THE PHYSIOLOGIST

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Cover: William F. Hamilton, 28th APS President, p. 64.

28th APS PRESIDENT

William F. Hamilton

It was stated in the student newspaper (3) at the Medical College of Georgia that William F. Hamilton "is noted for his stern appearance, kind heart, . . . and remarkable memory." Those who knew him will quickly agree. Dr. Hamilton's impact on physiology at the national and international levels as well as the high standards of teaching and research at his own institution were unusually impressive.

Dr. W. F. Hamilton was descended on the paternal side from 17th and 18th century emigrants from England and Ireland who settled chiefly in western Pennsylvania; on the maternal side his ancestors came from England, settling in colonial New England and later moving to Ohio and further west.

His father was Isaac Beeson Hamilton, the eldest of the large family of the Reverend William Ferguson Hamilton. Isaac Beeson Hamilton received a medical education and early in his career was practicing and teaching anatomy in Los Angeles, where he met Clara Eddy, a highly intelligent and widely informed young woman who was at that time running a neighborhood newspaper. They were married in 1892 and moved to Tombstone, Arizona, where W. F. Hamilton was born March 8, 1893. Dr. Isaac B. Hamilton practiced medicine chiefly in Arizona, California, and Mexico; at times he was in private practice, but mostly he was a company doctor at mining camps, for a railroad, and the like; unfortunately he was often tempted to invest unwisely in mining stock and other speculative ventures so that the family fortunes were uncertain.

After graduation from high school in Tucson, Arizona, W. F. Hamilton attended Pomona College in Claremont, California. There he was active in student government, worked to pay expenses at various jobs, and tried his hand at writing short stories for a campus publication. Of particular relevance was the development of a strong interest in biology; at Pomona College there was a biology professor who stimulated many students and there was an active program of field trips, marine collecting trips, and lab work.

By the time W. F. Hamilton received his A.B. degree in 1917, World War I had started and he enlisted in the Army. After basic training he was on a troop train to be sent overseas when he became ill, and after several months at Walter Reed Army Hospital, he was reassigned to Fort Sam Houston in Texas. There he was joined by his fiancee, Helen Folsom Dula, who was an elementary school teacher in San Diego, and they were married. Their first son was born in Berkeley, California. Another son was born in Austin, Texas; a daughter, in New Haven, Connecticut; and another daughter in Louisville, Kentucky.

Helen Hamilton was the major force in creating a home that combined warmth, humor, and mental stimulation, and friends of all ages were welcomed. She had a rare ease in entertaining that distinguished the many dinner parties and other gatherings which brought together friends of scientific, medical, journalistic, and business backgrounds. There were many lively exchanges of ideas with or without guests. Dr. Hamilton basked in this homelife skillfully managed by his talented and compassionate wife. He had a profound love for Helen and their four children.

When the children were young, a regular evening custom was the reading to them by their father of several chapters of a book, starting with *Treasure Island* and *Kidnapped* and continuing on through much of Dickens. Picnics were a favorite activity, usually with several families participating. Camping trips were enjoyed in warm weather. In later years Dr. Hamilton took up sailing. Another recreation or hobby he enjoyed much of his life was gardening. His seven grandchildren were a source of much interest and pleasure.

There were times of sorrow and distress. In 1943 his son, Lt. David P. Hamilton, Army Air Corps, was killed in an airplane accident while conducting experiments; he was a brilliant and personable young man and the loss was difficult. In 1956 Helen Hamilton died. (He subsequently married Mabel D. Bradley, who survived him for a number of years.)

After separation from the Army W. F. Hamilton entered graduate school and received the Ph.D. degree in 1921 from the University of California, Berkeley, in Zoology. While meeting the requirements of this degree he was appointed as an Associate in Zoology. He was appointed Instructor in Zoology at The University of Texas for the academic year 1920-21 and then Instructor of Physiology at Yale University 1921-23. He went to the University of Louisville as Assistant Professor of Physiology and Pharmacology in 1923, advancing to Associate Professor in 1926 and to Professor in 1931. He was also chairman of the department at the University of Louisville. The next two years (1932-34) were at George Washington University. In 1934 he made his final move to the Medical College of Georgia as Professor and Chairman of the combined Departments of Physiology and Pharmacology. In 1942 Pharmacology was established as a separate department. Dr. Hamilton remained as Chairman of the Department of Physiology until his retirement in 1960 and continued as Emeritus Professor of Physiology until his death in 1964.

