in a much higher oxygen consumption than similar levels of external work performed at high stroke volumes.

Up to this point we have assumed that there is tight coupling between the oxygen consumption of the heart muscle and its utilization of high energy phosphates. Drs. Pool and Sonnenblick determined the utilization of high energy phosphate stores in the isolated cat papillary muscle in order to relate the muscle's contractile activity directly to the breakdown of high energy phosphate stores, rather than to the more distant process of oxygen consumption. This was carried out under conditions in which no resynthesis of these stores could take place, i. e. by maintaining the muscles in an oxygen-free environment to block phosphate resynthesis through the Krebs's cycle, and by treating the muscles with iodoacetic acid to prevent high energy phosphate formation through anaerobic glycolysis. The high energy phosphate utilization of resting muscles could be determined by comparing the sum of ATP and CP in muscles which had been exposed to N_2 and treated with iodoacetic acid and allowed to rest for varying period of time (26). Identical results to those just described for papillary muscle use of oxygen were observed by Pool and associates in which the high energy phosphate usage of tension development (internal contractile element work) were compared with those of shortening against a load (external contractile element work) (23).

With this papillary muscle preparation, in which high energy phosphate usage is measured, it is possible to exclude uncoupling of oxidative phosphorylation as a possible cause of elevations of myocardial oxygen consumption. Examination of the effects of norepinephrine by this technique showed that this substance does not affect the resting utilization of high energy phosphate, but does augment the high energy phosphate utilization per unit of tension development (22).

Similarly, when papillary muscles were removed from cats rendered hyperthyroid by means of L-thyroxine injections, it was found that the high energy phosphate utilization per unit of tension developed was more than twice as great in muscles from hyperthyroid animals than in muscles from normal animals (25). Thus, the increased oxygen cost per unit tension development of hyperthyroid or catecholamine treated myocardium must be explained, at least in part, by the greater high energy phosphate costs of the contractile process which exist under these conditions.

In addition to hyperthyroidism, the studies on the oxygen and high energy phosphate costs of various aspects of myocardial contractions reviewed herein have many implications for pathophysiological states. Three examples will be presented.

The effects of mitral and aortic valvular regurgitation on myocardial oxygen consumption were studied by means of the preparation shown in figure 13 (41, 42). The right heart was bypassed and myocardial oxygen consumption determined, as described earlier. Aortic and mitral regurgitation were simulated by placing a steel cannula into the left ventricular cavity through the apex and connecting this through a flow probe either to the left atrium or aorta. When blood was permitted to flow from the left ventricle through the circuit into the left atrium, i.e., through circuit A, in Figure A, mitral regurgitation was simulated, while when blood was permitted to flow from the aorta into the left ventricle, through circuit B, aortic regurgitation was simulated.

The effects on myocardial oxygen consumption of opening circuit A and producing mitral regurgitation are shown in figure 14. This resulted in levels of regurgitation which were essentially equal to the forward cardiac output; that is, left ventricular stroke volume essentially doubled, (fig. 14, top left). It is of interest that only relatively small increases of myocardial oxygen consumption occurred (fig. 14, bottom left). Since this production of regurgitation was associated with an increase in left ventricular end-diastolic volume, left ventricular wall tension was augmented (fig. 14, center, left). Indeed, the modest increases in myocardial oxygen consumption induced by severe valvular regurgitation which were observed could be attributed entirely to the small increases in myocardial wall tension which occurred. When regurgitation was induced and these increases in wall tension were prevented, (fig. 14, right), the increases in myocardial oxygen consumption could actually be prevented, (fig. 14, bottom right). Similar results were obtained with aortic regurgitation (41) i.e., a large regurgitant volume resulted in a small increase in myocardial oxygen consumption which could be explained by the elevation of tension which occurred. These experiments serve to re-emphasize the differences in energy expended by the contractile elements in shortening

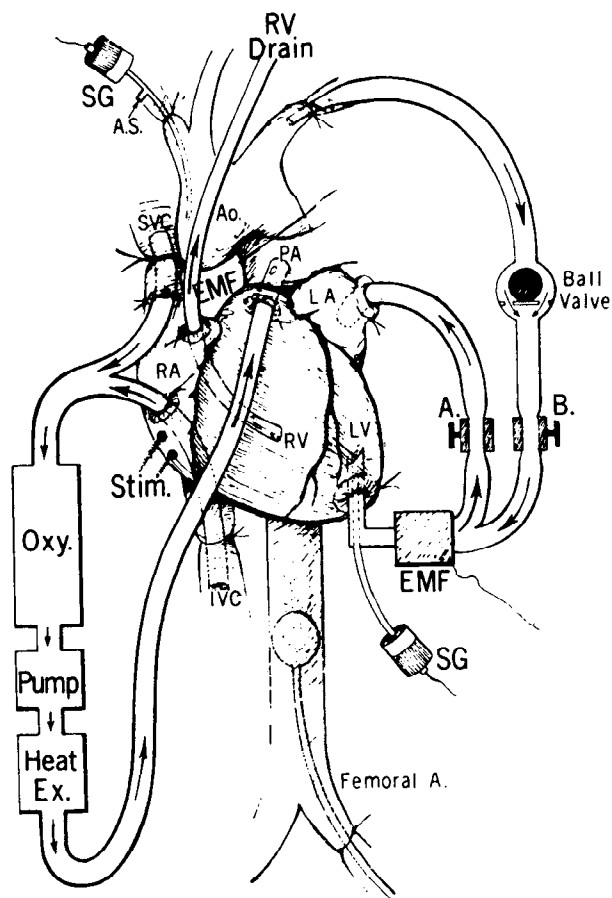


Fig.13. Experimental preparation. Blood was drained from both venae cavae (SVC, IVC) into a disk oxygenator (Oxy.) and pumped with a roller pump through a heat exchanger into the cannulated pulmonary artery (PA). A drain from the right atrium (RA) and ventricle (RV) allowed collection of coronary venous effluent. A stainless steel cannula was placed into the apex of the left ventricle (LV). By opening clamp A, blood was shunted from the left ventricle into the left atrium (LA) during systole (simulated mitral insufficiency). By opening clamp B blood was permitted to flow from the aorta (Ao) to the left ventricle during diastole. Aortic and shunt flows were measured with electromagnetic flow transducers (EMF). Peripheral resistance was controlled by a balloon catheter in the aorta. Stim. = electrical stimulator. A.S. = aortic sampling site, SG = Statham P23Db strain gauge. (Reproduced by permission from Urschel, C.S., J.W. Covell, T.P. Graham, R.L. Clancy, J. Ross, Jr., E.H. Sonnenblick, and E. Braunwald. Effects of acute valvular regurgitation on the oxygen consumption of canine heart. *Circ. Res.* 23:33, 1968)

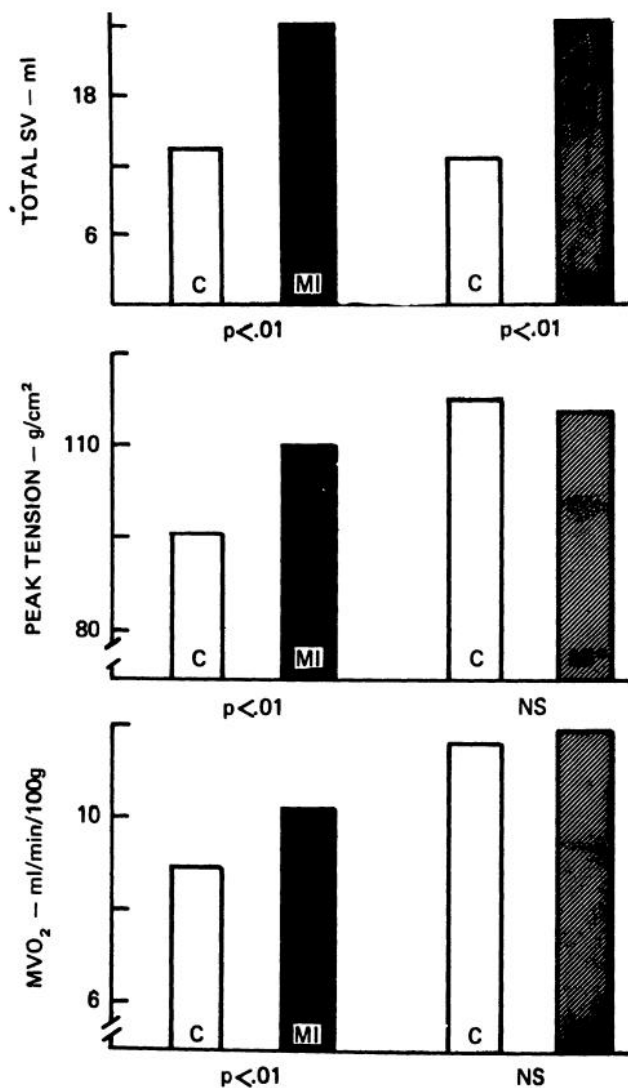


Fig.14. Summary of the effects of acutely induced mitral insufficiency in seven experiments. C = control; MI = mitral insufficiency; NS = not significant; SV = stroke volume; MVO₂ = myocardial oxygen consumption; MI* = mitral insufficiency with peak tension maintained at the same level as during the control period.

the myocardial fibers, as opposed to stretching the series elastic component, i. e., in developing tension. Valvular regurgitation allows a far greater fraction of the contractile activity to be manifest in shortening. When the experiments were carried out so that tension development remained constant when regurgitation is produced, this increased shortening work of the contractile elements did not produce a measurable increase in oxygen consumption.

Studies on myocardial energetics in congestive heart failure were carried out in papillary muscles removed from animals in which heart failure had been induced by constriction of the pulmonary artery one month earlier. Papillary muscles removed from these cats showed marked depressions of contractility *in vitro*, with reductions in the peak force which they could develop during isometric contraction and in the maximum velocity of isotonic shortening, that is, in the V_{max} , (39). It was observed, first of all, that oxidative phosphorylation and respiratory control in the mitochondria removed from these failing papillary muscles were entirely normal (35).

The concentrations of creatine phosphate and adenosine triphosphate in muscles isolated from normal cats, from cats with right ventricular hypertrophy without heart failure, and in muscles obtained from animals with heart failure are illustrated in figure 15 (27). Clearly, the stores of high energy phosphates were entirely normal in the latter group of muscles, even though, as already stated, their contractility was markedly depressed. It is evident, then, that their reduced contractility cannot be attributed simply to an inadequacy of the energy stores.

An attempt was then made to determine whether a defect exists in the utilization of energy in the contractile process of failing heart muscle, i. e., whether there might be a reduction in the efficiency with which chemical energy is converted into mechanical work in heart failure (24). Again, papillary muscles removed from animals with experimentally induced heart failure were employed, and the production of high energy phosphates was blocked with nitrogen and iodoacetic acid. It was observed that the heart failure state did not reduce either the resting rate of high energy phosphate utilization nor did it alter significantly the amount of energy utilized by the muscle per gram of tension development. From these studies it appears that the efficiency of the conversion of chemical energy to mechanical work is normal in this form of low cardiac output, experimentally produced, heart failure.

Elucidation of the determinants of myocardial oxygen consumption has also led to an approach to the treatment of one of the most common serious disease states, angina pectoris, i. e., the pain resulting from myocardial ischemia (2).

Since angina pectoris is a consequence of inadequate myocardial oxygenation, ideal therapy for this incapacitating symptom should be directed toward both increasing coronary blood flow and decreasing myocardial oxygen requirements. In the setting of severe coronary artery disease, however, the ability of the coronary vascular bed to dilate is limited so that methods designed to decrease myocardial oxygen

requirements may provide a more fruitful approach.

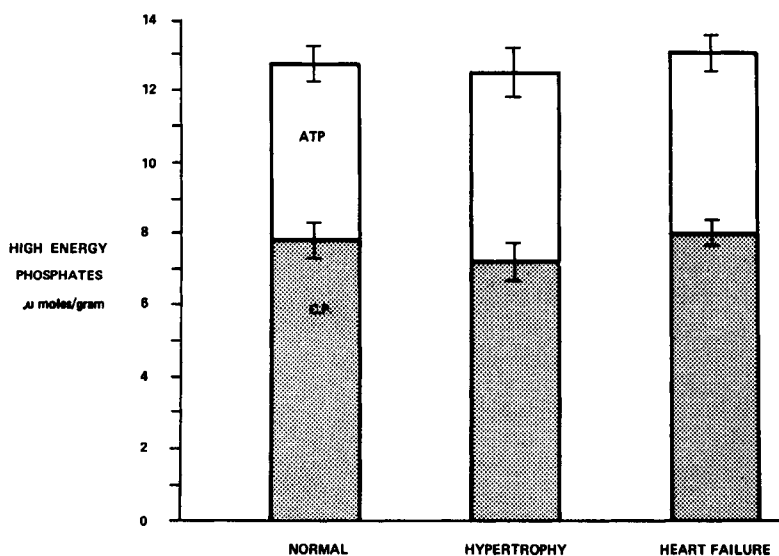


Fig.15. Average values (\pm SEM) of high energy phosphates (ATP= adenosine triphosphate, CP = creatine phosphate) in right ventricular papillary muscles obtained from normal cats, (left), cats with right ventricular hypertrophy without heart failure (center) and cats with experimentally produced heart failure (right).

Since the oxygen requirements of the myocardium are related largely to the number of contractions per minute, the tension development and contractility, it was considered that if cardiac frequency, arterial pressure and myocardial contractility could all be reduced, then myocardial oxygen requirements would also decline and perhaps, in this manner, a more normal relationship between myocardial oxygen availability and needs in patients with angina pectoris and myocardial ischemia could be re-established.

Stimulation of the carotid sinus nerves reduces heart rate, arterial pressure and myocardial contractility largely by reflex withdrawal of sympathetic activity. This approach was utilized for reducing myocardial oxygen requirements in patients with angina pectoris. Electrodes were attached to the two carotid sinus nerves and these were attached through wires to a subcutaneously placed radio-frequency receiver. The transmitter unit is worn outside the body and the patient is instructed to activate it manually when he experiences angina, or when he is about to participate in an activity which he knows is likely to induce angina.

Figure 16 is a representative tracing, showing heart rate, mean arterial and phasic arterial pressure in a patient with severe coronary

artery disease at rest and at various levels of exercise on a bicycle ergometer. Progressive increases in heart rate and arterial pressure occurred as the intensity of exercise was increased. The patient then developed angina pectoris, carotid sinus nerve stimulation was carried out, a prompt decline in heart rate and arterial pressure occurred and the angina disappeared, even though exercise was maintained. The stimulation was discontinued, heart rate and arterial pressure returned to their previously elevated levels while the patient continued to exercise, and promptly a second bout of angina occurred which could again be relieved with carotid sinus nerve stimulation.

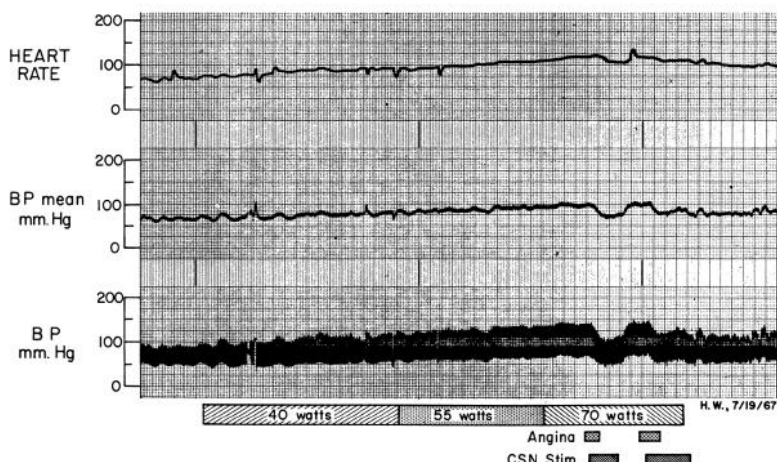


Fig.16. Representative tracing showing the abolition of angina during exercise by carotid sinus-nerve stimulation. The onset of angina occurred during exercise performed at 70 watts. At this point the stimulator was turned on, and heart rate and arterial pressure fell. This was immediately followed by complete cessation of the angina. The stimulator was then turned off. The heart rate and blood pressure rose, and angina re-occurred. Turning on the stimulator again resulted in decreases in heart rate and arterial pressure and disappearance of the chest pain. (Reproduced by permission from Braunwald, E., S.E. Epstein, G. Glick, A. Wechsler, and N.S. Braunwald. Relief of angina pectoris by electrical stimulation of the carotid sinus. *New Engl. J. Med.* 277: 1278, 1967.)

Similar favorable results have now been obtained with this radio frequency carotid sinus stimulator in more than 40 patients with severe, incapacitating angina pectoris operated upon in several institutions in this country and abroad. It is a relatively simple operative procedure and the patients who have recovered from the operation have demonstrated marked symptomatic improvement. The reductions in myocardial oxygen requirements brought about by stimulating the carotid sinus nerves have allowed the patients to increase the intensity of their activities greatly and most have returned to gainful employment. This experience serves to emphasize the manner in which an understanding of physiologic processes may lead to direct and useful clinical applications.

SUMMARY

The results of a number of investigations on the determinants of myocardial oxygen consumption have been summarized. The basal oxygen consumption of the resting heart is small, approximately 20% of that of the contracting organ. The oxygen requirements of myocardial depolarization and repolarization were studied in isolated hearts in which electromechanical dissociation was produced. The oxygen cost of depolarization was found to be extremely small, approximately 0.5% of the total oxygen consumed by the normally working heart. Studies in which the relative oxygen costs of cardiac output and aortic pressure were determined were reviewed and the far greater oxygen cost of "pressure work" as opposed to "flow work" was mentioned. The close relation between the area beneath the left ventricular pressure curve, that is, the so-called tension-time index, and myocardial oxygen consumption was pointed out. A series of experiments designed to determine the oxygen cost of changes in the velocity of cardiac contraction, reflecting alterations in myocardial contractility were reviewed. It was emphasized that the contractile state of the heart, as reflected in the maximum velocity of isotonic shortening, is a major and recently appreciated determinant of myocardial oxygen consumption. Thus, velocity of contraction shares the role of important determinant of myocardial oxygen consumption with developed tension.

While the precise costs of activation and maintenance of the active state of the myocardium have not yet been clearly defined, it is likely that they are relatively low. In studies on isolated papillary muscles in which contractile activity could be controlled with great precision, it was found that oxygen consumption is a function of the tension which is developed and the velocity of shortening of the unloaded muscle. Shortening against a load requires oxygen above and beyond that required for the development of tension. Thus, evidence was presented for the existence of a Fenn effect in cardiac muscle. However, it was observed that the oxygen costs of shortening against a load are substantially less than the oxygen costs of developing tension alone. It was also shown that almost the entire increase in myocardial oxygen consumption produced by the administration of catecholamines results from the increased contractile activity produced rather than from a direct stimulating effect of the catecholamines on myocardial metabolism.

The direct energy costs of muscle contraction were studied in papillary muscles in which the synthesis of high energy phosphates had been blocked. It was observed that, as with oxygen consumption, an increase in tension resulted in a far greater utilization of energy than did an increase in shortening. Also, the increased myocardial oxygen consumption produced by catecholamines and hyperthyroidism was found to be associated with an increased turnover of high energy phosphates. Thus, the energy cost of unit tension development is increased by these stimuli.

The relevance of these observations to a variety of disease states was reviewed. It was demonstrated that the production of severe degrees of acutely induced valvular regurgitation do not elevate myocardial consumption significantly when myocardial tension is held constant. Congestive

heart failure is associated with a depression of myocardial contractility, but this depression of contractility cannot be attributed to any reduction of high energy phosphate stores in the muscle. Normal utilization of high energy phosphates per unit tension development in failing heart muscle was also demonstrated. A technique for reducing myocardial oxygen requirements by stimulating the carotid sinus nerves was described and its application to the treatment of angina pectoris is demonstrated.