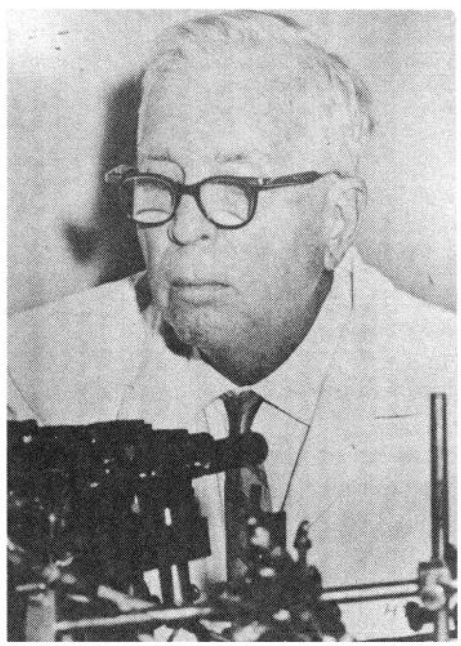
Dr. Hamilton had high standards for teaching, and he considered it was every department member's first responsibility when classes were in session. He emphasized small group sessions for the teaching of physiology to medical students and was particularly adept at stimulating discussions. His *Textbook on Human Physiology,* first published in 1947 by F. A. Davis Co. with two editions, attests to his dedication to his students' understanding of fundamentals.

Dr. Hamilton's early research dealt with animal behavior, including locomotion of the starfish. It was at the University of Louisville, however, where his highly significant contributions to physiology began to emerge. They were at first in the area of sensory physiology with particular emphasis on color vision. Also, in association with H. G. Barbour, the falling drop technique for determination of the specific gravity of biological fluids was developed (2). This method found considerable clinical application. It was later at this institution that the first of his "Studies on the Circulation" emerged which were the forerunners of his many researches that continued until his death. With these publications, he began his pioneering work on the relations between pressure and flow of blood in the cardiovascular system which continued at George Washington University and the Medical College of Georgia. This included the development of the Hamilton metal membrane manometer (5) for accurate measurement of pulsatile pressures and his contributions to the Stewart-Hamilton indicator-dilution principle (6) for the measurement of flow. His name is internationally recognized for these highly important accomplishments.

It should be emphasized that one of the important attributes of Dr. Hamilton and one that should be more seriously considered by present-day researchers is that the methods he developed were a means to an end and not an end in themselves. That is, the methods were for the purpose of gaining knowledge and understanding of physiological functions and their regulation. Philip Dow, who was Hamilton's long-time associate and eventual successor as chairman of the department at the Medical College of Georgia, stated "he was full of ideas and usually ways to test them, and he kept abreast of all the significant literature."

Dr. Hamilton's tenure at Georgia, as taken from the final report of his grant support that was written after his retirement, was generally regarded by him, as having three eras.