Acknowledgment. The work summarized here was carried out at the National Heart Institute, Bethesda, Maryland from 1955 to 1968 in close collaboration with a number of investigators. The important contributions of Drs. H. N. Coleman, J. W. Covell, J. Pool, J. Ross, Jr., S. J. Sarnoff, and E. H. Sonnenblick must be emphasized. The continuing critical advice, support and encouragement provided by Dr. R. W. Berliner, is gratefully acknowledged.

REFERENCES

1. Blain, J.M., E.E. Eddleman, A. Siegel, and R.J. Bing. Studies on myocardial metabolism. V. The effects of lanatoside C on the metabolism of the human heart. *J. Clin. Invest.* 35: 314, 1956.
2. Braunwald, E., S.E. Epstein, G. Glick, A. Wechsler, and N.S. Braunwald. Relief of angina pectoris by electrical stimulation of the carotid sinus. *New Engl. J. Med.* 277: 1278, 1967.
3. Braunwald, E., S.J. Sarnoff, R.B. Case, W.N. Stainsby, and G. H. Welch, Jr. Hemodynamic determinants of coronary flow: Effect of changes in aortic pressure and cardiac output on the relationship between myocardial oxygen consumption and coronary flow. *Am. J. Physiol.* 192: 157, 1958.
4. Coleman, H.N. Effect of alteration in shortening and external work on oxygen consumption of cat papillary muscle. *Am. J. Physiol.* 214: 100, 1968.
5. Coleman, H.N. Role of acetylstrophanthidin in augmenting myocardial oxygen consumption: Relation of increased O_2 consumption to changes in velocity of contraction. *Circulation Res.* 21: 487, 1967.
6. Coleman, H.N., E.H. Sonnenblick, and E. Braunwald. The Mechanism of the norepinephrine induced stimulation of myocardial oxygen consumption. In preparation.
7. Coleman, H.N., E.H. Sonnenblick, and E. Braunwald. Myocardial oxygen consumption associated with external work. The Fenn effect. *Am. J. Physiol.* In press.
8. Covell, J.W., E. Braunwald, J. Ross, Jr., and E.H. Sonnenblick. Studies on digitalis, XVI. Effects on myocardial oxygen consumption. *J. Clin. Invest.* 45: 1535, 1966.
9. Evans, C.L., and Y. Matsuoka. The effect of various mechanical conditions on the gaseous metabolism, and efficiency of the mammalian heart. *J. Physiol.* 49: 378, 1915.
10. Fenn, W.O. A quantitative comparison between the energy liberated and the work performed by the isolated sartorius muscle of the frog. *J. Physiol.* 58: 175, 1923.
11. Gibbs, C.L., H.H. Ricchiuti, and W.F.H.M. Mommaerts. Activation heat in the frog sartorius muscle. *J. Gen. Physiol.* 49:517, 1966.

12. Graham, T. P., Jr., J. W. Covell, E. H. Sonnenblick, J. Ross, Jr., and E. Braunwald. Control of myocardial oxygen consumption: Relative influence of contactile state and tension development. J. Clin. Invest. 47: 375, 1968.
13. Graham, T. P., Jr., J. Ross, Jr., J. W. Covell, E. H. Sonnenblick, and R. L. Clancy. Myocardial oxygen consumption in acute experimental cardiac depression. Circulation Res. 21: 123, 1967.
14. Gregg, D. E. Physiology of the coronary circulation. Circulation 27: 1128, 1963.
15. Gremels, H. Über den Einfluss von Digitalis Glykosidin auf die energetischen Vorgänge am Säugetierherzen. Naunyn-Schmeideberg's Arch. exptl. Pathol. Pharmacol. 186: 625, 1937.
16. Hasselbach, W. Relaxation and the sarcotubular pump. Federation Proc. 23: 909, 1964.
17. Hill, A. V. The heat of shortening and the dynamic constants of muscle. Proc. Soc. B. 126: 136, 1938.
18. Klocke, F. J., E. Braunwald, and J. Ross, Jr. Oxygen cost of electrical activation of the heart. Circulation Res. 18: 357, 1966.
19. Klocke, F. J., G. A. Kaiser, J. Ross, Jr., and E. Braunwald. Mechanism of increase of myocardial oxygen uptake produced by catecholamines. Am. J. Physiol. 209: 913, 1965.
20. Krasnow, N., E. L. Rolett, P. Yurchak, W. B. Hood, and R. Gorlin. Isoproterenol and cardiovascular performance. Am. J. Med. 37: 514, 1964.
21. Monroe, R. G. Myocardial oxygen consumption during ventricular contraction and relaxation. Circulation Res. 9: 3621, 1961.
22. Pool, P. E., B. M. Chandler, S. C. Seagren, and E. H. Sonnenblick. The mechanochemistry of cardiac muscle III: Effects of norepinephrine on the utilization of high energy phosphates. Circulation Res. 22: 729, 1968.
23. Pool, P. E., B. M. Chandler, and W. H. Sonnenblick. The mechanochemistry of cardiac muscle II. The isotonic contraction. Circulation Res. 22: 465, 1968.
24. Pool, P. E., B. M. Chandler, J. F. Spann, Jr., E. H. Sonnenblick, and E. Braunwald. The mechanochemistry of cardiac muscle IV. Utilization of high energy phosphates in experimental heart failure. Circulation Res. In press.
25. Pool, P. E., C. L. Skelton, S. C. Seagren, and E. Braunwald. Chemical energetics of cardiac muscle in hyperthyroidism. J. Clin. Invest. 47: 236, 1968.
26. Pool, P. E., and E. H. Sonnenblick. The mechanochemistry of cardiac muscle: I. The isometric contraction. J. Gen. Physiol. 50: 951, 1967.
27. Pool, P. E., J. F. Spann, Jr., R. A. Buccino, E. H. Sonnenblick, and E. Braunwald. Myocardial high energy phosphate stores in cardiac hypertrophy and heart failure. Circulation Res. 21: 365, 1967.
28. Ricchuiti, N. V., and C. L. Gibbs. Heat production in a cardiac contraction. Nature 208: 897, 1965.
29. Rodbard, S., C. B. Williams, D. Rodbard, and E. Berglund. Myocardial tension and oxygen uptake. Circulation Res. 14: 139, 1964.
30. Rohde, E. Über den Einfluss der mechanischen Bedingungen auf die Tätigkeit und den Sauerstoffverbruche der Warmbluterherzens. Arch. Exptl. Pathol. Pharmacol. 68: 406.
31. Ross, J., Jr., E. H. Sonnenblick, G. A. Kaiser, P. L. Frommer,

- and E. Braunwald. Electroaugmentation of ventricular performance and oxygen consumption by repetitive application of paired electrical stimuli. *Circulation Res.* 16: 332, 1965.
32. Sarnoff, S.J., E. Braunwald, G.H. Welch, Jr., R.B. Case, W.N. Stainsby, and R. Marcruz. Hemodynamic determinants of oxygen consumption of the heart with special reference to the tension-time index. *Am. J. Physiol.* 192: 148, 1958.
 33. Sarnoff, S.J., R.B. Case, G.H. Welch, Jr., E. Braunwald, and W.N. Stainsby. Performance characteristics and oxygen debt in a nonfailing metabolically supported, isolated heart preparation. *Am. J. Physiol.* 192: 141, 1958.
 34. Sarnoff, S.J., J.P. Gilmore, A.G. Wallace, N.S. Skinner, Jr., J.H. Mitchell, and W.M. Daggett. Effect of acetyl strophanthidin therapy on cardiac dynamics, oxygen consumption and efficiency in the isolated heart with and without hypoxia. *Am. J. Med.* 37: 3, 1964.
 35. Sobel, B.E., J.F. Spann, Jr., P.E. Pool, E.H. Sonnenblick, and E. Braunwald. Normal oxidative phosphorylation in mitochondria from the failing heart. *Circulation Res.* 21: 355, 1967.
 36. Sonnenblick, E.H., J. Ross, Jr., and E. Braunwald. Oxygen consumption of the heart. Newer concepts of its multifactorial determination. *Am. J. Cardiol.* 22: 328, 1968.
 37. Sonnenblick, E.H., J. Ross, Jr., J.W. Covell, G.A. Kaiser, and E. Braunwald. Velocity of contraction as a determinant of myocardial oxygen consumption. *Am. J. Physiol.* 209: 919, 1965.
 38. Sonnenblick, E.H., J.F. Williams, Jr., G. Glick, D.T. Mason, and E. Braunwald. Studies on digitalis, XV. Effects of cardiac glycosides on myocardial force-velocity relations in the nonfailing human heart. *Circulation* 34: 532, 1966.
 39. Spann, J.F., Jr., R.A. Buccino, E.H. Sonnenblick, and E. Braunwald. Contractile state of cardiac muscle obtained from cats with experimentally produced ventricular hypertrophy and heart failure. *Circulation Res.* 21: 341, 1967.
 40. Spann, J.F., Jr., E.H. Sonnenblick, T. Cooper, C.A. Chidsey, V.L. Willman, and E. Braunwald. Studies on digitalis, XIV. Influence of cardiac norepinephrine stores on the response of isolated heart muscle to digitalis. *Circulation Res.* 19: 326, 1966.
 41. Urschel, C.W., J.W. Covell, T.P. Graham, R.L. Clancy, J. Ross, Jr., E.H. Sonnenblick, and E. Braunwald. Effects of acute valvular regurgitation on the oxygen consumption of the canine heart. *Circulation Res.* 23: 33, 1968.
 42. Urschel, C.W., J.W. Covell, E.H. Sonnenblick, J. Ross, Jr., and E. Braunwald. Myocardial mechanics in aortic and mitral valvular regurgitation: The concept of instantaneous impedance as a determinant of the performance of the intact heart. *J. Clin. Invest.* 47: 867, 1968.

MEDICAL PHYSIOLOGY STUDENT LABORATORY

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During the past five years, freshmen medical students and first year graduate students enrolled in the introductory medical physiology course at this University have participated in a laboratory exercise which required that they perform thoracotomies, implant electromagnetic flowmeter probes and blood pressure gages in the ascending aorta and in the cardiac chambers of experimental animals, and subsequently, record responses of these and other variables during a prescribed experimental protocol. In spite of the apparent complexity of these procedures, our students have successfully completed the experiments in about 90% of the cases. This experience indicates that instrumentation, previously limited to relatively few cardiovascular research laboratories, can be used to advantage by relatively unsophisticated students. This laboratory exercise is a practical and valuable learning experience. The report which follows describes details of the procedures and instrumentation and includes a critique of our experience.

Medical physiology courses typically include a laboratory exercise which provides the student with first hand experience in cardiac dynamics and the cardiac cycle. Although such exercises take many forms, they usually involve the recording of ECG and the blood pressure in acute animal preparations. In most instances, the laboratory requires active participation and provides the student with opportunity for his first look and feel of the live cardiovascular system. Such experience is, in general, valuable, for it provides a first hand demonstration of mechanical, electrical, and other dynamic concepts basic to understanding normal cardiovascular physiology and also lays the groundwork for understanding abnormalities in cardiovascular function. The most sophisticated modern cardiovascular diagnostic workup is, after all, only an extension of this experiment involving a human patient.

Most of today's cardiovascular research laboratories utilize one or more of the modern methods of measuring and recording phasic blood flow. In this department, extensive use has been made for over ten years of electronic approaches to blood flow measurement and, indeed, several blood flowmeters have been developed or refined. Use of these devices in research projects is commonplace. Five years ago we felt that our experience with techniques for measuring blood flow was sufficiently wide and the instrumentation sufficiently simplified that measurement of phasic flow could be included in the routine part of the medical student physiology laboratory. For reasons described below, we selected electromagnetic flowmeters as the teaching model and redesigned our student laboratory experiments involving hemodynamics and the cardiac cycle to take advantage of this and other modern instrumentation.

Mechanics. Our medical physiology classes number 96 students subdivided into three sections of 32 each which rotate through three laboratories. The cardiovascular laboratory has eight stations, each

manned by a team of four students. For this experiment, the four students are assigned roles as surgeon, assistant, engineer, and director. Each station is equipped with a table, respirator, surgical instruments, and an Offner Recorder with appropriate plug-in units to accommodate two Statham strain gage manometers, an electromagnetic flowmeter, and an electrocardiograph. The flowmeter selected for this laboratory is an inexpensive instrument designed around a commercially available chopper amplifier, so that it is possible to measure blood flow using only a chopper input amplifier, a flow probe, and an audio amplifier as a magnet drive.

Before the laboratory, the dog is anesthetized and a tracheal cannula inserted. This frees the student's time for attention to the experiment. Large dogs are used in order to insure that the flowmeter head fits the ascending aorta securely. A 20 kg dog usually requires about a 20 mm diameter probe. Students have received the laboratory directions beforehand and have been requested to read them. Two faculty members and two lab assistants are on hand to provide guidance. These individuals are familiar with the dissection and the instrumentation.

The student surgeon and assistant perform a thoracotomy through the fourth or fifth left intercostal space and expose the heart and origin of the great vessels. Before proceeding with the implantation of the flowmeter, they explore the chest and identify a number of anatomical landmarks (sympathetic chain, vagus and phrenic nerves, coronary artery and sinus, etc.). Dissection of the aorta from the pulmonary artery is less of a technical problem than predicted; during the past five years, the great majority of our students have been able to seat a flow probe around the origin of the aorta within a half hour of entering the chest. Once the probe is seated, the engineer initiates recording of phasic flow and ECG. Since the electrodes of the electromagnetic flowmeter probe can serve also as the ECG pickup, it is possible to arrange for recording of either the ECG or aortic flow by simply moving a selector switch. Next, the surgeon places polyethylene cannulae into the left ventricle and aorta. If these cannulae are connected to a single Statham strain gage manometer by a stopcock, it is possible to use the single gage for selective recording of the pressure at either site. Thus, if only two recording channels are available, it is possible to record any combinations of two of the following four variables by simply moving a switch or lever: ECG, pressure #1, pressure #2, aortic flow. The students can record these variables two at a time using the ECG as the initial reference tracing and can then go through recording various combinations in order to compare the mechanical and temporal relationships. At the conclusion of this inspection of normal relationships, certain of these recordings are repeated while introducing perturbations into the system. These include observing the effects of electrical stimulation of the vagus and sympathetic nerves, injection of cardio-active drugs, mechanical interference with venous return and with aortic outflow. Later, the effects of coronary artery ligation are recorded, and terminally, ventricular fibrillation is induced. Afterwards, students report on their findings and the results are reviewed. In preparation for this, students align their records in time to construct a set of curves of the events of the cardiac cycle. The laboratory discussion reviews

the timing of the electrical, mechanical, and hydraulic events of the heart beat.

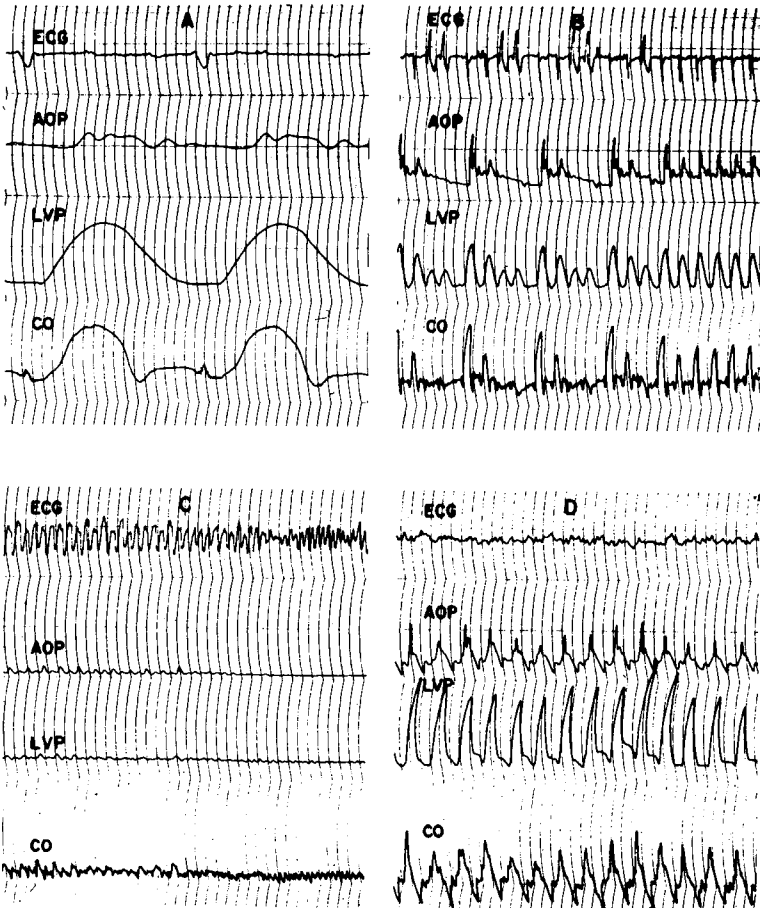


Fig.1. Excerpts from a student record demonstrating electrical and mechanical correlation during normal and pathological states. a) Normal cardiac cycle. Paper speed 100 mm/sec. b) An arrhythmia is present. Some of the ventricular contractions do not generate enough pressure to open the aortic valve; this is reflected in the record of aortic pressure and aortic blood flow. Contractions preceded by prolonged diastole are super normal as indicated by elevated aortic pressure and increased stroke volume. c) Transition from ventricular tachycardia to ventricular fibrillation about five minutes after coronary artery ligation. The entire hemodynamic sequence which followed coronary ligation was recorded; this excerpt demonstrates reduced perfusion pressure and stroke volume during ventricular tachycardia and the absence of coordinated cardiac activity during ventricular fibrillation. d) Hemodynamics during manual

cardiac massage by the medical student. This procedure gives the student a firsthand appreciation of the work of the heart.

Other physiological and pharmacological maneuvers included sympathetic and vagal stimulation, manipulation of venous return and outflow resistance, administration of cardioactive drugs, etc.

Discussion. Over the past five years, 120 student groups have attempted this experiment; only ten failed to complete it, usually due to perforation of the pulmonary artery during placement of the flow probe. The presence of experienced instructors has practically eliminated delays due to technical problems with the flowmeter. Although the Offner control panel is a challenge to students, it rarely takes more than a few minutes of the instructor's time to acquaint them with rudiments of its operation. None of the instrumentation has been damaged by the students.

We feel that these experiments have proved to be well within the capabilities of first year medical and graduate students and have added significantly to their understanding and appreciation of cardiac function. In an era in which electronic means for measurement of blood flow constitutes a standard tool in most physiology laboratories, we find little justification for continuing to use out-moded methods or for ignoring this opportunity. Student acceptance and response to this laboratory exercise have tended to agree with our appraisal of its effectiveness as a teaching approach.

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SHOULD PHYSIOLOGY TRAINING BE DIVORCED FROM THE MEDICAL CURRICULUM*

INTRODUCTION

F. J. HADDY
Michigan State University

Each year the Education Committee of the American Physiological Society considers some currently interesting aspect of teaching. Last year the topic was teaching physiology to the medical student (1). This year the subject is teaching physiology to the graduate student in a medical school.

Many Departments of Physiology are administratively and fiscally in medical schools. Consequently, graduate students in these departments interact with medical faculty and medical students. They frequently take courses with medical students. From time to time the question has been asked whether this arrangement is in the best interest of the physiology graduate student and, since the discipline of physiology is perpetuated through the graduate student, in the best interest of physiology. Some of the goals of physiology and medicine differ; some physiologists, by the nature of their training, are more committed to teaching medical students than graduate students; and some departments are small and lack the breadth necessary for individualization of the graduate students program. Over the years, occasional attempts were made to solve these problems. In general, however, the attempts were not very vigorous because there are redeeming features in the arrangement. Some of the goals of physiology and medicine are synergistic; the graduate student benefits from the interchange; and there are practical reasons for the association. Since the pressure for change was not really great and the system seemed to work, the question was soon forgotten.