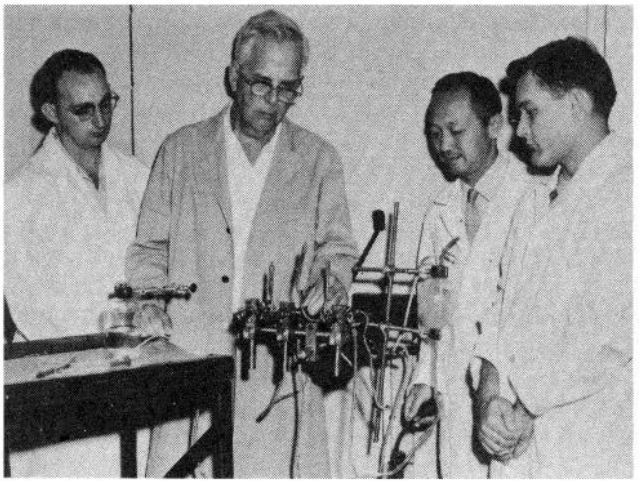
The first era covered the years from 1934 to 1946, when there was no grant support and a "budget" of $2,000 per year for teaching and research supplies and equipment. Interestingly enough this is the period when much fundamental work (65 papers) was accomplished, including recordings of human pulse pressure arteriograms under various conditions, measurement of pulse wave velocity and its transformation throughout the arterial tree, relation of the pulse pressure curve to the pattern of cardiac ejection and total stroke volume. Using the indicator-dilution method for measuring cardiac output Hamilton published a theory of cardiac output control that required 20 years for its acceptance. During this period a number of the Hamilton manometers (made in his departmental workshop) were sold to other laboratories, providing additional research funds. The major collaborators in these studies were Robert A. Woodbury, Philip Dow, and John W. Remington.



The second era covered the years of grant support from the Life Insurance Medical Research Fund and the National Institutes of Health (NIH). During this period Hamilton's group branched out into clinical physiology. This included the establishment of a cardiopulmonary laboratory successively directed by Don M. Fowell M.D., Robert G. Ellison M.D., and Lois T. Ellison M.D. During this same period comparison of the indicator-dilution method and the Fick procedure in collaboration with Nobel Laureates Andre Cournand and D. W. Richards, Jr., of Columbia University showed that both methods were measuring the same thing and with equal accuracy (7). This resulted in the wide acceptance and development of the indicator-dilution method. Philip Dow and John W. Remington were major collaborators with Hamilton during this period.

Andre Cournand in his Nobel lecture (4) of December 11, 1956, honored Dr. Hamilton with the following quotes. "To guide our hand . . . we had all the knowledge accumulated through the years by physiologists in their studies on animals: and to one, Dr. William F. Hamilton, I owe a more personal debt of gratitude for his constant advice and kind criticism." In regard to the Hamilton manometer, he stated "Although the Hamilton manometer was subsequently replaced by a strain gauge in association with electronic recorders, it is well to recall that most of our early knowledge of pressure pulses was obtained by using this device." In regard to the dye-dilution technique he stated "The use of the dye dilution technique . . . provides an indirect means of measuring this volume (central blood volume), according to a principle first correctly stated and then experimentally established by Hamilton and his school."

The third period was that of the NIH- and American Heart Association-supported training course for cardiovascular investigators, which began in 1953 with the move of Dr. Robert S. Alexander from Western Reserve University to join the department. The expansion of physical facilities for research also occurred at this time. This postdoctoral training program was jointly operated by Dr. Hamilton and Dr. Raymond P. Ahlquist, Chairman of Pharmacology and originator of the theory of α- and β-adrenergic receptors. The first classical paper of this theory was published in the *American Journal of Physiology,* to whose Editorial Board Dr. Ahlquist had submitted his paper following the suggestion of Hamilton (1). From 1954 to 1963, 32 postdoctoral trainees came from all over the United States and the world to study, and most of them are still active in cardiovascular research.



During the second and third eras six areas of research concerned Dr. Hamilton, the other Department members and the postdoctoral trainees. These were *1*) the theory and practical techniques of the dye-dilution method; *2*) the physics of pulsatile flow and elasticity of tissues; *3*) the measurement and control of blood volume in shock; *4*) cardiopneumographic changes and electrocardiographic norms; *5*) renal blood flow and intravascular volume; and *6*) congestive failure of the circulation.

In 1924 Dr. Hamilton joined the American Physiological Society, which became an integral part of his scientific life; he regularly attended its meetings for 40 years. He was one of the founding members of the Circulation Group,[1] which has now become the Cardiovascular Section. He served the society as Councillor (1942-49) and in 1954 the Society honored him with selection as President-Elect and in 1955 he became President of the Society. His major interest in the society was the publications. He served on the Editorial Boards of the society journals from 1940 to 1958 and on the Board of Publications Trustees from 1951 to 1954 and again from 1957 to 1959. His final service to the society's publications was as Section Editor of the three volumes of the Circulation Section of the *Handbook of Physiology.* This prodigious task, which included close editorial attention to every chapter, was completed only a short time before his death. He also served the Society by organizing the second fall meeting in 1949 and was active in the Visiting Scientist Program and opportunities for senior physiologists. He was one of the leaders in the purchase of Beaumont House, which is now the headquarters of FASEB.

For many years there had been attempts to devise a seal or emblem for the American Physiological Society. Dr. Hamilton was most interested in this activity and proposed an emblem that was presented to the Council of the American Physiological Society on September 12, 1957. The initial use of this emblem was as the first page decoration of the first issue of Volume 1, November 1957 of *The Physiologist.* On the first page of that issue it is stated that "the seal at the top of the page was designed by William F. Hamilton and has been adopted by Council as an official emblem of the Society." This emblem can be found on the cover and first page of current issues of *The Physiologist* as well as stationery and other official documents of the Society.

Dr. Hamilton served on several research review boards, including the NIH Physiology Study Section and that of the Life Insurance Medical Research Fund. He was a founder and first chairman of the Basic Science Council of the American Heart Association.

Dr. Hamilton was accorded prestigious honors in recognition of his accomplishments. In 1953 he presented the Connor Lecture of the American Heart Association and received the Gold Heart Award from this organization in 1958. The Georgia Heart Association in 1960 presented him with its Distinguished Service Award. He received the Gairdner Foundation Award in 1960 as well as the Modern Medicine Award in 1960. At the time of his retirement from the Medical College of Georgia a symposium was held in his honor entitled "The Physiological Frontiers of Congestive Circulatory Failure" with a panel of speakers including Dr. Eugene A. Stead, Jr., Dr. James O. Davis, and Dr. Eugene M. Landis. Dr. Hamilton was permanently commemorated by the Medical College of Georgia on May 10, 1979 with the dedication of the William F. Hamilton Wing of the Sanders Research and Education Building. This included a ceremony involving members of the College Administration, his daughter Dr. Clara Hamilton Schoenborn, and an address by Dr. Harold C. Wiggers. The ceremony was followed by a symposium entitled "Physiology of Atrial Pacemakers."

Dr. Hamilton is fondly remembered by his many colleagues and students as both a friend and a teacher.

[1]See "History of the Cardiovascular Section," by R. S. Alexander, p. 67.

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History of the Cardiovascular Section

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As with the invention of the wheel, it would be futile to attempt to identify the first occasion when a group with special interests convened their own private meeting during the course of a scientific conclave. Nevertheless, inasmuch as the cardiovascular physiologists were the first to organize one of the groups that evolved into what have more recently become formalized as "Sections" of the American Physiological Society, it is of interest to trace the history of this group. The idea was born during the 1932 APS meetings in Philadelphia at a luncheon attended by Drs. Henry Bazett (Pennsylvania), George Fahr (Minnesota), Charles Greene (Missouri), William Hamilton (George Washington), Louis Katz (Chicago), Forest McCrea (Duke), Walter Meek (Wisconsin), Isaac Starr (Pennsylvania), Maurice Visscher (Illinois), and Carl Wiggers (Western Reserve), now recognized as the founding fathers of the group. (It is of interest that 7 of these 10 individuals became presidents of the APS.) The group decided to arrange a dinner session during the following spring meeting at Cincinnati to which 45 of the leading cardiovascular physiologists would be invited. The dinner was held on April 10, 1933, and was attended by 17 of those on the invitation list plus 7 guests. After a stimulating discussion of a variety of scientific issues, the idea of making such a dinner meeting an annual event was enthusiastically endorsed. The question was raised as to how the group should be identified, and a wide assortment of suggestions were forthcoming, including "The Bloody Squirts," "The Cardioquacks," "The Hales and Harveys," and "The His Bundlers." A subcommittee finally settled on Yandell Henderson's suggestion of "The Hearties," but by common usage this was soon displaced by the less imaginative title of "The Circulation Section of The American Physiological Society." Three decisions of more significance to the future of the organization were made: that membership would be restricted to a select group, that members might bring scientific guests but not their spouses, and that the management of the organization would be the responsibility of a three-member Steering Committee, one of whom would retire each year and be replaced by a new member.