But now the question is asked more frequently and, once asked, is not so quickly forgotten. Medical education is experiencing a great revolution. Hardly a week passes without another medical school announcing a major curriculum revision. The trends are clear and include more emphasis on service and on the behavioral and social sciences; earlier involvement with the patient; more individualization of the medical student's curriculum, particularly through the medium of elective courses; increased relevance of basic science teaching to the problems of the patient; and abbreviation and integration of basic science offerings.

These trends in medical education may affect graduate education. For example, it is argued that the new medical curriculum is more time-

*Session on Teaching sponsored by the Education Committee of the American Physiological Society at the Annual Meeting of the Federation of American Societies for Experimental Biology, April 16, 1969, Atlantic City, New Jersey. Session organized by J. R. Brobeck and chaired by F. J. Haddy.

consuming and thus leaves less time for thoughtful research and graduate student teaching; that an abbreviated and integrated medical physiology course is not appropriate for the graduate student; that the small specialized medical school Department of Physiology is now even less able to meet the needs of the graduate student; and so forth. It has been suggested that the needs of the graduate student can better be met by a broadly based all-university Department of Physiology, serving many disciplines in addition to medicine, because such a department can afford many kinds of physiologists and a large variety of strong graduate courses.

The Education Committee is therefore perhaps justified in asking whether physiology training should be divorced from the medical curriculum. Certainly the problem should be thoroughly discussed. The purpose of this Teaching Session, then, was to hear arguments on both sides of the question. The Teaching Session had several unique features. It was introduced with a broad examination of physiology and its relation to medicine by one who currently views the scene from Washington. There then followed six short presentations by graduate students or recent graduate students, three on each side of the question. The "debate" was concluded with summaries for the affirmative and negative by two more mature physiologists who are also trained in medicine.

- (1) The Teaching of Physiology. The Journal of Medical Education. 43: 1143, 1968.

PHYSIOLOGY: THE N-DIMENSIONAL PROFESSION

H. P. JENERICK
National Institutes of Health

When I started considering various facets of the subject of this meeting, namely, should physiology be divorced from the medical curriculum, I began by examining the viewpoints of my fellow speakers. In support of a separation, some feel that the goals of medicine and physiology are different; that training in physiology must be individualized; and one critic even feels medical faculties neglect the training of graduate students! The other group stressed the fact that both the medical and graduate students benefit from the interchange; there are practical reasons for continuing the association; and that the goals of medicine and physiology are synergistic. Continuing this "penetrating and critical review," I even pretended to put myself in the position of the medical school dean. As I sat behind my new mahogany desk and pondered this question, the only answer I could come up with and still keep my membership in the deans' union, was silence.

I'm giving you this bit of background to make it clearer why I chose the particular title I did for my address. We already have a number of different but equally valid answers to our general question, and it seemed comfortable to pass on by and discuss physiology in broad terms, for in the end it will be for each person here to answer the question for himself. Not so much by what he says about it, but by what he does about it. The answer he finally gives must be made in the larger context of the relationship between the two sister disciplines - medicine and physiology -

and it is this that I want to talk about.

Without implying that physiology derives its sole existence from medicine, it's safe to say that there are strong ties and interconnections. Physiology has been welcomed for centuries in the medical school and during all that time has been cheerfully housed and nurtured. In return, physiology has taught and researched into the foundations of normal and abnormal bodily functions. As biologists we might recognize this relation as a form of symbiosis (where both partners benefit) rather than commensalism (where both happen merely to live together on friendly terms). In following this analogy we might go even further and consider who is the host and who is the guest? Perhaps that oversteps the analogy of symbiosis and we better settle for the concept of a partnership or co-habitation as being realistic and generally more interesting. In any event, physiologists will eventually be concerned if our shared roof starts to leak, and there are definite signs that it is. What are some of the findings an appraiser would make if he came in and looked over one of the houses physiology lives in - the medical school?

Modern medicine is a complex system involving more than 300,000 physicians, 75,000 dentists, 600,000 nurses, and more than 1 million allied health personnel directly involved in patient care. The tremendous advance of medical knowledge during this century (in which physiology has participated) has necessarily led to a great increase in specialization, so that now more than 75 percent of all physicians are in one of the specialties. In consequence surgery has grown quite complex; automatic systems are being introduced for patient monitoring; there is a shift to preventive medicine, bringing with it a need for increased sophistication in diagnosis. Should physiology be concerned with these changes or should it stay removed and uninvolved? If so, bioengineering, as the emerging science of systems and control, will fill in the gaps we leave. Let me add parenthetically how incredible this development now seems. Last year at this same teaching session Dr. Harry Patton of Seattle said:

"Physiology is concerned not only with the functional properties of cells, tissue, and organs, but more especially with their regulation and control. The physiologist is the control-system analyst of biology. Interest in control and regulation, above all, is the glue that makes physiology a coherent discipline."

I'm sure that many of us here still agree with Dr. Patton; yet, somehow within the past year, an independent Biomedical Engineering Society has been organized and its membership is growing rapidly. How could we let that happen? Many members of this Society will know what I mean when I say shades of 1957! (For those who don't, that was the year the Biophysics Society was splintered off and organized.)

In light of what I said earlier about the growth of the specialties, medical practice is being reoriented and, in turn, so is the medical curriculum. That raises the next question which I believe is the real subject of today's debate; namely, who is ultimately responsible for a medical curriculum? All members of the faculty? If not all, then just

who? When considering answers to these questions, the physiologist in the medical school should also consider what his answer may imply; for if he abdicates from this responsibility, he also must accept the consequences. It is a natural human trait for all of us to accept what we're doing now as somehow right and proper in all respects. If someone else even raises questions about it, an automatic alarm goes off and our castle is stoutly defended even if it's the Christians outside trying to break in. But sooner or later, we're due for a big surprise if our purposes and activities become too divergent from what society requires and expects of us.

Many years ago Dr. William Salter of the Department of Pharmacology at Yale was addressing a group of anesthesiologists. He warned that "no professional group can maintain itself on the basis of service alone." We can make a modern paraphrase - "physiology cannot maintain itself on the basis of its research alone." The message for today is that physiology, as a whole, has to concern itself not only with fundamental research and graduate training, but also with medical education and with medically relevant research. Now that doesn't mean you're asked to stop being physiologists - but it does ask that you consider from time to time what are the larger dimensions and purposes of your research and teaching.

Last year Dr. Thomas Reeves, a professor of medicine, speaking at the education symposium of this society, described what he believed a physiologist to be; namely, one whose training and experience allows him to understand and to teach the functions, regulation, and interaction of the parts of the body. Dr. Reeves went on to describe how he sees physiology playing a continuing central role in medical practice, since a physician's selection of any course of treatment or therapy must be played out against the background of what normal physiological function should demand. It is chiefly through his training in medical school that a physician receives the information about physiology needed to guide him through the rest of his career. This is a serious obligation that physiologists cannot easily set aside or retreat from into a laboratory.

The extent and content of physiology's future contributions to medical education could be the subject of a month-long debate. As a start, I suggest you might read the published papers from last year's symposium "The Role of Physiology in Medical Education." You'll find there echoes of today's discussion, so we're not voicing something entirely new. For instance, Dr. Walter Randall expressed concern over the apparent de-emphasis of teaching as a worthwhile activity. The outlook in some departments has become so narrow, he said, that most of their activities are no longer relevant to the training of medical students. Dr. Reeves, who I have already quoted, said further, "by virtue of the rigorous and disciplined nature of his training, the good physiologist should be in the best position to integrate into a meaningful whole, the knowledge that continues to be amassed regarding the function of the parts of the body. This is the primary role of the physiologist in the modern medical curriculum. If he abdicates this responsibility for directing the teaching of integrative systems physiology, the hope of achieving a truly excellent

curriculum will be seriously diminished." Other members of that symposium placed similar emphasis on coordination, integration, and the keystone position of physiology in the medical curriculum.

The old standard medical curriculum of two preclinical years and two clinical years had evolved for good reasons. It gave the student an understanding of the major areas of medicine and of the general sciences on which medicine is based. The latter knowledge was and still is essential to medicine because the physicians received a broadly based understanding that enabled them to comprehend the entire disease process in their patients. This basic science core also permitted communication between the general practitioner and the specialists about the problems they were dealing with in their patients.

But medical knowledge has increased greatly in extent and depth and the medical curriculum now represents a compromise between a number of competing basic and clinical specialties. Although more clinical material is packed in, particularly by the emergence of new medical specialties, this does not diminish but rather increases the need for basic science training. I mentioned earlier that specialty practice is increasing. It is now estimated that five out of six medical students will eventually enter one of the specialties. These clinical disciplines, especially in academic medicine, are marked by active research which draws on a base of physiology as a preclinical science, much as physiology draws on the natural sciences base.

But, on the other hand, in many medical teaching programs relatively little time is devoted after the first year to the science upon which these medical advances are based. Since such a large fraction of medical students are now planning to enter one of the specialties, it can be seen that our total system of medical education faces a very real challenge to develop more appropriate mechanisms for the effective transfer of knowledge from the advancing front of basic medical sciences to the physicians in training who will need this knowledge in their medical practice.

Part of this need will be met by curriculum revisions which introduce more advanced physiology training to the regular curriculum as well as the specialties. This shift in educational pattern will call for development of special programs such as seminar series, lecture and laboratory courses, etc. that will provide opportunity for advanced medical students, residents, and practicing physicians to obtain an in-depth background in physiology essential to their selected specialty area. Does anyone need to be convinced that physiology has much to say to internists, anesthesiologists, neurologists, surgeons, and others. There are many who believe a well developed and extended curriculum which provides the student and the resident access as needed to advanced areas of physiology may be one of the most significant developments yet to come. One can also predict that in the long run, medical research will continue to expand and also to evolve in new directions other than through the classical academic department. Broadly-based, imaginatively directed clinical research programs are now being mounted. There is a need there for a strong basic research component that is recognized by the clinical

researchers and I hope by the preclinical scientists who must man these research positions. In addition, there are related needs for us to develop graduate training programs which will permit physiologists to participate with physicians and engineers in the type of complex health care systems of the future which we are just now beginning to see evolve. While it's a little early to sketch out the dimensions of this development, we will gain valuable experiences by our increased participation at various levels of medical training. So you see, rather than posing a threat, the growing sophistication of the clinical sciences creates a host of opportunities for further interfacing and collaboration by physiologists.

These then are several of the many dimensions of physiology, all arising from the growing involvement with clinically-oriented research and teaching which greatly augments and extends physiology's traditional position early in the curriculum. While we can also anticipate changes there too, that subject (the medical physiological course) is so close and perhaps so painful, I will leave it at that.

When the dust settles, we may find the following. The medical curriculum has become individualized, with a minimum number of integrated, core courses. These are supplemented and extended by larger blocks of electives in clinical, preclinical, and even graduate school subjects. As a consequence, the medical school will be drawn back more tightly into the university, a development that will bring much relief as well as great opportunities for the regular graduate programs of the basic medical sciences. You can see by now, I hope, physiology stands to gain in the long run in direct proportion to the work and involvement each of us puts in now.

In practical terms what does a modest sized, modest budgeted department do in the face of these demands? Should they push for unity or diversity? On the one hand, a staff chosen on the basis of having unified or closely related research programs will clearly have much to say to each other at the bench. But, one wonders if they will attract many graduate students unless these students are already committed to that specific research area. Why is that? It's a fact that the ordinary candidate for graduate school often has a fuzzy notion about physiology since it is not often taught as such in college. In this connection, one particularly rough question to ask yourself is this. Suppose you were appointed to a chairmanship and asked to build up a modern, but modest-sized physiology department. How many offers would you extend to your present and former graduate students? Would you select specialists in axon research, or would you search for a staff with broader capabilities? So, if a department staff is to do their graduate training well, they should train the young people for both aspects of an academic post - training them in depth for future research and broadly in the fundamentals of physiology for future teaching. This balance is not an easy one to make and I know that you have been concerned over it long before hearing this speech. Not only that, matters are rapidly getting more complicated. As a result of upgraded high school curricula, colleges are now teaching more advanced material. This in turn requires adjustments in the professional schools. Just for example, one-third of the entering class was excused from biochemistry this year at a prestigious Boston medical

school. As physiology penetrates the undergraduate curriculum, we can anticipate the need for similar adjustments. Depending on our responses, that time will signal either the gradual demise of physiology as such in the medical school, or an opening of new opportunities for broader and stronger professional involvement of the types I have discussed earlier. We do not need change for change's sake, but because physiology must continue to make, in our jargon, "homeostatic adjustments to environmental changes." This is even an inappropriate analogy, since homeostasis implies a return to what was before. In the present case, the environment has changed irrevocably, so adaptation will bring us to some new position.

The parameters and conditions of that new position are still hidden from us in the future. Even the systems physiologists here among us could not predict where or how we are going because they don't know the variables or even the constants. In general terms, this suggests that diversity is a good general strategy because there is no best way. Physiology needs to be broadened and extended, not constricted down by processes of exclusion. Disregarding the titles, there should be room for biophysics as well as bioengineering and clinically-related research and teaching. The hallmark that distinguishes physiology is its concern with synthesis and integration, with the fitting of individual parts into the assembled whole. Under this rubric there should be space for molecular and cellular physiologists as well as organ and systems physiologists.

However, as we change and evolve, we face a very great challenge and that is how do physiologists meet the widely diverse needs that have been discussed here. We can't be all things to all men. The day is nearly gone when a department could go it alone and by itself attempt to meet the needs of all of its students and its academic colleagues. So, one of the greatest challenges is how a limited faculty can attempt to establish collaborative research programs and to hand-tailor the education of 100 or more medical students coming through each year. Here, as in the rest of life, the greatest challenge also offers the greatest opportunity to advance. Faced with this problem, some departments of limited means may very well seek to develop strength out of a concentration of effort. Taking any unique or special resource, like a staff interest in cardiovascular problems, or in neurophysiology, they can build these up to a high level of excellence. (Note: I'm not contradicting what I said earlier about the hazards of overspecialization; I'm talking about a matter of degree.) Such small-scale centers of excellence can intermesh, as appropriate, with related interests, both clinical and preclinical, in other parts of the school. They can be supplemented in their areas of weakness by still other groups, but the key elements of this development is to provide enough concentration in something to carry it beyond the critical mass and enable it to make meaningful contributions in medical and in graduate training. One shrewd observer of the dynamics of academia has predicted that to the extent physiology links itself with other groups in the medical school, to that extent will she again grow and flourish.

In closing, I confess I have largely avoided the related and equally

complicated problem of physiology graduate teaching, particularly in medical school based departments. These groups experience great frustration in providing their students an adequate exposure to the cognate natural sciences of physics, physical chemistry, mathematics, or psychology, since these latter departments are all too often located on distant campuses. Although there are no easy solutions for this problem, there are possible long-range solutions as I have sketched out. Finally, I have intended throughout this presentation to suggest very strongly that a severance of physiology from the medical curriculum would be fatal. Not now - not when the demands and the opportunities for the partnership are greater than ever.

(The next three papers by Roe, Hersey, and Whitehorn are for the affirmative of the question; Should physiology training be divorced from the medical curriculum?)

GOALS OF MEDICINE AND PHYSIOLOGY ARE DIFFERENT

D. H. ROE

Graduate Student, University of Illinois

In analyzing the resolution, "That Physiology Training Should be Granted its Divorce from Medical Education," it is important to examine the goals of physiology and medicine. Medicine has as its goal the curing of disease and the saving and prolonging of useful life. On the other hand physiology has as its goal an understanding of the functions of life in all forms of life. The two goals obviously overlap to a certain extent. Also most people will agree that medical students should have some training in physiology. When you combine this with the fact that medical goals are most apparent and immediate to the majority of people, you have the reasons for the marriage of physiology and medicine. This marriage has been long and profitable; however, certain problems are becoming apparent in the marriage.

These problems arise from two situations. In outlining these situations I am generalizing and ignoring the exceptions; however, the generalizations are valid for the most part.

1. Medical schools and their associated physiology departments tend to be separate in location, bureaucratic structure, or both, from the main university campuses. This because of the need to be near large metropolitan areas where there are large hospital facilities and numbers of patients. This situation makes sense from the standpoint of medical goals, but makes things difficult for good physiology training for the graduate student.

2. Medical school physiology departments tend to have their strengths concentrated in one or two areas of physiology and these areas are usually closely connected to mammalian or systems and organs physiology. Again this makes sense from the standpoint of medical goals, but it certainly narrows the scope of training available to the physiology graduate student.

In order to efficiently pursue the goals of physiology, I feel physiology

departments must meet certain requirements. These requirements include: a) having a broad base of expertise within the faculty of the department, b) being a part of the main campus so that there can be continuous interrelationships with other departments on the campus. c) being able to attract good graduate students in reasonable numbers. d) being able to provide the kind of education which will adequately prepare the physiology graduate student for his career in physiology.

By broad base of expertise within the department faculty, I mean the research interests and abilities of the faculty should include at least the following broad areas of physiology; mammalian or systems and organs, comparative, and cellular and molecular physiology. Mammalian physiology is of course the classical base of physiology. Comparative physiology includes such stories as adaptations of insect flight muscles to permit many wing beats for each excitation, temperature regulation in moths, abilities of fish to maintain internal ionic balance in both sea and fresh water, the isozyme story and many others. In short the adaptations of organisms which permit them to live in the wide spectrum of ecological conditions found is one of the most fascinating stories physiologists have to tell. Ultimately to understand the complete functioning of organisms, it is necessary to know the cellular and molecular functions. The fact that physiology departments did not broaden their scope unfortunately contributed to the breaking away from physiology of such disciplines as biochemistry and biophysics. Many in these disciplines are physiologists at heart, and they should have a home in physiology departments. Individuals doing research in this area who are associated with physiology departments are more likely to ask critical questions about the physiological environment of the cell or molecule. In other words it is fine to be able to draw the kinetic curve of some enzyme, but more important is what this curve looks like when the enzyme is exposed to substrate and inhibitor concentrations it experiences in the organism and at the ionic strength and pH of the organism.

Being part of the main campus is becoming exceedingly important. Physiologists today need more and more training in math, physics, biochemistry, physical chemistry, and depending on their research interests, psychology, electrical engineering, and computer science. Philosophy should probably be included as well, when one sees the implications involved in applying various biological advances to society. To have the necessary training in these areas and to have the kind of interrelationship with these departments which leads to cross fertilization of ideas and techniques makes it imperative for physiology departments to be an integral part of the main university campus.

Being able to attract good graduate students in reasonable numbers is crucial to the future of the discipline of physiology. Departments meeting the first two requirements I have outlined can do this. I am not sure departments falling short of these requirements can.

Being able to provide the kind of education which will adequately prepare the physiology graduate student for his career in physiology is what this debate is all about. Obviously I feel the student should be exposed to the broad spectrum of physiology and then be allowed to specialize

in the area that excites him or her the most. I do not see how this is possible unless a department meets the first two requirements I outlined. The education given the graduate student must be flexible so that it can be individualized to meet the needs and desires of each student. One of my colleagues for the affirmative will amplify this vital point. Finally an important part in the education of a graduate student is to put him into the role of teacher. The graduate student should have the opportunity - perhaps even be required - to teach a course or courses to undergraduate students. This experience brings home to him the importance to a scientist of being able to clearly communicate ideas and concepts. It is amazing how much you learn about a fundamental concept when you are trying to make it clear to a blank-faced undergraduate student who just can not understand.

In conclusion, for physiology to efficiently pursue its goals it must have a broad base, must be a part of the main campus, must attract students, and must provide these students with the kind of education which will prepare them for full and rewarding careers in physiology. Therefore, physiology training should indeed be granted its divorce from medical education.

TRAINING IN PHYSIOLOGY MUST BE INDIVIDUALIZED

S. J. HERSEY

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The resolution under consideration represents one aspect of a multifaceted problem, namely, "what is the best way to educate physiologists?" The particular facet with which we are concerned here deals with the question of what is the best psychological, and perhaps by extrapolation the best physical environment in which to accomplish this task. In order to discuss the resolution then it is advisable to first interpret the terms involved and put them into the proper context. For the purpose of this discussion, I have taken the term physiology "training" to mean that set of educational experiences which are designed to produce a physiologist. (Let me make it clear that I do not believe a physiologist can be "trained," rather physiologists must be provided with a set of educational experiences which will lead to their development as physiologists.) I have also interpreted the term "medical curriculum" to mean that set of educational experiences which are designed to produce a physician. With these interpretations in mind we may properly re-phrase the resolution to read something like the following:

"What set of education experiences ought to be offered, to both the physiology graduate student and to the medical student."

This interpretation of the resolution requires the answers to essentially two basic questions. First, what should physiology "training" be? How does one go about educating a professional physiologist? The second question is; what experiences within the medical education program are relevant to producing a professional physiologist? Thus I shall not discuss the relationship of physiology as a science to medicine nor shall I discuss the role of physiology in the education of a physician. While

both of these topics are valid subjects for discussion, I do not believe that they are the central issues in the resolution under consideration. Let me first consider what physiology education ought to be and then entertain what, if any, educational experiences ought to be shared by such a program and medical education.

Everyone, I think, agrees that physiologists are a very heterogeneous group. While there are some basic aspects which are common to all physiologists, for the most part, physiology is made up of individual scientists and any, other than a general specification, must refer to sub-groups of physiologists and not to physiologists as a whole. How then, with such an individualized and diverse group, can one expect to produce a physiologist? The answer is that physiologists must be educated as individuals not as a group. The individualized education of physiologists has indeed been the tradition and I strongly feel that this tradition of individualized education is and has been the main key to producing a high quality of scientists, who subscribe to the title "physiologist."

The bulk of the responsibility for the individualized education of the physiologist rests, of course, with the dissertation advisor. It is under the advisor's guidance that the physiology student develops as a scientist and as an individual. A physiology "training" program provides little more than a super-structure or set of guidelines during this stage of the educational process. But what about the initial phases of physiology graduate education; what about the first years of graduate study? Is this period simply a matter of biding time until one chooses a dissertation advisor? Is it simply a period to make up deficiencies from ones undergraduate training or to pass language exams? If that is the case, then I submit that an organized program in physiology during the first year or two is of little importance and the function could be just as well accomplished without any sort of formal program. Fortunately, however, I don't believe that this is the case. At least it is not intended to be a time-biding period, nor a period of making up deficiencies. I believe that it is intended rather to serve as a time for the development of the student to act as an individual. A time to develop the capacity to undertake the more individualized aspects of his or her education. If the purpose of the initial years of graduate education is indeed to develop the student's capacity to act as an individual, I feel that it is a grave mistake to subject him or her to a program which is designed according to mass education policies. We must provide individual training right from the onset, and not expect a student to suddenly become an individual the day he walks into his advisor's lab. The individualized education in the initial stages of a graduate program should be based upon the individual's background, his immediate specialization or research interest, and upon his future goals. It should be designed to develop the basic skills which the trainee will need as an individual scientist. The sorts of skills to which I refer are literature criticism, the ability to design meaningful experiments, the ability to make use of technological advances, and the ability to express ones ideas in a professional manner. The student should also be introduced, at the very earliest opportunity, to the research goals, the research philosophies, if you will, within the department in order to facilitate his choice of an

advisor and more importantly to gain an understanding of what physiology research really is. These are the sorts of things which will make him independent, the sorts of things he will need as professional physiologist. We should not, I believe, subject the student to routine course work which is for the most part totally irrelevant or at best satisfies some curiosity which might just as well be satisfied by reading a text. I submit, that rather than offering a basic course in physiology or biochemistry or any other science, as most training programs do, that graduate programs ought to offer basic courses for physiologists, courses designed to emphasize the needs of the individual student. Such courses could provide basic information in physiology as well as other disciplines, depending upon the individual student's requirements, and at the same introduce the student to the skills needed for his professional development. Only in this way will the program be, from beginning to end, truly designed to produce a physiologist.

How then does this sort of physiology education relate to medical education? Medical education programs, I believe, have a fundamentally different approach. They are designed to produce a rather well-defined group of people. They are not individualized programs nor are they designed to produce individual scientists. This is evidenced by the fact that a nationwide exam can be given for physicians. While some may argue about the value of national board exams, the fact remains that physicians can be given a common exam at the end of their educational program. I think no one would be so foolish as to suggest a nationwide exam for graduate students in physiology. I do not suggest that physicians are stereotyped, I only submit that it is after the M.D. is obtained that specialization really occurs for the physician. Indeed the range of interests and positions occupied by physicians is perhaps even more diverse than that of physiologists. However, this diversification occurs at a different stage in the educational process for the two groups of scientists. The sorts of educational experiences provided the predoctoral physician are therefore, designed for group education rather than individualized education. From the point of view then of the nature and fundamental design of the educational programs there would appear to be no real relationship between "physiology training" and "medical education." On the one hand physiology education is designed to produce individuals to develop their skills or capabilities as individuals, whereas predoctoral medical education is designed to produce a group of similar people and to provide them with a common basis, from which they can subsequently specialize. If then the very design of the educational systems are not related it is perhaps unnecessary to ask that "physiology training" be granted a divorce from the "medical curriculum" since little more than an historical marriage even exists.

INADEQUACY OF GRADUATE EDUCATION

D. WHITEHORN

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The future of physiology as a discipline depends heavily upon the quality of graduate education in the field. A decision concerning the separation of graduate and medical training should take into account the

adequacy of graduate education as presently formulated within the framework of a medical school environment. If an acceptable quality of graduate education can not be attained in that environment, the separation should be carried out. In judging the adequacy of graduate education in physiology it should be emphasized that the student is being prepared for a career which will span the next thirty years. What skills a physiologist will need to function effectively in that world of the future is unknown, yet a prediction of future conditions is essential to any judgement of graduate education. In the present discussion, I will not attempt to deal with changes related to research activities which will undoubtedly occur within the field. Rather, I will concentrate on changes in the society in general which have important implications for physiology and for all of the sciences. It will be argued that at present, graduate education is not properly preparing the future physiologists to understand and deal with these changes and that a separation from medical education could provide a partial solution for this inadequacy.

How do social and political changes in our society effect physiology and science in general? It is clear that we live in an age of scientific revolution. Advances in technology, with their reliance on basic science, are rapidly changing the nature of our society and of ourselves. The enormous effect that scientific advancement is having upon our way of life has not gone unnoticed. A cursory examination of current social thinking reveals a prominent role for science and technology. Some believe that all of man's problems can be solved by intensive application of technology. Others point out the possibilities for increased personal freedom in an affluent society, but warn of the dehumanizing effects of present technological trends. How the fruits of the scientific revolution should be applied is, in fact, an important issue of our times and may become more evident in the future. If the young people of today are any example, the detrimental, as well as the useful applications of scientific information will be of increasing interest to the citizens of the future. There is already discussion concerning ways in which scientific applications can be introduced into the society in a more reasonable manner. It would be unfortunate if scientists, and physiologists in particular, with their interest in systems and their interactions, were unable, due to inadequate background, to participate effectively in the important decisions which must be made in this area.

These are disturbing developments for those who wish the sciences to be an objective search for truth, uninvolved in social and political issues. But to maintain that science is not intimately involved in the evolution of our civilization is to close one's eyes to the world around him. Unfortunately, many scientists appear to adhere to this position, a stance which may exclude scientists from a constructive role in the evolution of our society. This attitude is transmitted to the student during his graduate education.

The student enters graduate school with the beginnings of an understanding of the social climate; often these days with considerable interest in it. However, during graduate training the student is rewarded only for efforts within the scientific discipline. The demands made upon his time and energy are increasingly large as faculties strive to produce

"better" physiologists. A strong interest in the world outside the laboratory often becomes a luxury for the student who hopes to seriously pursue his research. This inward viewpoint, concentrating on building the conceptual framework which is the discipline of physiology today, leaves little time for understanding of social and political events. Without this understanding, changing attitudes, particularly toward education and science, seem threatening and repugnant. With such a reaction to change, rational action is impossible.

Graduate education is an obvious point at which to begin to provide the physiologist with an understanding of the broad and ill-defined problems of social evolution. A variety of techniques could be employed. Faculty-student discussions of the area could be initiated, for example, probably to the mutual benefit of both parties. It must be admitted, however, that neither student nor faculty are competent to deal at this time with the social and political implications of scientific advancement. A closer working relationship with the social sciences would thus seem essential. Whether an alliance with the social sciences can be carried out without severing ties with the medical school is an administrative question which I won't attempt to answer.

The time is ripe, however, for a radical shift in the concept of graduate education for physiology. Current trends in medical education place less emphasis on the basic sciences. Further, machine teaching may soon eliminate the lecture as a teaching method, supplanting it with individual or small group consultation. Physiologists may attempt to fight the trends, arguing for more time for the basic sciences, but this would seem to miss the point. "Factual" material can be transmitted more easily, and probably more clearly, via machine teaching, while the flavor of the scientific life can be transmitted better by close personal contact with the medical student. If the physiologist no longer is required to the extent he once was in medical education, the field should find new outlets for its abilities.

The problem of how scientific achievement can be used effectively for the good of man is generally left to politicians and retiring scientists writing their memoirs. As these questions gain wider interest within our society, the scientist must be capable of rational participation in the development of solutions which will be in the good of society, as well as protecting the age-old right of man to freely investigate the world in which he lives.

(The next three papers by Rankin, Keyes, and Clopton are for the negative of the question; Should Physiology Training be Divorced from the Medical Curriculum?)

BOTH MEDICAL AND GRADUATE STUDENTS BENEFIT FROM THE INTERCHANGE

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I appreciate your asking for this view from the other side of the

generation gap, but as you have asked, I must urge you to exercise tolerance should these views differ materially from those of the establishment. By establishment, I mean members of this Society.

First, to avoid tilting at windmills, let us establish that we have a subject, that is, is physiological education married to medicine? I am sure that there are facts and figures expressing the view of the Society on this point, but I have applied a simpler criterion. I examined the last issues of the four journals of this Society and found that 84% of the articles came from medical schools or medical centers. Therefore you, or to be more accurate, you who are doing the work, are married to medicine. Having ascertained where you are, the question arises should you teach physiology? I shall consider first the teaching of medical students. In my opinion if M.D.s teach medical physiology the end product is a technician. If the M.D. is to be considered a professional man then he should be taught by professional men and you are the professionals in physiology. I think therefore that you should teach medical students and of course, you do.

You are in medical schools, teach medical students, therefore the question proposed reduces to this: should you train your graduate students in what you do. There are several arguments that persuade me that we should be taught in the environment in which we will work. These are as follows:

1. It is difficult to teach something you have never experienced. To teach an effective course in medical physiology, it would be beneficial to have experienced the course as a student.

2. More important we should experience the people. As a result perhaps of admissions policies or the training system as a whole, the medical student is not like other people. He is very intelligent but his approach to science is very utilitarian, as compared to physiologists who are more esoteric. The truth may very well be in between, but we must face facts as they are, and the pragmatism displayed by the medical student in his approach to science must be seen to be believed and is best seen and experienced as a fellow student.

3. A department obliged to teach medical physiology is, theoretically at least, obliged to consider the whole of physiology rather than focus a few specialties. I seriously believe that if medical physiology were not a part of the physiology department's responsibility, then the students in that department would be led to understand that the mammalian organism consists solely of some neurons served by a cardiovascular and respiratory system. The void below the diaphragm being largely ignored. It is my belief that the depth of field to which a physiology graduate is exposed would be seriously compromised if physiological education was divorced from medicine.

4. In close association with this point is the concept of reality as viewed by the physiologist and the clinician. Professionals as they are, esoteric as they are, physiologists tend to put on their blinkers and focus down on their own area so that the world becomes a frog skin or

the placenta becomes a set of equations. On the other hand, a clinician is concerned much more closely with the real world. To an obstetrician a placenta is a large mass of tissue, he holds in his hands several times a day. To such a man the calm statement "let us assume that the placenta consumes no oxygen" is faintly humorous, yet most physiological studies of this organ make this assumption. Where physiology is taught in a medical school, some of this gross reality is bound to infiltrate the cloistered halls of the physiology department to the great advantage of the recipients. To divorce physiological education from medicine is to divorce it from reality.

5. My final argument is on a more personal plane. I have been led to understand that in the past the relationship between M.D. and Ph.D. has not been conducive to useful cooperation between the two. In recent years this relationship seems to have improved although even now it is not what it might be. I submit that separating physiological education from medical schools would not improve the atmosphere of mutual respect that precludes cooperation between the M.D. and the Ph.D., further the proposed divorce may lead to a degeneration of the relationship which would be especially damaging in this era of sophisticated quantitation and instrumentation in research. In brief, the current marriage between physiological education and medicine permits the indigenous population of a medical school to see the physiologist as he would be:

1. A teacher.
2. A potential co-investigator with an ability to focus on aspects that are the specialty of his profession.
3. A reference source.

To summarize my arguments, training physiologists in a medical environment has the following advantages:

1. We experience the course for which we will ultimately be responsible.
2. We experience the type of people whom we will eventually help to train.
3. Our training is presented on the broader front covering the whole of physiology rather than a narrow range.
4. We are exposed to an essential element to reality to counteract our natural tendency to migrate towards the trivial.
5. Our mutual relationship with medical personnel is improved.
6. By our presence we advertise ourself as useful and productive members of the biomedical community.

THERE ARE PRACTICAL REASONS FOR CONTINUING THE ASSOCIATION

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I am speaking against the resolution for the following reasons:

To begin with, an individual who has no desire to be involved with

medical education in his graduate training or his teaching activities has more than ample opportunity to obtain training in a non-medical environment. I am referring to those universities and colleges where advanced degrees in life sciences are offered in non-professional schools. An individual can obtain advanced training in general and comparative physiology, plant physiology, biophysics, bioengineering, and others, to name just a few. Thus since there are alternatives available for graduate training in physiology, the resolution is unnecessary.

However, the bulk of the research in mammalian physiology is carried out in medical institutions. The individual who wishes to study mammalian function will probably want to take his graduate training at a medical school rather than a non-medical institution. Furthermore, many physiology graduate students and professional physiologists are interested in human and mammalian physiology as it applies to medicine. These individuals will be interested in being associated with a medical college and medical education. It seems to me that these people should not be denied the opportunity to receive their training in that environment which is most closely related to their interests. If graduate training in physiology were divorced from medical education, the graduate students would be deprived of this opportunity.

What the question really boils down to is this: Should the physiology graduate student take any of his training with medical students as a part of the medical curriculum, or should he have a separate and presumably more rigorous, more concentrated schooling? It has been argued that the general course in human physiology offered as a part of the medical curriculum does not have sufficient depth for graduate students and is therefore unsuitable for their needs. I should like to take exception to this argument. A first course in physiology should serve as a survey of the field. It should provide the beginning framework upon which future depth of understanding will be built. It is far too easy to lose perspective in the forest of physiology because of the masses of trees known as minutiae. More understanding and depth can easily be obtained in any specific area with reading and conferences with individual professors. In addition, this survey course will probably be one of the last opportunities for the graduate trainee to have an overview of the discipline of physiology.

However, let's assume for the moment that the divorce were in fact carried out and that graduate training in physiology, even in the beginning courses, were separate and distinct from the medical curriculum. What might be the consequences of such a separation? There are several, of course, but I should like to focus our attention on one that I consider of utmost importance to both physiology and medicine. Such an arrangement would result in essentially no interaction between the medical students, their educational curriculum, and the graduate trainee. The graduate student would be as isolated from the medical environment as he would be if he were at an institution without a medical education program. It is quite analogous to the situation that exists at the undergraduate level where a science major has a completely separate program of study from that of the student who majors in one of the humanities. The only point they have in common is their physical surroundings. Would such a completely separate program really fulfill all the needs of the graduate trainee

in physiology? I think not. Because there would be no interchange between the two programs, there would be no opportunity for the graduate trainee to gain insight into the informational and attitudinal needs of the medical students. As his training progressed the graduate student would become less and less involved in those topics of physiology that would be of mutual interest and usefulness to both physician and physiologist. When the graduate student completed his training and was ready to begin teaching medical students he would have essentially no knowledge of the topics that would be appropriate to the needs of the student of medicine.

This problem of selection of appropriate material for medical student courses in the basic sciences is already a hot issue between clinical and basic science departments. Many clinicians are stating publicly that the teaching of physiology to medical students should be left to members of the departments of surgery and medicine, because they believe they know better than professional physiologists which aspects of physiology should be taught to medical students. I should like to refute this argument with a quote from the past-president's address to the APS given by John Brookhart:

"I think the needs of the young physician for a foundation upon which he can build in the future can be defined better by us as physiologists looking ahead to the physiology of tomorrow than they can be by internists, surgeons, and pediatricians looking back on the physiology of the past and relating this to their past experiences. Unless we give some recognition to the existence of this problem, I anticipate that this prerogative will be taken away from us and that physiology as a discipline will be diminished in importance."

In order to make the proper selection of material from the entire discipline of physiology appropriate to the needs of medical students, the graduate trainee should receive at least a portion of his training in a medically oriented environment. Thus a major factor in the education and training of a physiologist who contemplates teaching in a medical school should be interaction with medical students and educators in course work in both the lecture and laboratory sessions.

I have had the opportunity to experience graduate training in both medical and non-medical environments. I have observed that the emphasis in teaching and research in a non-medical environment tends to be channeled into those topics that have little relevance to medicine. I am not saying that these topics are irrelevant to science or human knowledge, only that they are not appropriate to medical education.

In summary, I have tried to make three points:

1. The resolution is really unnecessary since the opportunities for physiology graduate training independent of medical education already exist.
2. The resolution would actually deprive some individuals from studying physiology in a medical environment unless they became medical students.
3. Medical education itself would be the lesser, because those in-

dividuals assigned the teaching of physiology would not be adequately prepared to handle their assigned responsibility.

THE GOALS OF MEDICINE AND PHYSIOLOGY ARE SYNERGISTIC

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The goals of medicine and physiology are different, but the goals of medical and physiological education are people. It is their nature that is the true subject of the resolution. Dissatisfactions on the part of those trained and those doing the training are the real motivations for any changes that might be made in medical and physiological training. I don't argue for the status quo, because I believe there are valid reasons for a change, but to implement a complete separation of physiology training from the medical curriculum is, I feel, to attack the problem with a meat cleaver when some deft plastic surgery is called for.

I can not accept a planned separation in the physiological training of graduate and medical students for two reasons. Physiology benefits from graduate training that is partially concerned with medical problems, and both physiology and medicine benefit when "academic" training in physiology is available to medical students. I would like to expand on this second point with two considerations. First, the physiologist has more to offer the medical student than a review of human physiology in preparation for pathology. Personal contact with the methods and viewpoints of physiology benefits the medical student by helping him put limits of confidence on physiological and clinical knowledge. Secondly, medical education has a significant effect on the quality of a large amount of physiological research. I don't think physiologists can ignore the opportunity to affect the quality of this research. Both of these considerations indicate interactions in medical and graduate training in physiology.