Louis Katz, Walter Meek, and Carl Wiggers were elected as the first Steering Committee. For anyone able to recall these personalities, it is not surprising that they established the tradition that the Committee would run the organization according to its own best creative instincts and never allow democratic principles involving the entire membership to encroach on the autocratic power of this triumvirate. A ritual in keeping with this proud tradition was the annual "election" of the new member of the Steering Committee by unanimous acclamation after eloquent nominating speeches staged by the Steering Committee. This denial of democratic responsibilities to the membership as a whole backfired on just one occasion. It was discovered that a Sunday scheduling of the dinner conflicted with a local Blue Law which prohibited operating the cash bar. The only means for providing appropriate beverages was to operate by private club rules whereby the Steering Committee picked up the tab for the drinks. This almost bankrupted the Committee that year when many members left without reimbursing them for their libations. It evolved that the newly elected committee member became keeper of the archives and screener of nominations for membership, the second year man had the responsibility of dinner arrangements, and the senior member was responsible for the scientific program.

The nature of the scientific programs in those early days has become so foreign to the decorum of contemporary scientific discourse as to be difficult to convey to younger generations. The purpose of the meetings was defined as "promoting frank discussions between active investigators." In modern terms, this translates into merciless heckling of colleagues, employing scathing criticism, penetrating logic, biting sarcasm, and lightning-swift repartee in attempts to win points. It was in part a game, but a fascinating and stimulating game, employing techniques that would no longer be tolerated in the dignified halls of science. In that era, several factors made this possible. The group was relatively small, closely knit, and all very familiar with each others work. Hence one had little fear that the fireworks of the debate would be taken personally. In addition, both the knowledge base and the technology were thoroughly familiar to all combatants; no one could resort to authoritarian claims of having a sophisticated technique whose fine points were not appreciated by the others. There was also a universal skill among this group to know how to make use of comic relief—or outright buffoonery—so that sufficient humor was mixed with the acrimony to sustain a level of entertainment equal to the intellectual intensity of the debate. Sessions tended to alternate between a cardiac and a peripheral vascular focus, and to capitalize fully on this format, controversial topics were chosen and discussion leaders selected whose views were most provocative. Members and their guests garnered profound insights into the frontiers of their science by listening to these excoriating examinations of new concepts.

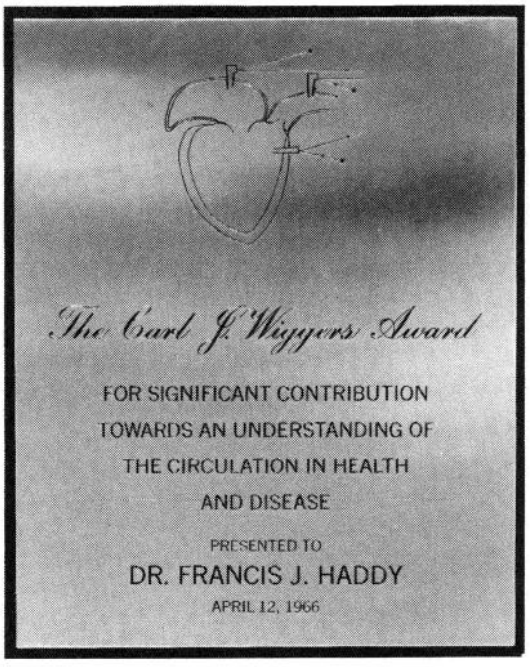
The organization thrived on this format for well over a decade, but by the 1950's a number of difficulties were arising. The success of the enterprise led to an ever increasing pressure for membership, and the group was growing so large as to defeat its original purpose. It was therefore decided to limit the membership to 100, which