The adequacy of medical education bears on the first consideration. I believe a significant dissatisfaction exists inside and outside the medical profession over many medical training programs. It is well expressed by two M.D.'s both concerned with medical education. The first, Dr. J. C. Whitehorn (1) has said: "The educational programs generally experienced by the physicians of the past few generations have tended to inculcate an expectation of certainty of knowledge and a phobic aversion for and intolerance of uncertainty. . . . the worst offenders have been teachers of science." He goes on to point out that scientific knowledge is often presented as a group of facts, not as a viewpoint based on lines of evidence and subject to change. I feel this is an indictment that should and has come from students and teachers in physiology. It has and must continue to evoke changes in physiological training, whether allied with medical education or not. It does not argue for a separation of training. It implies that as physiologists we have, at times, presented physiology as more a source of textbooks for the medical student than as an evolving science of biological systems. The medical student certainly needs a thorough foundation in body systems, but physiology has more to offer him.

Dr. E. C. Rossi of Marquette School of Medicine argues for the blend

of "physician-scientist" as the true goal of medical education(2). He says that "until clinical teaching becomes less authoritarian, the best place for students to learn human values in medicine is in the research laboratory... Here there is no place for personal or group authority. Statements must be supported by data... Research experience provides the highly humanizing experience of proving to the student that he (and others) can be wrong." I believe that the view of medical education as primarily infusing a collection of knowledge into the medical student is responsible for defects in clinical training and, because of its frequent association, physiological training. The physiologist should be skilled in the creative approach to problems, and to the degree the physician encounters novelty in every patient, he also should possess the same skills. This strongly argues for a reappraisal of present training in physiology, but not for a separation from the medical curriculum. In fact, it indicates the need for, even an increase in the overlaps in medical and physiological curricula.

The other consideration concerns the crossover from clinical training to medical research. In today's society where money is often readily available for those engaged in medical research, the M.D. researcher is common. Many full-time workers in physiology have medical educations. This is reflected, to some exaggeration, by the statistic that 49% of the regular membership of the APS have medical degrees with 83% devoting more than a quarter of their time to research (3). The situation is not likely to reverse itself, for when questioned on their career plans about one-third of all medical students indicated an interest in an academic-scientific career (4). To remove contacts with the physiologist early in their training, hinders these medical students in deciding their role in research. If they choose to devote all or part of their time to research, the physiologist is best suited to guide their training in these areas. In the face of this, the question of a separation of medical and physiological curricula becomes central to the quality of a large segment of future research in physiology. As long as research plays a major role in the functions of many medically trained personnel, they should have an exposure to productive research procedures, and have the option of pursuing their research training as far as their ability, interests, and work demand. The motives of the resolution disregard this and would suggest only the academically trained physiologist is responsible for advancing knowledge in physiology. I contend the goals of physiology in reality are significantly affected by what goes on in the medical curriculum. In summary, I have given two reasons why I think the physiologist should contribute his knowledge of research to medical training: 1) to contribute importantly to the scope of clinical training, and 2) to further the goals of physiology.

The reasons for changes in physiological training remain. Perhaps the association with medical education helps to ease the teaching of physiology into a didactic preaching of facts. Whatever the cause physiology students as well as medical students suffer. The result is a knowledgeable graduate student who doesn't know how to begin his thesis research, or the medical student who is a compendium of truths, until after the exam. Claude Bernard (5) said that, "The unique and fundamental rule of scientific investigation is reduced to doubt." That expresses what the physiologist

as a scientist-teacher must do: indicate the appropriate doubt to associate with a physiological finding. For the graduate-student and medical-student researcher, he must also provide the techniques for resolving this doubt in the lab, in the library, or in the clinic. The physiologist has knowledge to offer, certainly, but as a scientist-teacher his talent lies in nurturing an inquiring attitude, resolving problems, developing concepts, evaluating knowledge. He is able as no one else to attach a rating of confidence to what he passes on to others.

I feel these considerations indicate a clear justification for overlap in medical and graduate education. The burden is on the teacher of physiology not to compromise his role in the interaction. If he fulfills this role, his role as a scientist, the goals of both medicine and physiology will be approached. These goals may be said to be different, but they can be synergistic in their achievement through a considered educational interaction.

REFERENCES

1. Whitehorn, J. C. Education for uncertainty. *Perspectives in Biology and Medicine*. 6: 277-279, 1963.
2. Rossi, E. C. Why is the medical profession estimable in the individual but not in the generality. *Perspectives in Biology and Medicine*. 8: 230-240, 1965.
3. Comparative statistics of APS regular members. *The Physiologist*, 11: 24-25, 1968.
4. Brown, J. H. U. Behavioral sciences and the medical school. *Science*, 163: 964-967, 1969.
5. Hoff, H. E., et al. Claude Bernard on experimental medicine - some unpublished notes. *Perspectives in Biology and Medicine*. 8: 30-49, 1964.

SUMMARY FOR THE AFFIRMATIVE

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The problem for debate is an administrative question: In order to meet their teaching responsibilities, where might physiologists best be situated, in a medical school or in a graduate school? Let us recognize at the outset that the administrator does not have the power to make changes, but only to make plans and decisions. The changes take place owing to social developments largely beyond administrative control, and the administrator merely predicts the direction and timing of these developments and responds accordingly with an administration plan of action. I conclude, therefore, that the task for each of us is to predict three developments for the next 30 years - the development of physiology, that of the university, and that of medical education - and then to propose some realistic administrative responses.

Let us begin with the first question; Where is Physiology headed? Physiology can be defined very simply as the study of biological machines. Over the past century it has enjoyed such phenomenal success that there are only two remaining types of biological machines that are poorly understood. These are the brain and the cell.

From this point of view the future development of physiology can be expected to follow two dominant lines. One of these is the study of interactions among aggregates of neurons. The current study of small and isolated groups of neurons will yield to the analysis of ever more complex networks and populations of neurons, and will eventually provide the basis for rational analysis of the mechanisms of animal behavior. Cell physiology is concerned with molecular aggregates within cells, which form ever more complex assemblies of macromolecules. This study at present revolves around mechanisms that control macromolecular construction and energy transduction. In the future it will lead to the analysis of the mechanisms of cell maintenance and repair, of cell development and growth, and of organogenesis.

At this level of understanding the lines of research in cell physiology and neurophysiology will begin to converge. Some of the ultimate questions in biology will then be approached concerning the mechanisms controlling the development of form and function of the human body, and the cellular mechanisms underlying the processes of learning.

In order to create this new level of understanding physiologists will require the kind of environment that is best offered in our major universities. This is only in small part because of the presence of faculty colleagues in physics, chemistry, and mathematics, and in other biological sciences, and our younger colleagues, that is, our graduate students and post-doctoral fellows. In the larger part it is because the healthy university offers the priceless opportunity for leisure. I do not mean by this the summer vacation or semester break, but rather the encouragement and subsidy for long hours and weeks of uninterrupted meditation in the laboratory and library. According to Aristotle: "As play, and with it rest, are for the sake of work, so work, in turn, is for the sake of leisure".

As an apostate M.D. I can attest to the agnosia in the trained medical mind for leisure in this sense. Most M.D.'s tend to identify leisure with golf and sailing and consider it to be a self-indulgent and slightly immoral activity for any one who has not yet passed his Boards. It is quite true that physiologists often appear to their clinical colleagues to have time on their hands, but it is my impression that in the competition between abstract and utilitarian values, physiologists tend too easily to be caught up in the frenetic round of medical activities, owing to the pervasive demand in the medical environment for service. Any one who has attempted simultaneously to meet commitments both in research and in patient care will apprehend this sense of urgency directed away from leisure. Yet without leisure physiologists are unlikely to solve or even to conceive their major problems.

Physiologists in a medical setting tend to take up problems arising

in and defined by disease processes. Such work, though limited in scope, is often of great practical value and may, as in the case of steroid hormones, yield important insights into some basic mechanisms. My point is that physiologists holding the Ph.D. in physiology are well qualified for such work, but that physiologists holding the M.D. are rather less well qualified for the working of less tightly structured and more basic problems. Unless academic physiologists construct a leisure environment for their activities, they will not realize their full potential. Realizing this, many physiologists will re-locate their laboratories in universities.

For the second question, where is the university headed, the answer is rather uncertain. It is difficult to maintain the activity of leisure under the pressures of student militancy, political interference, and the demands for faculty administrative service. Potentially the most damaging current trend is toward the bureaucratization of university teaching and research processes, in which numerical estimates of such items as percent of effort, contact-hours per week, number of lectures per quarter, faculty productivity in terms of M.A.'s and Ph.D.'s per capita per year, and so forth, become the basis not merely for provisional budget allocations but for the evaluation of faculty performance. It is bad enough to have one's papers counted each year, but intolerable to be asked how many hours it took to write them. But the costs of medical schools have risen many times over the increase in general population in the past three decades, far more than the costs of letters and science colleges. In the next three decades they will be subject even more to cost control and the time-and-motion studies of bureaucratic numerologists. Moreover it is reasonable to expect that faculties will only maintain the academic environment required for unstructured teaching and research, if they refuse to trade their independence for high levels of personal and research support. It is uncertain whether physiologists will conclude that they can afford their independence, and still less so for medical faculties. In either case the university offers the better hope for adequate leisure.

It is my prediction that the center of gravity for physiology as a discipline will lie wherever the most basic and exciting new work is being done. If this in the universities, then perhaps paradoxically, physiologists will find there greatly expanded areas for effective service, in helping their non-medical colleagues to deal with such important social problems as population control, environmental pollution, the stresses of urban living, and so forth. Medical schools simply are not structured to offer this broad sweep of opportunities for participation by physiologists in team research on solutions to these problems.

In answer to the third question, medical education is headed in the direction where physiology will be even more unwelcome than it has been these past two decades. As a former medical student I can well remember the strong resentment felt by clinical faculties and by almost all medical students about the kind of physiology being taught and the timing of it. As many of you will recall, our former colleague August Krogh wrote, that having devoted the major portion of his life to teaching physiology to medical students, he would like at some time before

his retirement once to teaching physiology to a group of students who were interested in it (2). Indeed the only props now holding physiology in the first year of the medical curriculum are the Flexner Report and Part I of National Boards. We all know that the ability of students to pass a course in physiology has little correlation with the ability to practice medicine, and that it is absurdly anachronistic for the anatomist, the biochemist and the physiologist to stand like Cerberus guarding the gates to the clinical Elysium.

Moreover, the practice of internal medicine in the most literal sense is applied physiology, because, in the words of Evans (1), "the nosology of medicine has moved from syndrome diagnosis to more explicit description of patho-physiological states." These states can best be taught, and therefore will be taught, by those who treat them. In point of fact most physiologists have for years been learning their mammalian physiology from clinicians, in as much as many of the better monographs on organ systems have been written by clinicians.

Even more compelling is the shift of medical attention away from the basic sciences to problems in medical sociology and economics. As Willard Rappleye (2) wrote: "Medicine today is as much a social as it is a biological science. Our responsibilities are not for the individual patients alone; they are responsibilities related to the whole field of medical care - industrial medicine, hospital insurance and various kinds of plans for medical services. We are concerned with providing adequate medical care to the entire population of the country. . . ." Unfortunately these words were written in 1947, and medical schools have made only the most marginal adaptations to their message in the succeeding two decades. But there are strong forces currently at work to initiate some long-needed changes in this conservative and self-sustaining structure. One of these is student protest. Medical students have known for years that medical education was lagging far behind the society it was constructed to serve. The student of the "silent generation" passively if resentfully accepted this, but when the current generation of undergraduates from Berkeley, Columbia and other turbulent campuses get to medical school, they will not remain silent, and the medical faculties will not be able to ignore them. A second force for change is the public demand for more medical care at more reasonable cost. The public is paying for medical education, and it is a basic premise in American society that he who pays the piper calls the tune.

The future provision of effective medical care will require an enormous increase in the health-related bureaucracy of this nation. Many of the most important decisions about such care will be made on behalf of the individual physician, unless he is properly trained to plan for them. An effective medical education for this kind of decision-making will require that basic medicine, surgery and psychiatry occupy the first two years of medical school and that the second two years continue these with additional courses in areas such as priorities in patient care; priorities in medical research; the organization of paramedical personnel; the use of computer systems in recording, diagnosis and therapy; the use of community hospitals in psychiatry; dietary management of the pre-school ghetto child; and so forth.

These new activities will require time and facilities for instruction. Medical education slowly but inevitably adapts to technological advance; the replacement of surgical anatomy by the pharmacology of antibiotics is a classic example. By extrapolation basic physiology will sooner or later become a pre-requisite for medical admission as is now the case with organic chemistry. There are many signs of the move in this direction already, such as the first year program in the new medical school at San Diego. It is essentially a one year program in basic biology, which can easily become the last year of undergraduate pre-medical education, as the pressure builds for additional training in the new medicine at the other end of the curriculum. Alternatively students having done this work already will be admitted directly to the second year. On a nation-wide scale this shift will require that many physiologists emigrate to the undergraduate universities, either in a Diaspora into departments of biology or by transfer of whole departments of physiology into colleges of letters and science.

Here we come full circle, because, not only for research but for the sake of teaching, physiology will be established in many universities in the undergraduate curriculum. The field has already reached a high level of sophistication and now requires that kind of definition which comes best, when it offers a basic course, year in and year out, for students interested in acquiring a disciplined point of view about a major entity in our world. Biological machines are such an entity. The discipline will become widely available not only to future medical students, but to future nurses, technicians, optometrists, therapists, criminologists, scientists of many kinds, and especially to future engineers, who have an urgent need to understand the living systems of our world, before they inadvertently destroy them. In this manner physiology will be defined on its own terms and not as a stepping stone narrowly directed toward medical practice.

Please note that I am not predicting that medical schools will become divorced from universities, but that physiology will yield place to the new kind of university connection that medical education desperately needs. To quote Evans again, "The elements essential for medicine's continued growth can be found only in the university, provided the university... sees in medicine unique opportunities to observe and study certain crucial aspects of the nature and behavior of man over and above the mere teaching of skills and techniques of a group of practicing professions."

In regard to the problem of an administrative plan, I wish to conclude with two points. First, I say to Physiology: "When your divorce is granted, marry Anatomy. You can have exotic affairs with psychology, biochemistry, mathematics, and even bioengineering, but unless you enter a contract with the stodgy character down the hall, who won't even come to Federation Meetings, you will not have sturdy offspring". The experience at Berkeley has shown that it is virtually impossible to teach physiology effectively at the undergraduate level without the active collaboration of the professional anatomist. The students quite literally do not know what the physiologist is talking about. Any planned move of physiology and anatomy from the medical school to letters and science must be a combined transfer. This point can easily be overlooked because of

the long stand-off between these two faculties, in which each has taken the other too much for granted.

The second point is that letters and science departments typically have a useful lifetime of about 15 years. The faculty and their courses and research then tend to become dogmatic and over-specialized. The institution of tenure, which was designed to protect political nonconformance (and is doing that poorly), provides a very effective shield for technological obsolescence. University presidents know this and know also that the best way to revitalize a sagging department is to enlarge it with new men and to give it a new mission. Over the past two decades universities have introduced numerous splinter departments in biophysics, cell biology, molecular biology, and most recently neurobiology. Such small and limited-purpose units are especially prone to rapid senescence. I suggest that those of you here between the ages of 25 and 40, in the next 15 years when many of you will be called upon to introduce the teaching of physiology and anatomy at the undergraduate level, choose as your administrative vehicle an aging department of biophysics, cell biology, molecular biology or neurobiology. Broaden its focus, create its new courses, and re-name it the Department of Physiology.

REFERENCES

1. Evans, Lester J. The Crisis in Medical Education. Ann Arbor: Univ. of Michigan Press, 1964.
2. Trends in Medical Education. Institute on Medical Education. New York: Ed. by Mahlon, 1947.

SUMMARY FOR THE NEGATIVE

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Although this debate has been formulated in terms of the divorce of physiology training from the medical curriculum, and is intended to focus on the value, or otherwise, of training graduate students of physiology, I believe that it is impossible to keep the subject constrained within these narrow limits. To me it is axiomatic that no healthy academic department can survive without a healthy graduate program of its own. In the practical politics of today's situation the divorce of graduate training in physiology from the medical curriculum would inevitably mean its eventual divorce from the medical faculty, and the eventual disappearance of physiology as an academic discipline from medical schools. Furthermore, we cannot blind ourselves today to the fact that precisely that is being discussed seriously as a matter of policy at many medical schools.

In my view the speakers for this motion have made many cogent points which cannot be disputed as defects which exist in many physiology departments today. However it is my contention that these defects need not exist if only medical faculties can be persuaded of the real importance to them of physiology and other basic sciences. The defects we see are, in other words, of administrative origin rather

than matters of unalterable principle.

The proposal entertained in this debate is an old one, but the very fact that we are considering it today suggests that the marriage between medicine and physiology is indeed in some danger. As Dr. Jenerek has reminded us so fully, the broad scope of physiology is itself a serious barrier to fruitful discussion of the problem. There are very few academic disciplines which are closely comparable so that the application of general principles and the use of analogy is fraught with pitfalls.

As long ago as 1904 the eminent physiologist W. H. Howell argued that physiology should remove itself from the medical faculty in the main. His main reason was that the requirements for teaching medical students were too limited and would constrict the healthy development of the basic sciences related to medicine. As Howell put it, "there must be an outlying division of workers who will keep the subject in touch with practical medicine, though the flower of the army, the imperial guard, is busy elsewhere!"

The debate has continued forcefully for nearly three quarters of a century. Today we have heard many old grievances, and the picture often has been of physiology in the role of insulted and neglected wife claiming her rights of release from an insensitive, overbearing and crude husband. For years she has been denied recognition as a fully mature person, treated as a slave, given miserable quarters and a miserly fraction of the pay packet! She knows she is a queen and that she will only receive her due by obtaining a divorce and flying to the welcoming arms of that much more cultured gentleman, the University Faculty of Science.

The defendant in this case tends to complain that the wife is a somewhat shrewish, snobbish lady, over-concerned with her own activities and refinements and unresponsive to her husband's real needs, particularly in the education of medical students. She is accused of a considerable lack of balance and narrow-minded self interest. When he comes in from the garden hot from digging and looking for a mug of beer and a robust sandwich, she provides him with an expensive Moselle and asperges vinaigrette. When other wives turn up to a barbecue in blue jeans and blouses, she insists on coming in full evening dress bedecked in all her jewels. Even worse, she won't recognize her age. When other women are recognizing that the glories of youth are past, she insists on putting on ever thicker rouge and brighter lipstick in a vain and foolish attempt to outshine younger and more beautiful women, such as Mrs. Molecular Biology, Mrs. Bioengineering, and even the once flashy but now ever-so-mature Mrs. Biochemistry. She is so jealous of Mrs. Anatomy's recent face-lift that she keeps badgering her husband for an electron microscope of her own so she can get a face lift too! On cross-examination the husband is likely to admit that sometimes he is tempted to get rid of the whole harem. He is quite sure that his own housekeeping is just as efficient as any provided by his basic science wives. With a beautiful house and a fine place in society he sometimes wonders whether the advantages of women in the house are all that they are cracked up to be.

When we turn to the wife's pleas we find a situation which is all too familiar in the divorce court. She admits she is extravagant in her dress and her taste in cooking, but this is all she has left to do, since her natural charms and reasonable pleadings seem to have had so little effect upon her husband for so long. Her husband forgets that he had a very poor place in society before she and the other wives in the harem came along. The house was damp and drafty, and had no curtains, and the garden was full of weeds. Thanks to the efforts of her and the other girls the house is now light and airy, is centrally heated, and the garden is full of beautiful flowers. Her husband's lack of appreciation is perhaps the most galling when it shows itself in the form of public boasting about the beauties of his estate for which she and the other girls are given no credit at all. Only the other day she discovered that one of her husband's business friends had no idea that she and the girls had made all these domestic improvements, and was quite unaware that nearly all of the Nobel Prizes in Domestic Arts and Sciences for the past 10 years had been won by them and not by her husband. He had always been stingy with money and gave the girls the poorest rooms in the house, but even worse, it was he who took nearly all the extra money that was donated by wealthy visitors who had been unusually impressed by the house and its gardens.

What really worried her now was that she knew that her husband was having difficulties in his job and getting a bad name in the neighborhood because of his failure to cultivate the meadows beyond the garden which were rapidly becoming a public scandal. His only reaction to rising public criticism was to try and get his wives to do more work without giving them any extra help. She and the other girls had managed to keep a decent household up 'till now because her academic mother had given them money in a bank account to which her husband fortunately had no access. This help was now gravely jeopardized since some of the neighbors, who seemed unaware that the husband was even married, had persuaded her aunt that the neglected fields would only be cultivated if she gave him money for more tractors and agricultural machinery. The situation is going from bad to worse and before the whole household collapses in ruin she is determined to seek her freedom at last.

As in any divorce, however, there are three parties to the matter and not two. As a physiologist who has often reflected on the truth of many of the complaints we have heard today, I can perhaps be allowed to emphasize that this third party is society or mankind at large, and that in a divorce the plaintiff wife, be she ever so virtuous, is always in danger of appearing to be a bit of a shrew to this third party. My position is that the marriage of physiology and the medical faculty is indeed in grave shape but that society must demand that the marriage be saved. The difficulties of this marriage are due to causes far wider and deeper than is suspected by the couple involved. My main reason for this suggestion is not that the wife can expect to be very much better off without a heavy course of marriage counseling - mainly, but not solely, directed at the husband - but that if a divorce is granted the husband will go to pot! This will be contrary to society's best interest. In passing I would mention that the case for supposing that the wife has an exaggerated idea of the devotion of her proposed second husband is certainly an

arguable one which she would be well advised to reflect upon. This argument, however, is not as important as the case for society's interest in the preservation of this marriage.

Let us now examine society's view of the matter. I believe that society requires its health to be the concern of a profession rather than of a trade. However we look at it, health is a matter which affects every level of an individual's or a society's life and being. Its professional guardians must therefore be educated to a level of proficiency, and above all to an attitude of mind, which allows, at least potentially an understanding, and appreciation of the effects of their activities on every level of an individual or society. This is what we mean by the distinction between a profession and a trade. A profession is effectively granted a charter by society and not just a license. It is a corollary of the granting of such a charter that a profession is responsible for sufficient research and education to maintain and advance itself to the fullest possible extent so as to fulfill its duty to society. Having provided the power and the privileges of self-determination to a profession, society expects the professional body so honored to fulfill its duty in return.

I believe that society can reasonably complain, and indeed shows many signs of complaining already, that medicine as a whole has fallen far short of this ideal in the last thirty years or so. Thus although the provision of certain types of remedial treatment has improved enormously during this period we are presently faced with an increasing barrage of public complaint which is by no means wholly due to unreasonable demands or expectations. The best American medicine is undoubtedly the best or equal to the best in the world. Nearly all of it, however, is far too expensive, and much of it confined to limited geographical regions and to a limited fraction of the population. The profession has continually failed to educate enough doctors to meet the demand so that approximately 20% of medical practitioners in the U. S. A. were trained abroad and even this addition to the ranks has not enabled the provision of medical services on a wide enough scale.

Nor is this all. It is now well recognized in business circles that hospital management is one of the most inefficient and backward areas of management in this country. The public is becoming increasingly aware that most of the improvements in public health and life expectancy over the last 50 years are due more to the efforts of pharmaceutical chemists and sanitary engineers than to the medical profession itself. The AMA is spoken of in some circles in terms which used to be reserved for the Teamsters Union, and Dr. Kildare is having a hard time keeping up with anti-M. D. jokes in other T. V. programs.

Perhaps the most serious indication of the declining position of medicine in society today is the minuscule contribution of doctors to discussion and legislation on some of the most pressing socio-biological issues of the last 10 years. By and large doctors seem to discuss salaries, the dangers of socialized medicine, golf or technicalities during their leisure hours and it is the laymen, churchmen, or other academics who discuss the population problem, pollution, child psychology, organ transplantation, malnutrition, and "genetic engineering." Doctors are far from being

pace-setters in these or a dozen other important fields in which health or human biology are at issue.

In summary, society today shows evidence of considerable dissatisfaction with the medical profession and appears to have at least partly reasonable grounds for this dissatisfaction. The situation seems to be remarkably parallel in practically all the industrially well-developed countries of the world. Not unexpectedly the governments of all these countries are in various stages of losing patience with the medical profession and of seeking to establish means for the provision of adequate health care outside the existing framework of private or group medical practice. In some countries this has gone as far as the establishment of fully nationalized medical services.

It is easy to see that in this situation society looks on the marital problems under debate today from a far wider point of view than that of the marriage partners themselves. Many of the arguments we have heard today resemble the petty domestic details which are often so tiresome in divorce proceedings. To return to our metaphor, society's main concern today is whether the erring husband should be rehabilitated by induction into the military services or whether good psychotherapy will make him into a sufficiently reliable person to be trusted as a private citizen. If society decides upon the former course the question of whether his wife should be allowed to live in married quarters on the base is of strictly secondary significance.

My own preference is for the strong belief in the United States that the system of free enterprise should be used as a social force whenever possible. I am therefore prejudiced in the direction of maintaining the independence of the medical profession if it is socially and politically possible to do so. I believe that the chances of doing this depend critically upon the preservation, and hence the improvement, of this somewhat rocky marriage and that the retention of physiology and other basic biological sciences within the medical faculty is probably the single most critical factor in determining whether we can succeed or not.

I would now like to summarize some of the reasons supporting my argument. In making such a large claim for the value of the basic sciences to the medical faculty and thus to the practice of medicine as a whole, my remarks should not be confined to the role of physiology. Because of its breadth and almost undefinable scope, physiology is probably the most valuable single basic science for a medical faculty, but practically everything said below would apply to any of the established disciplines of the "pre-clinical" field of education and research in medicine. It is probably instructive to start by dealing with some of the general statements which are commonly made by the protagonists to arguments on this topic. Most arguments of this sort tend to be confused by matters of academic prestige and by a lack of genuine understanding of certain basic principles which are currently unfashionable.

The first thing required for a healthy medical faculty is to recognize that the basic science departments are not just "service" departments to the rest of the school and must be allowed a vigorous life of their own.

The advance of the medical specialities would be seriously hampered without vigorous programs for the post-graduate training of interns and residents. General practice will flounder or become ossified without vigorous programs of refresher courses and further training. In exactly the same way a department of basic sciences must be given the opportunity and facilities to conduct a vigorous and healthy program of graduate training in its own discipline. Such a viewpoint is very rarely heard in the councils and committees of the majority of medical schools. When it is heard it often appears to be more a question of lip service than of genuine concerns. More often we hear that the basic sciences should remember that they are not in a medical school to teach graduate students but to teach doctors and that the main job of a medical school is to "train doctors." Such statements are true enough but do not cover the whole problem. They neglect the fact that a department representing any discipline of major importance must be in a position to reproduce itself by a strong graduate program; and fail to consider what is meant by a "doctor." Despite all claims to the contrary, training received by medical students in the clinical departments of the majority of medical schools is a technical training provided by a mixture of apprenticeship and more or less dogmatic presentation of "facts" and techniques. As with any complex modern technology this vocational approach is probably necessary for the large majority of students and should not be criticized for these characteristics. Nor is this view of the matter concerned with the actual relevance or quality of the content of such a curriculum. It is simply a question of a different approach.

The basic sciences are required in the medical faculty for the provision of the conceptual ground work upon which subsequent clinical training must be founded. Precisely because this training is not vocational for medical students, a method of education can be adopted which is closer to that found in other graduate schools in universities. It is quite right for the clinical departments to concentrate upon a vocational type of training for the majority of their students, but this will only be successful in providing doctors who are truly capable of forming a profession rather than a trade if it is superimposed upon a genuinely non-vocational presentation of the basic sciences. If, however, the basic sciences are asked or forced to train medical students in a vocational manner the whole of the training of a medical student will become vocational and the majority of the student body will be fitted only for the practice of a trade.

On the other hand, there is a genuine basis for some of the clinicians' complaints about the basic sciences in general and physiology in particular. Both parties to this argument usually miss the point by confusion of essentially different purposes and activities in education. Both frequently end up in a position of people living in glass houses throwing stones. For example, the physiologist is anxious to teach medical students a considerable amount of material dealing with excitable tissues. In perfectly sensible academic fashion he talks a lot about the nerves of the invertebrates and lower vertebrates because these are the objects from which the experimental evidence supporting his theoretical picture have been drawn and because the history of work on these objects constitutes a large part of the history of this part of his discipline. It is a perfectly

legitimate exercise to convey to students a "feel" for their discipline by tracing its professional and conceptual history in this way. Often however, the manner of doing this neglects another important factor in education namely the motivation of the student. It is right to demand of the physiologist teaching medical students that he make a special effort to find examples of medical interest which will be more likely to secure the medical student's interest, and that he reduce his dependence upon the lower forms of life so that he uses them to give an occasionally exciting glimpse of the background of his discipline rather than a complete and thorough survey which would be appropriate for a graduate student. To suggest however that he should forego all mention of squids, crabs, and frogs is a destructive and phillistine example of the "all or none" principle which physiologists and other basic scientists have every right to resist.

To any medically trained physiologist, however, it is strange how often such complaints of irrelevance are raised by clinicians who appear to be completely unaware of the long-standing criticism of medical schools that their concentration upon specialized and difficult problems of disease is highly inappropriate for the vast majority of doctors! Such criticisms have been made to me by gynecologists who have failed to give their students any account of the complications and consequences of the use of contraceptives, and of the consequences of the many variations of human sexual behavior in and out of marriage, or of the handling of the problems of the menopause: by physicians who have spent hours with their students on the use of the artificial kidney and the identification of rare amino-acidurias but who have failed to give more than passing reference to the management of cystitis and acute pyelitis: by neurologists who have spent hours on the detailed role of the substantia nigra in Parkinson's disease but have omitted to cover the management and diagnosis of disorders of sleep; and by ophthalmologists who have given an excellent account of the slit-lamp, but who have never demonstrated the technique and principles of removing a foreign body from the eye!

Another argument commonly heard today is that physiology is a dead science anyway. Critics of this sort are sometimes willing to admit that this is because it has done its job so well and has so effectively spawned a number of more modern daughters such as biochemistry, biophysics, and pharmacodynamics, but the practical consequences of this viewpoint in the medical school tend to be grave. This criticism is often coupled with the implication that the modern clinical department is normally so well staffed with research workers of high ability that these departments could easily provide all the teaching in basic sciences that would be necessary for medical students. I have now been in two medical schools in which at least one Chairman of a major clinical department and a number of Deans have in all seriousness proposed that the Physiology Department should be abolished for these reasons. Such criticisms seem to stem from an alarming mixture of blindness and arrogance. There are excellent physicists at the Bell Telephone Company, and many brilliant biochemists and physiologists in the laboratories of the pharmaceutical companies. Many of them run excellent training programs within those organizations. No one has ever been so foolish as to suggest that this means that universities should drop their departments in these areas.

The idea that physiology is dead has often been supported by other basic scientists in the biological field. It is a sad commentary upon present times that so many academic gentlemen should apparently suffer from the same compulsive desire to be fashionable at all costs that appears to be afflicting society at large.

One difficulty in countering such arguments is that with its very broad scope physiology has indeed been practiced by clinicians or others who were not administratively classified as physiologists. The works of Harvey (physician), Beaumont (general practitioner), Bowman (ophthalmologist), Blalock (surgeon), Wolff and Wolff (physician, psychologist), Hargitay and Kuhn (physical chemists), and of Penfield (neurosurgeon) spring immediately to mind as a very incomplete list. To my mind both physiologists and clinicians have been to blame in drawing false conclusions from this very real aspect of physiology.

The disagreements which have led to the divorce proposed in our debate today all too often result from the taking of sides on questions which have not two but many possible answers. Physiology probably has suffered more than other disciplines because it is difficult to match its huge scope with a coherent professional or departmental structure. Physiologists are not without blame for the situation we find ourselves in today. Most of them sided with departments of chemistry and of medicine in obstructing and deflecting the healthy growth of biochemistry in the 1920's in a thoroughly shameful manner. The biochemists were not only skillful and possessed of an immense and self-justifying field of endeavor, but, were also lucky in attracting industrial support because of the practical applications of their discipline outside medicine. To a lesser extent the same can be said of physiologists' attitudes toward pharmacology 20 years earlier and to biophysics and bioengineering 20 years later. These restrictive and conservative attitudes of physiologists were however aided and abetted by medical faculties who gave little encouragement to the possibilities of sensible and coherent expansion of physiology on a divisional basis.

If anything we could be working in medical schools for the expansion of their basic sciences as a nucleus of academic departments which will eventually include a wider range of disciplines than the traditional "pre-clinical sciences." Medical schools should take a leaf from the book of M. I. T. who long ago realized that engineers must be provided with both basic sciences and humanities in their education if they were to remain a profession worthy of the name.

I would like to believe that the best in medicine have always appreciated these basic considerations and that if physiologists can take a broader and more confident view of their future they can persuade the majority of their clinical colleagues to see the question in a balanced perspective. If, however, the current pressures to increase the number of medical students being trained and to improve medical services are allowed to override these considerations and to make the position of the majority of the departments of physiology even more tightly confined to the position of a vocational service department then physiology, whatever the difficulties, will have the responsibility as an academic discipline of

major importance to detach itself and enter the fold of the faculty of science in universities. The fact that our discipline is technically relevant to medicine is more of a hindrance than a help. This technical relevance is to my mind quite unimportant compared with its role in providing, with the other basic sciences, the essential academic leavening without which medicine will continue its current downward progress towards becoming a trade. Both parties to the squabble should attempt to rise above petty questions of academic prestige and politics and recognize that their social responsibility demands a more enlightened approach to their problems. The situation in my mind is depressing but not hopeless and society's demands should be met by vigorous marriage counseling to both sides rather than by granting a divorce.

REFERENCES

1. Howell, W.M. Congress of Arts and Sciences. 5: 434, 1906.
2. Flexner, A. Medical Education in the U.S.A. and Canada. Carnegie Foundation, 1910.

DISCUSSION

Haddy: Should physiology training be divorced from the medical curriculum? We have heard powerful arguments on both sides of the question. We now enter a thirty minute discussion period during which you on the floor can add your opinions or question the speakers. I would only remind the audience that today we are not so much concerned with the training of the medical student as we are with the training of the graduate student. This is a session on graduate education. Teaching of the medical student had its hearing last year.

Unidentified: Dr. Jenerick has reassured us that it is only rumored that physiology is not getting a fair share of the training grant funds. I have recently come across three facts - I believe they are facts - which I would like him to interpret for us in the sense of trying to dispel this rumor. The first fact is that the number of training grants in physiology from the National Institute of General Medical Sciences has fallen over the last five or six years to approximately half of the number in 1963. The second fact is that the number of training grant programs in biochemistry, which are in the same pool with physiology training grants, has increased markedly over the same time period. The third fact is that the number of programs in biomedical engineering, which admittedly is small compared to the numbers in the other two programs, also increased markedly over the past five or six years. Could you put these facts into a frame of reference in terms of your rumor.

Jenerick: It wasn't my rumor. I don't know who started it. I guess I cannot deny that these are facts. Now, what might they imply? Concerning the growth of the awards in bioengineering, clearly new disciplines continue to emerge and run the gauntlet of competition. There is no way to exclude these new disciplines. They may be at the expense of some of the older programs that don't continue to mature. The number

of physiology training grants is falling; that's a fact. There were a number of seed grants made earlier, when funds were relatively more abundant in relation to the number of applications, to departments attempting to organize themselves and start graduate programs under the conditions we have been discussing here - perhaps where physiology was just developing or where physiology was separated from its undergraduate base. As a consequence, when - and this is a fact - these applications were reviewed by physiologists sitting on the training panels, they simply were not recommended for continuation. That's a fact.

Mommaerts: I would like to express a few opinions on the side of the negative, which is not to be construed in any sense as being in the defense of the status quo. I would also like to greet my young colleagues. This is, I believe, the first time that this establishment has recognized their existence. Let's be very glad about this. While it is recognized that physiology has many objects - invertebrate, vertebrate and human - there seems to be a prejudice that human physiology is somehow not a pure science. I believe that it is not impure and that it is possible to have an academic group chiefly devoted to the study of animal, molecular, biophysical, comparative and human physiology, with a touch of the chemical, and that this is intellectually a most satisfactory enterprise and that it is technically feasible. If you don't believe me, come and look.

On two occasions, the criticism has been made that physiology is not very molecular. I do not consider this a reason to run away from contact with human physiology. On the contrary. And with respect to maintaining this contact, Howard Jenerick very beautifully indicated how thousands of us can serve and influence several millions very directly. But what disturbs me, looking at the other side of the generation gap, is that while there is a great concern with social values, social needs and social criticism, much of this seems to be in the nature of disruption, confrontation and indulgence. And when we ask them to do something responsible and practical, such as teaching nurses, they say it can't be done. I hope physiologists will not say it can't be done. But I will admit that physiology and medical education should be practiced on the university campus. The idea that medical schools should be built in great sociological centers stems from another era of transportation. We can no longer justify the building of medical centers in the large cities, though the medical student will indeed do well to receive clinical training in these areas. But medical schools, medical faculties and ivory towers should be in the university. I will also admit that there are likely to be changes in the pattern of medical education, very much along the lines described by my colleague, Dr. Freeman. Such changes will occur. They will change the pattern of medical education, but I hope to God they will not detach physiology from it because this would be very much akin to the effects of detaching the military from civilian influence. I hesitate to think what the medical profession would be like if detached from our civilizing and intellectualizing influence. It doesn't cost us anything and will greatly strengthen our position. I believe medicine is not complete without the science of physiology.

Freeman: I would like to make one comment in response to Dr. Mommaerts.

I fully agree that medicine should not ever become divorced from the university and that - I think this is an important point also raised by Dr. Bush - it is exceedingly important that medicine retain this contact with the university setting, in order that it not be reduced to the status of a trade. But I think that physiology is not the connection which will prevent the reduction of medicine to a trade. Over the past fifty years the basic sciences have been enormously important in giving medicine the momentum, the breadth of vision, and the technical expertise to achieve many incredible accomplishments. But there are equally grave problems which have now arisen, in part because of these various successes. Medicine now needs to not diminish but rather to expand its connection with the university. If it relies mainly on the basic sciences, that connection is going to shrivel in my view. However, if the medical schools push forward and if the university pushes forward to establish new levels of connections with the Departments of Economics, Political Science, Sociology, Business Administration and so on, if these new areas of interaction and contact develop and become as effective as the basic science contacts have been in the past fifty years, then medicine will be in a very healthy and vigorous condition. I think that, to the extent that they rely on the connection with the basic sciences, medicine is not going to get what it needs and we cannot promise this kind of support. We can't deliver it any longer. I think that our connection should serve as the model for the development of this kind of university affiliation continuing on in the future, but in other areas.

Bower: It seems to me that the problems spoken to in terms of the need of physiology departments to obtain more diversity and more contact with the other sciences cannot really be properly looked at in terms of a problem in teaching anatomy to medical students or really in terms of administration problems. Rather they should perhaps be examined strictly in terms of logistics. The problem of the number of areas represented in our physiology departments, it seems to me, could be relieved by the physiology departments establishing real teaching programs for the baccalaureate undergraduate degree. In that way they would automatically enter into the university community as one of the sciences. The problem is from the logistic standpoint; how to keep a viable relationship between people who are separated by some distance.

Bush: Yes, I agree with you and I'd like to expand on Dr. Mommaert's comments in this area. Too many physiologists have their own little sets of prejudices about what physiologists ought to do or not do. The question of teaching nurses or physical therapists is a case in point. The negative attitude is to elevate your nose and say, "Well, you know, it's not really for me." The positive attitude is to say, "Yes, sure, let's teach the nurses", establish a foothold in the area, do a good job with it and use it as a lever to impress your colleagues for the deserved expansion of your activities. Then we will begin to solve the logistic problem. I'd also like to comment on Dr. Mommaert's point concerning human physiology. There's a very important factor here. Many people have the prejudice that human physiology is not really much more than an extension of dog physiology. There are good grounds for believing that there are still many surprises in store via human physiology. However, for legal and ethical reasons, you cannot succeed in this area,

especially nowadays, without strong contact with your clinical colleagues and medical centers. Success depends on the patient achievement of good working relationships with the clinicians. I think we'll be abdicating our responsibilities if we don't try.

Barker: One brief comment. Many years ago the non-medical school physiologists were complaining that those of us who are connected with medical schools were treating them with arrogance. I think some of the M.D. arrogance may have brushed off on us and I would like to remind all of us physiologists that our colleagues who have been known in the past as simple biologists may have a very strong point.

Metcalf: I am an M.D. in the Department of Medicine at the University of Oregon Medical School. I want to speak despite the chairman's admonition that the father in this marriage spoke last year, because it does seem to me that the children had their day in court - and I do think that they should have, that is, I agree with Dr. Mommaerts that they may be, indeed, are the most important witnesses of our past relationship. I do think, however, that the concept of marriage and divorce has somewhat strained our relationship and threatens to strain it further, by constricting the way we look at one another. I would only suggest that a divorce is a very bad way to start an expanded relationship. If indeed it's true - and I sincerely believe that it's true - that medicine needs physiology and many other disciplines, in some sort of a harem sense, I'd like to suggest that our relationship be used as an expanding model by which we can develop a more casual and easy relationship with the social sciences rather than starting off with the prejudice of a past failure, a divorce.

Unidentified: I am a dentist and a physiologist and all the mention we've had today is that there are 65,000 of us tradesmen. Somebody did mention that, I believe. I would address myself not to the question of dentistry but more especially to the title of the teaching session. The title implies that physiology is one entity. We've heard quite enough about the diversity of it and my comment would be that surely some parts of physiology and graduate training in physiology could be divorced from the medical school but since some of physiology and physiology training is not in the medical school, there is clearly no one sweeping solution for the problem.

Unidentified: I think we are obviously facing a question of identity and I want to expand on what Dr. Metcalf said. Clearly medicine needs physiology and physiology needs medicine but medicine does not need only physiology and physiology does not only need medicine. I was appalled by Dr. Freeman's juxtaposition of pointing out that physiology had given birth to a number of subdisciplines and then to suggest that we had an anachronism. Clearly this is a retrogression that is difficult to understand. The answer seems to us in terms of our identity, is to devise an adequate mechanism for expanding the physiology department so that it will truly begin being the mother of biological sciences and in that sense serve as a bridge for medicine - for dentistry to be sure - and for all other biological sciences in that sense. Now whether this is best done in a university setting with service to all different depart-

ments is a matter that depends a good deal on tradition and on existing facilities but surely our aim should be to expand and widen our view and our training in such a way as to make it possible to serve all of the aspects of physiology that Dr. Mommaerts talked about and not put up our nose and say to those who deal with gingival tissue, "That isn't physiology" or - to take the other way - unless we are looking at the molecular messenger of RNA, why then we are not really dealing with physiology. Clearly it is unity of biological sciences that physiology stands at the very center of.

Jacobs: I wish we did not have to wait a year to see these papers in print. I'd like to underscore Dr. Freeman's remarks concerning bureaucratization of university as well as medical teaching and research processes. We are scientists trying to do our jobs but estimates of such items as percent of effort spent on this function and that function do not help. I'd like to see his comments concerning this problem copied and sent to the proper administrators in our institutions.

SEMINAR ON CARDIOVASCULAR EPIDEMIOLOGY

The Second Ten Day Seminar on Cardiovascular Epidemiology will be held September 14-26, 1969 in Italy. Fifteen student fellows can be accommodated. Nominees should be at the postdoctoral level, with some residency training or its equivalent, planning on academic or research career, and interested in cardiovascular epidemiology. Limited funds may be available to pay for room and board during the Seminar, and for transportation in the amount up to \$200 per accepted fellow. Nominations should be submitted to Jeremiah Stamler, Room LL 139, Chicago Civic Center, Chicago, Illinois 60602.

ERRATA

Molnar, George W. Newton's Thermometer: A Model for Testing Newton's Law of Cooling. *The Physiologist* 12: 9-19, 1969.

The legends for Figure 4, page 16, and Figure 5, page 17, should be interchanged to read as follows:

Fig. 4. Semi-log plot of the course of cooling of a mercury thermometer with a bulb 4 x 15 mm and a stem with a fine capillary bore. 0 = still air. ● = air moving 5 miles/hr. From 200° toward 29°C.

Fig. 5. Semi-log plot of the course of cooling of a sphere of water under conditions maximizing the fraction of heat transfer by radiation. Data of Ericsson in 1876 (3).

The errors are entirely those of the author.

In addition on page 10, first sentence, third paragraph from the bottom should be changed to read:

"...the Crucible containing the mixture of lead, tin, and tin-glass [bismuth], was taken off the fire and set upon the ground.

SECOND INTERNATIONAL MEETING OF THE INTERNATIONAL SOCIETY FOR NEUROCHEMISTRY

The International Society for Neurochemistry will meet in Milan, Italy, September 1-5, 1969. For further information write Professor Rodolfo Paoletti, Institute of Pharmacology, University of Milan, Via Vanvitelli 32, 20129 Milan, Italy.

NEWTON'S LAW OF COOLING APPLIED TO NEWTON'S INGOT OF IRON AND TO OTHER SOLIDS

GEORGE W. MOLNAR

I. Introduction. In the preceding communication (7) Newton's thermometer was made use of to test his law of cooling. It was shown that his own instrument 'disobeyed' his 'law' because cooling proceeded faster in the stem than in the bulb of the thermometer and because there were convection currents mixing the linseed oil between stem and bulb. A mercury thermometer with a fine capillary bore however cooled geometrically in moving air. Because these thermometers had liquid contents however it is not possible to generalize these findings to the cooling of solids without testing the law on solids.

With respect to biothermal investigations, a segment of an organism is essentially either a liquid mass (e.g., a vasodilated finger) or a solid mass (e.g., a vasoconstricted finger). For a clear understanding of the cooling of an organism or part thereof, therefore, it is necessary to know how Newton's law relates to both liquids and solids. It is a curious state of affairs however that the information on the cooling of solids available in the engineering literature is not immediately applicable to biothermal problems. The mathematics of the unsteady state has been thoroughly developed but the examples presented with respect to solids in the engineering literature are usually only hypothetical, contrived by substituting values in the equations. For example, Williamson and Adams (10) published equations, tables and curves illustrating the cooling of solids. Their cases were based on the assumption that the surface temperature changed either suddenly from initial to final temperature or else at a constant rate of 0.1 degree per second. The first condition however is a very special one, and the second condition holds only for a short interval of cooling. Their examples do not help a biologist very much.

II. Newton's Ingot of Iron. As mentioned in the previous paper (7), Newton's primary objective was the establishment of a scale of temperature (9). For temperatures up to the melting point of tin (232°C), he used his linseed oil thermometer. For higher temperatures he resorted to a stratagem which has always been considered to be ingenious. He heated an ingot of iron until it was glowing and with a pair of tongs placed it in a constant air stream. He then put pellets of metals and alloys on the iron and noted the times at which each began to harden. To convert these measured values of time to calculated values of temperature, he made two assumptions: 1) That the rate at which heat passed from the iron to the moving air was proportional to the temperature difference between iron and air. (This assumption about rate of heat transfer is sometimes mistakenly referred to as Newton's law of cooling.) 2) That at equal intervals of time these temperature differences or excesses were in constant ratio. (This assumption is about the time course of the fall in temperature and is therefore Newton's 'law' of cooling.)

By means of these assumptions and a table of logarithms, he was

able to calculate the higher temperatures presumably by starting with the time values for metals having melting point temperatures measurable with his thermometer and extrapolating backwards.

Newton did not give the dimensions of his ingot of iron beyond saying that it was 'ferrum satis crassum' or 'iron sufficiently thick'. (He did not use the word 'ingot' nor any equivalent such as block or bar.) Since he carried it with a pair of tongs, it probably did not weigh more than 10 to 20 pounds, or 5 to 10 kilograms. A bar 5 x 10 x 20 cm would weigh about 17.2 lb. or 7.8 kgm.

In order to test Newton's results, the cooling curve for an ingot of these dimensions was calculated on the basis of the following assumptions: 1) That the temperature of the iron was uniform from center to surface because of the high thermal conductivity of iron. 2) That the rate of heat transfer was uniform from all surfaces to the air because Newton specifically stated that he placed the iron in a constant wind. He did not say how he generated the wind nor on what he rested his hot ingot. A possible setup is shown in Figure 1 which is based on a woodcut in Agricola's *De Re Metallica* (1), a book owned by Newton (3).

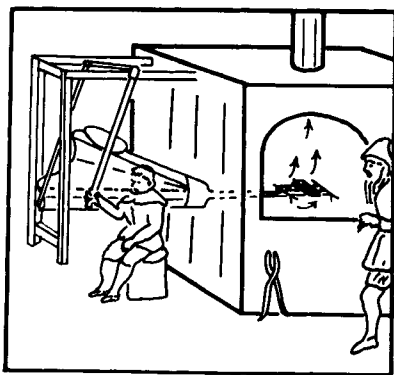


Fig.1. A plausible 'wind tunnel' for Newton's cooling experiments, an unfired furnace normally used for heating and melting metals. Based on a woodcut in Agricola's *De Re Metallica*, 1556, about 125 years before Newton performed his experiments. The assistant operated a pair of bellows which forced a stream of air under the ingot resting on a grate. The air went up the chimney. Newton did not have a beard.

It is plausible that Newton placed his bar on a grate under which, in an unheated furnace, he directed a stream of air from a pair of bellows. Newton performed his experiments in his quarters on the second floor directly above the Porter's lodge to the right of the main gate of Trinity College, Cambridge University. This area is a private apartment not open to the public and so it was not possible to ascertain by direct inspection what sort of equipment could have been installed by Newton. 3) That the heat capacity of iron diminishes with fall in temperature. According to the table of data in a handbook (5) based on measurements made in 1918, the specific heat of iron falls linearly from 0.1850 cal/gm-C at 700°C to 0.1055 at 0°C. 4) That the air temperature was 20°C.

The fall in temperature during consecutive one-minute intervals

was calculated by the formula:

$$Q = h(T - T_a)At = V\rho c \Delta T t \quad \text{Eq. 1.}$$

$$\Delta T = \frac{hA}{V} \cdot \frac{(T - T_a)}{\rho c} \quad \text{Eq. 2.}$$

where Q = quantity of heat.

h = heat transfer coefficient = $0.066 \text{ cal/cm}^2 - \text{min-C}$
(assumed).

T = iron temperature, with 700°C as the initial value
(assumed).

T_a = air temperature = 20°C (assumed).

A = surface area of ingot = 700 cm^2 (assumed).

t = time in minutes.

V = volume of iron = 100 cm^3 (assumed).

ρ = density

c = specific heat, cal/gm-C .

ΔT = fall in temperature during one minute.

At the end of each minute the calculated ΔT was subtracted from T for the beginning of the minute. The value of c for this new T was then determined by means of the linear equation fitted to the data in the handbook (5), and used in Equation 2 to calculate ΔT for the next minute. $(T - T_a)$ for each succeeding minute was divided by the initial value arbitrarily taken to be $700^\circ - 20^\circ = 680^\circ$. The ratios were plotted on semi-log paper as shown in Figure 2. (At 700°C the glow color is dark red (5).)

The curve in Figure 2 is a plausible first approximation of the cooling curve of Newton's ingot of iron. It is decidedly non-linear because of the fall in the heat capacity of the iron as it cooled from 7000 to 200°C . Values for the true melting points of Newton's pellets of metals and alloys (obtained in a current handbook (5)) were plotted as open circles on this curve. Directly below each was plotted as a solid circle the value reported by Newton. His values were all low with the error increasing progressively up to 200° for antimony. This could have been caused by the extrapolation from the boiling point of water through the melting point of tin as shown by the dashed curve in Figure 2. Unfortunately Newton's melting point for tin as measured with his thermometer was in error by 20° and this gave the wrong slope for the extrapolation backwards. It may be that his tin was not as pure as he supposed or that his technique for ascertaining the melting point, as quoted from Desaguliers above, was in error. At any rate because of a techni-

cal error and because of the inconstancy of the heat capacity of iron, his data do not support his law of cooling.

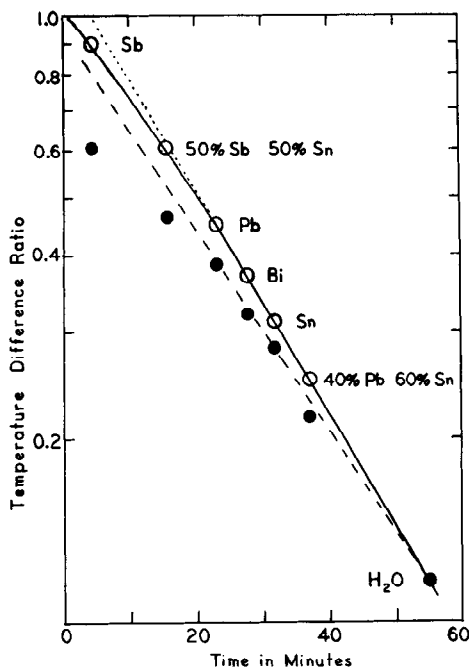


Fig.2. Calculated cooling curve for an ingot of iron 5 x 10 x 20 cm represented by continuous curve. Dotted segment = backward extrapolation from lower linear segment along which cooling would have proceeded had the heat capacity remained at a constant value. o = true melting points of Newton's metals from a handbook (5) • = Newton's melting points (9). Dashed curve = linear extrapolation of curve starting at the boiling point of water and passing through Newton's value for the melting point of tin.

III. Musschenbroek's Pyrometron. Peter van Musschenbroek (1692-1761) was the next person to report measurements of cooling of solids in 1731 (8). He made these measurements with an instrument he called a pyrometron. As shown in Figure 3, a bar of metal was fixed at the right end of the instrument and attached to a rack and pinion, gear train, and dial hand at the other end. By this means a contraction of 1/25,000 rhenish inch could be measured. The bar of metal, 5.8 inches long, and 0.3 inch on a side, was heated either by alcohol lamps or by a coal fire. When the whole apparatus except for the dial was immersed in boiling water, an iron bar expanded by 53 divisions above the length in room air at 0°C; therefore 1 div. = 1.89 C. In a coal fire the iron bar expanded sufficiently so that by the time it was placed in the pyrometron it still contracted 276 divisions in a room at 0°C. Therefore cooling was followed from about 521.6°C down to 0°C. For tin the expansion was 102 divisions for 100 C and cooling was followed from 141.1° to 0°C. Similar conversion factors were not given for the other metals. Musschenbroek published his data in tables with columns of time in minutes-seconds and of dial divisions. These results were tested by converting them to temperature difference ratios as with Newton's data and plotting them on semi-log paper. The results for an iron and a lead bar are shown in Figure 4. The linearity is surpris-

ingly good except for an acceleration at the tail end. Similar results were obtained with steel, brass, copper, and tin. This linearity means, of course, that cooling proceeded geometrically, i.e., according to Newton's law. For the iron bar the linearity extended from about 520°C to 20°C. According to the calculated curve in Figure 2, however, there should have been a curvature in the trend in Figure 4 because of the fall in the specific heat of iron with cooling. This accelerating effect must therefore have been opposed by a decelerating factor. Musschenbroek performed his experiments under still air conditions, not as Newton did in moving air. Therefore the heat transfer coefficient fell as cooling proceeded and this served to counter the accelerating influence of the fall in specific heat. As a result Musschenbroek's bar of iron speciously obeyed Newton's law of cooling.

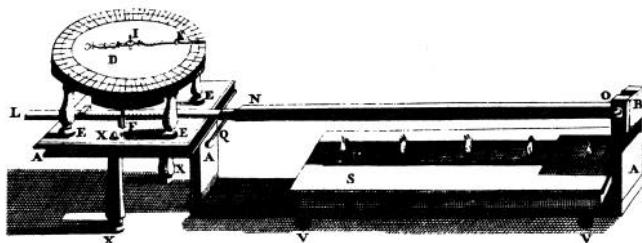


Fig.3. Musschenbroek's pyrometron, 1731. The metal bar at O was fixed to the frame A by clamp B. At N the bar was connected by a screw Q to the rack L, which turned the pinion F. The dial D was roughly 5 cm in diameter. The alcohol wicks T preheated the metal bar. The alcohol vessel R covered by a stone slab S and resting on feet V could be slid along under the bar for even heating.

IV. Elementary Mathematics of Cooling. Although Newton was the secretive inventor of the calculus, he did not use it to analyze the course of cooling. Indeed he presented no formulation whatsoever. The first person to derive a cooling equation was Lambert in 1779 (6). His presentation was almost the same as it is in a textbook today:

y = heat excess above air at time τ .

$y = Y$ when $\tau = 0$.

$$-\frac{dy}{y} = \frac{d\tau}{7}$$

$$\ln \frac{y}{Y} = -\frac{\tau}{7}$$

(ln = logarithm)

$$y = Y e^{-\tau/7}$$

Eq. 3.

7 = 'subtangent'

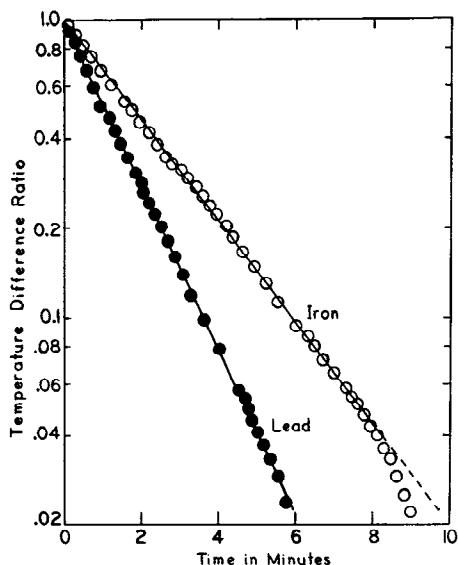


Fig.4. Examples of cooling curves based on measurements made by Musschenbroek with his pyrometron (8).

Our representation of Equation 3 today is:

$$y = (T - T_a)t$$

$$Y = (T - T_a)_0$$

$$(T - T_a)_t = (T - T_a)_0 e^{-kt} \quad \text{Eq. 4.}$$

where T = temperature of cooling object.

T_a = ambient or air temperature.

t = time

k = Cooling constant.

It is obvious that Lambert's subtangent is the reciprocal of the cooling constant, $\tau = 1/k$.

The meaning of the cooling constant can be deduced by letting t equal a unit of time, say a minute or an hour. Then Equation 4 can be written:

$$\frac{(T - T_a)_1}{(T - T_a)_0} = R = e^{-k} \quad t = 1 \text{ unit}$$

$$\ln \frac{(T - T_a)_1}{(T - T_a)_0} = \ln R = -k$$

k is therefore the natural logarithm of the ratio, R , of consecutive temperature differences and

$$R = \text{antiln}(-k).$$

Now $(T - T_a)_0 - (T - T_a)_1 = \Delta T$, and

$$\frac{\Delta T}{(T - T_a)_0} = r = (1 - R) = [1 - \text{antiln}(-k)] \quad \text{Eq. 5.}$$

As Figure 5 shows r is very nearly equal to k for values of $k \leq 0.1$ but r increases less as k increases. Multiplied by 100, $r\%$ is the per cent rate of fall in temperature difference per unit of time and this is actually the useful measure of the rate of cooling.

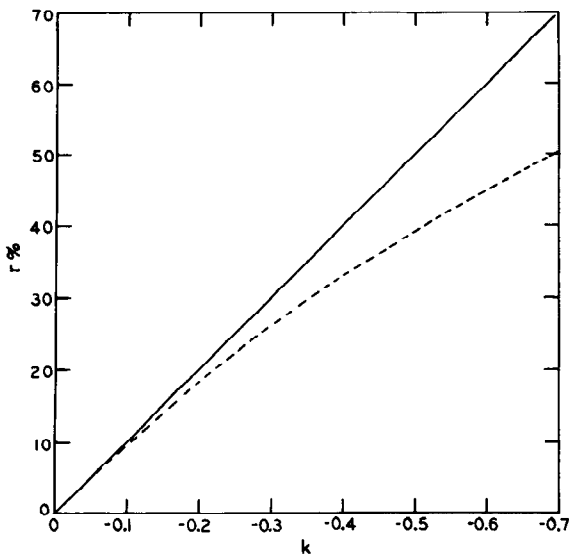


Fig.5. The relation of r to k in Equation 5, that is, of the percent cooling rate to the cooling constant.

Equation 4 holds only when the following conditions obtain:

1) Uniformity of temperature from center to surface. This can be so only when there is instantaneous conduction of heat from center to surface, a condition approached by a bar of metal, a well stirred liquid, and approximately by a vasodilated organism. 2) Constancy of heat capacity, internal heat conductivity, and external heat transfer coefficient.

3) Neutralization of opposing tendencies as acceleration of cooling due to diminution in heat capacity by deceleration of cooling due to diminution of the heat transfer coefficient.

In the case of a solid with low conductivity, condition 1 does not obtain and it is necessary to resort to a mathematics more elaborate than that of Lambert. This was developed by Fourier and published in his celebrated treatise, *Théorie Analytique de la Chaleur*, in 1822 (4).

The formula for the system with non-uniform temperature distribution varies with the shape of the object. There is a separate formula for a sphere, cylinder, slab, etc. Since biological segments are more or less cylindrical, only the formula for the cylinder will be considered and at that for the simplest conditions possible: no heat input, heat flow only radially and not longitudinally (an 'infinite' cylinder), uniform thermal properties in all directions (isotropy), and uniform temperature distribution initially. The formula is (2):

$$\frac{(T_r - T_a)_t}{(T_r - T_a)_0} = \sum_{n=1}^{\infty} \left[\frac{2AJ_0\left(\frac{r}{a}\beta_n\right)}{(A^2 + \beta_n^2)J_0(\beta_n)} \right] e^{-\beta_n^2 \frac{a^2}{\alpha} t} \quad \text{Eq. 6.}$$

T_r = temperature on a radius at a distance r from the axis.

n = number of term from 1 to infinity.

$$A = a \frac{h}{K}$$

a = radius.

h = heat transfer coefficient.

K = thermal conductivity.

J_0 = Bessel function of order zero, first kind. Bessel functions are something like sines and cosines and are used in problems concerned with cylinders.

β_n = roots of $\beta_n J_1(\beta_n) = AJ_0(\beta_n)$ obtainable in Carslaw and Jaeger (2).

J_1 = Bessel function of order one, first kind.

$$\alpha = \text{thermal diffusivity} = \frac{K}{\rho c}$$

ρ = density.

c = specific heat.

This formula is a remarkable creation of the human mind. It looks formidable but it can be subdued and made easily useable. It states that the temperature difference ratio at any point along a radius from center to surface at any moment of cooling is equal to the sum of an infinite number of terms each of which is the product of a constant (in brackets) and an exponential term which diminishes with time.

Usually it is sufficient to know the course of cooling at the center and at the surface. At the center $r = 0$. Therefore

$$J_0\left(\frac{r}{a}\beta_n\right) = J_0(0).$$

In a handbook of mathematical tables we find that $J_0(0) = 1.0000$.

Equation 3 then simplifies to:

$$\frac{(T_c - T_a)_t}{(T_c - T_a)_0} = \sum_{n=1}^{\infty} \left[\frac{2A}{A^2 + \beta_n^2} J_0(\beta_n) \right] e^{-\beta_n^2 \frac{d}{a^2} t} \quad \text{Eq. 7.}$$

where T_c = temperature at the center.

At the surface $r = a$, $r/a = 1$, and $J_0(r/a\beta_n) = J_0(\beta_n)$.

But this cancels the corresponding term in the denominator and Equation 3 simplifies to:

$$\frac{(T_s - T_a)_t}{(T_s - T_a)_0} = \sum_{n=1}^{\infty} \left[\frac{2A}{(A^2 + \beta_n^2)} \right] e^{-\beta_n^2 \frac{d}{a^2} t} \quad \text{Eq. 8.}$$

where T_s = temperature on the surface.

Although the formula calls for the summation of an infinite number of terms, in practice it is rarely necessary to use more than the first 6 terms. Moreover as time progresses each term becomes smaller and after a while the 6th term is so small that it can be dropped. Then the 5th term can be dropped, etc., until only the 1st term is left. The series is said to converge to the 1st term. After convergence has taken place Equations 7 and 8 simplify to:

$$\frac{(T_c - T_a)_t}{(T_c - T_a)_0} = \left[\frac{2A}{(A^2 + \beta_1^2) J_0(\beta_1)} \right] e^{-\beta_1^2 \frac{d}{a^2} t} \quad \text{Eq. 9.}$$

$$\frac{(T_s - T_a)_t}{(T_s - T_a)_0} = \left[\frac{2A}{(A^2 + \beta_1^2)} \right] e^{-\beta_1^2 \frac{d}{a^2} t} \quad \text{Eq. 10.}$$

Now equations 9 and 10 differ from Equation 4 only in having the constant enclosed in brackets. The cooling constant $-k$ in Equation 1 corresponds to $-\beta_1^2 \frac{d}{a^2}$ in the exponents of Equations 9 and 10. It

is of practical interest to find that this cooling constant has the same value at the center and at the surface (and all intermediate points) because often measurements can be made only on the surface.

On a semi-log grid Equations 9 and 10 plot as parallel straight lines with Y-intercepts equal to the constants in brackets and slopes,

$$-k_1 = -\beta_1^2 \frac{a}{a^2} \quad \text{Eq. 11.}$$

Since our test for Newtonian cooling has been linearity of the semi-log trend, we can conclude that theoretically a solid can cool geometrically after convergence has taken place. This occurs when:

$$\frac{(T_s - T_a)_t}{(T_c - T_a)_t} = J_0(\beta_1) = a \text{ constant} \quad \text{Eq. 12.}$$

as can be seen by dividing Equation 10 by Equation 9.

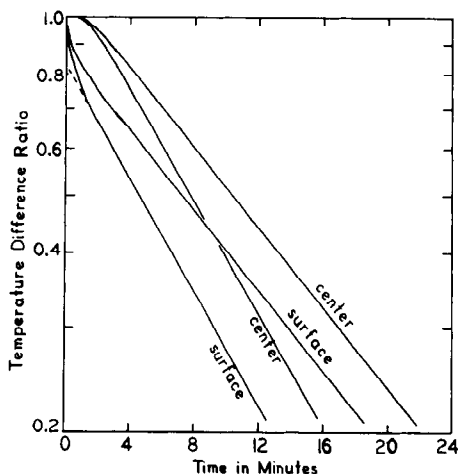


Fig. 6. Cooling curves calculated by means of Equations 7 and 8 for an infinite cylinder having the thermal properties of water. Radius = 1 cm (finger dimension). For the upper pair of curves, $h = 0.044 \text{ cal/cm}^2\text{-min-C}$ (air flow about 1 mile/hr.). For the lower pair $h = 0.066$ (about 2.5 miles/hr.).

Figure 6 shows the cooling curves for an infinite cylinder of finger dimensions having the thermal properties of unstirred water as calculated by means of Equations 9 and 10 for two values of the heat transfer coefficient (air flow of 1 mile/hr. and 2.5 miles/hr.). Convergence takes place after about 2 minutes; thereafter the curves for the center and surface are parallel and cooling proceeds geometrically. Before convergence the curve for the surface is concave upwards and for the center convex upwards. Figure 7 shows a family of curves relating r_1 to the radius and to the heat transfer coefficient, h . (k_1 of Equation 11 has been converted to r_1 by means of Equation 5.) As the radius increases an increase in h has less and less effect on r_1 . Thus a high wind can be expected to increase the rate of cooling of a finger very greatly but not that of the trunk.

V. Cooling of a Beaker of Water. Although the mathematical analysis of cooling leads to Equation 6 as a deduction, the physical picture

of things and events depicted by this synthesis in symbols is not immediate obvious. What is happening during the cooling of a solid when the several terms of the equation peel off like the layers of an onion and disappear? The events during this interval of cooling can be most easily detected and reflected upon by observing the course of cooling in a simple model, namely, a beaker of water. This was done, as shown in Figure 8, by measuring temperatures at equal intervals on a radius from center to surface by means of thermocouples.

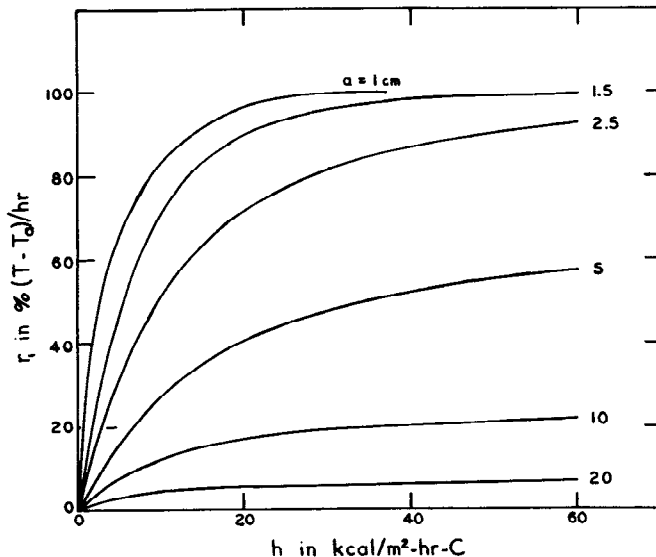


Fig.7. Relation of r_1 (from k_1 , Equation 11, for the first term of Equation 7) to the heat transfer coefficient for infinite cylinders having the thermal properties of water and radii ranging from 1 cm to 20 cm.

When the water was stirred with a propeller, all points on the radius except in contact with the glass cooled on the same linear trend shown by the dashed curve up to about 26 minutes in Figure 9. The slope then diminished slightly and cooling continued along another linear trend (dot-dash curve). This change in slope was probably due to the fact that the thermal diffusivity (α in Equations 6 and 11) becomes a minimum around $4^\circ C$. ($\alpha = 0.00141$ at $10^\circ C$, 0.00137 cm^2/sec at $4^\circ C$.) Except for the slight deviation caused by this small change in a physical constant, therefore, stirred water cooled according to Equation 4 in conformity with Newton's law.

When the water was not stirred with a propeller, cooling proceeded according to the dotted curve in Figure 9. It followed a linear trend up to about 26 minutes with a slope only a little less than that for the

adjacent curve for the stirred water. There followed a hump during which cooling slowed. After about 36 minutes cooling again proceeded linearly with a slope slightly less than that for the adjacent stirred water curve. When the water was not stirred by a propeller it was very effectively stirred by the thermal convection currents which reversed directions (because water at the surface cooled below 4°C at which the density is the greatest) during the interval of the 'hump' of the dotted curve in Figure 9. Thus preceding and succeeding this hump water again cooled essentially in conformity with Newton's law.

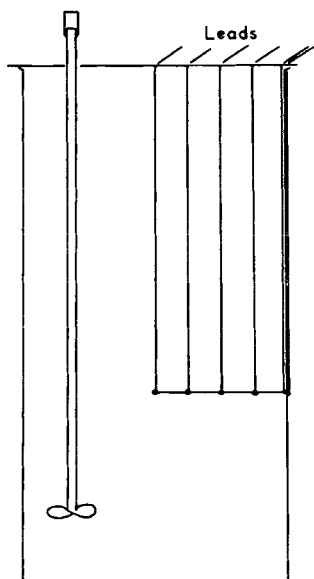


Fig.8. A beaker of water or of 2% agar jelly showing the positions of thermocouples on a radius.

When the currents were arrested by gelation with 2% agar, however, the water cooled very much in accordance with Equation 6 with the trends shown by the continuous curves in Figure 9. At the center cooling did not start for more than 15 minutes and then proceeded slowly with a convex curvature until finally becoming linear at about 40 minutes. At the surface (inner side of beaker) the temperature plunged down and gradually turned with a concave curvature to a linear trend. Thereafter even the surface of the solid water cooled more slowly than the center of the liquid water did.

The question is: What happened during the first 40 minutes when the cooling trends varied from convex to concave courses depending upon the distance out from the center? The answer is demonstrated by the plot of temperature distribution in Figure 10. Initially all points from center to surface were at the same temperature, about 21°C .

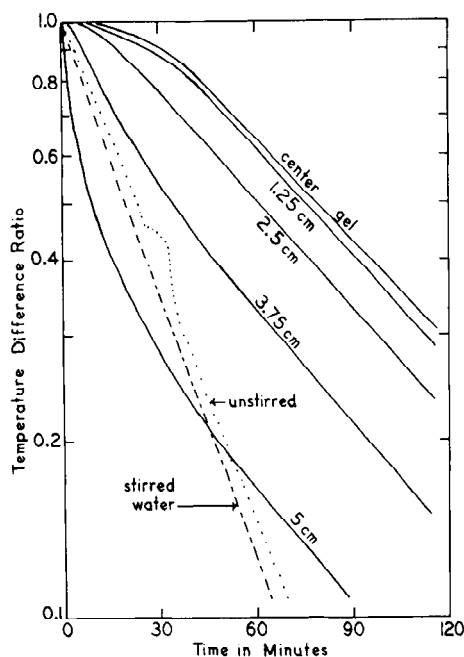


Fig.9. Comparison of cooling curves (continuous curves) of a 'solid' (agar gel) at points along the radius shown in Fig. 8 with the cooling curve of unstirred water (dotted) and the cooling curve of stirred water (dashed).

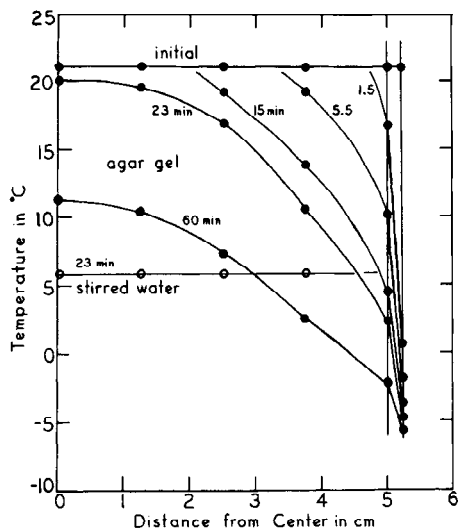


Fig.10. Temperature distribution along the radius in Fig. 8 at 1.5, 5.5, 15, 23 and 60 minutes after immersion in a bath at -6.9°C . \circ = stirred water. \bullet = agar gel. The vertical lines at the right represent the inner and outer surfaces of the beaker.

Cooling began when the beaker was immersed in a bath at -6.9°C . When the water in the beaker was stirred, all points continued to be at the same though falling temperature, e.g., as shown for 23 minutes of cooling, at about 6°C . After the water was immobilized *in situ* however the progress of cooling was quite different. Following immersion the temperature of the outer surface of the beaker plummeted to reach about 1°C within 1.5 minutes. In the same time the inner surface cooled to about 17°C . Cooling however had not yet penetrated to the couple 1.25 cm within (3.75 cm out from the center). Five minutes later it was within this point. After 1¹/₂ minutes it was within the half way point. After 23 minutes the temperature at the center finally dropped 1 degree. Obviously during this time the cold has slowly penetrated from the surface to the center and a non-linear center-to-surface temperature distribution has been established. As can be seen in Figure 9, at this time the several curves are not yet linear and parallel. At 60 minutes they are, however, and for this condition the internal temperature distribution is shown in Figure 10.

It thus becomes understandable that in the cooling of a solid the summation of several terms is necessary during the time that the cold penetrates to the center. As the cold penetrates the several terms of Equation 6 drop out except the first. This convergence to one term occurs when a particular center-to-surface temperature distribution becomes established, namely, that conforming to Equation 12 for an infinite cylinder. Thereafter cooling proceeds geometrically for all points with the same cooling constant.

The beaker of gelled water was of course not an infinite cylinder; there was much heat transfer across the bottom of the beaker. This may partly account for the fact that the curves in Figure 9 are not quite parallel. It is also of passing interest that, as shown in Figure 10, the temperature on the outer surface of the beaker had not reached that of the bath even after 23 minutes. Yet the experimental conditions here were close to the ideal for producing the condition assumed by Williamson and Adams (10) as mentioned in the Introduction, namely, that of a sudden change in the surface temperature from initial to final temperature. Finally in all of these experiments the water supercooled but eventually the temperature jumped up to the freezing point and remained there during the change of state.

VI. Conclusion. An analysis of the cooling of an organism or part thereof in relation to Newton's law can be informative and useful. If it passes the linearity test on a semi-log plot, then the cooling constant can be calculated and used for comparison with cooling under other conditions, etc. If it does not pass the test, then further investigation to determine the cause of the deviation is informative. The important external factor which can cause a deviation is a change in the heat transfer coefficient. Important internal factors can be changes in physical constants, changes in heat transport by convection, and changes in temperature distribution. Formal mathematics is helpful in showing the interrelationships of variables, but in experimentation it is probably best to proceed empirically because conditions are rarely if ever as simple as they are assumed for the mathematical derivations.

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REFERENCES

1. Agricola, G. De Re Metallica. Basel, 1556. Trans.by H. C. Hoover and L. H. Hoover, 1912. (later President and First Lady of the USA). New York: Dover, 1950.
2. Carslaw, H. S., and J. C. Jaeger. Conduction of Heat in Solids. London: Oxford Univ. Press, 1950.
3. de Villamil, R. Newton: The Man. London: Knox, 1932.
4. Fourier, J. The Analytical Theory of Heat. 1822. Trans.by A. Freeman, 1888. New York: Dover, 1955.
5. Handbook of Chemistry and Physics. C. D. Hodgman, editor, 33th ed. Cleveland: Chemical Rubber, 1954.
6. Lambert, J. H. Pyrometrie oder vom Maasse des Feuers und der Warne. Berlin, 1779.
7. Molnar, G. W. Newton's Thermometer: a model for testing Newton's law of cooling. Physiologist 12: 9-19, 1969.
8. Musschenbroek, P. van. Tentamina Experimentorum Naturalium Captorum in Academia del Cimento. Additamentum. Leiden, 1731.
9. Newton, I. Scala graduum caloris. Calorum descriptiones & signa. Philosophical Trans. Roy. Soc. London: pp.824-829, 1701.
10. Williamson, E. D., and L. H. Adams. Temperature distribution in solids during heating or cooling. Physical Res. 14: 99-114, 1919.