now prompted charges of elitism. To prevent inactive retirees from occupying membership slots, in 1952 a category of "Distinguished Member" was created and gradually expanded to include most senior members so as to make room for younger members. This did little to silence the criticism of elitism because in the post-Sputnik era our science was growing too rapidly. Complaints reached the Council of the APS, which became distressed that such a restrictive group was identified as part of the Society, and they decreed that it could no longer present itself as a Section of the APS; for a number of years thereafter the organization was renamed "The Circulation Group." Of much greater importance, however, was the fact that the old format was dying. The crowd was too large, the field was splintering into ever smaller subspecialties with their own sophisticated technologies, and the sparkling give-and-take of yesteryear no longer flourished. Instead, the meetings became a marathon of countless members striving to get to the podium to show "a few slides they just happened to have in their pocket." Various techniques were tried in largely futile attempts to salvage something worthwhile. The most disastrous of these was an arbitrary termination of the discussion so that the stage could be turned over to a couple of night-club entertainers imported from New York. The hapless entertainers used their most ribald stories and employed every trick known to their profession trying to elicit a spark from their audience; they were rewarded with nothing but blank stares.

It was following this fiasco that John Remington became the senior member of the Steering Committee responsible for the scientific program and decided that a radical change in format was in order. In 1962 he originated the idea of shifting the main scientific thrust to the organization of a symposium scheduled on the regular Federation program and hence open to all. The speakers at this symposium were then invited to be guests at the closed dinner meeting of the Group. The concept was that following dinner the material of the symposium would be thrown open for a complete rehash, with no holds barred other than a prohibition against showing more than one lantern slide. The open symposia were an outstanding success and shortly established a reputation for excellence, but the evening discussions sputtered and faltered. Chairmen endeavored in one way or another to return to "the good old days," but it became obvious that the newer generation was not able to engage in the intellectual tango of former years.

A new factor emerged with the death of Carl Wiggers in 1963. Following his memorial service at Western Reserve, Louis Katz spoke to some of Wiggers' former students who were reminiscing on the lawn in front of the chapel. Katz urged that something must be done to commemorate the contributions of this "Dean of Cardiovascular Physiologists." In due time all former associates of Carl Wiggers were solicited for contributions to a "Wiggers Fund," and three of his students, R. M. Berne, W. C. Randall, and R. S. Alexander, endeavored to establish a suitable memorial. By coincidence, just about the time that the solicitation was completed, Alexander came up the line as Chairman of the Steering Committee of the Circulation Group. All parties concerned readily agreed to try a variation of the format: to retain the symposium concept established by Remington but to follow the dinner by a "Wiggers Memorial Lecture" designed to give a more comprehensive overview of the topic of the symposium. The income from the Wiggers Fund was used to purchase a plaque to constitute "The Carl J. Wiggers Award." In the design of the plaque, the wording was taken from the title of Wiggers' classical text and use was made of one of his very early diagrams depicting the optical registration of intracardiac pressures, drawn by Wiggers himself and used in numerous of his classical publications. The 1966 meeting of The Circulation Group was preceded by a symposium on "The Chemical Control of the Peripheral Vasculature" and featured the first Wiggers Lecture delivered by Dr. Frances J. Haddy as recipient of the first Carl J. Wiggers Award.

Stringent efforts were made to avoid committing future Steering Committees to this same format, but the idea was so well received that, with minor modifications, it has remained the choice of successive Steering Committees. With the dinner meeting now transformed to a formal lecture, restricting the audience no longer made sense, and it shortly became the practice to open the Wiggers Lecture to the public. Membership is now open to anyone who is interested; the only remnant of elitism is the identification of members who have made scientific contributions as "Fellows." The organization was no longer tainted and thus was eligible to be restored as a formal Section of the APS under the modified title of "The Cardiovascular Section." Now representing one of the 12 sanctioned Sections – as a recognized constituency within the Society – somewhat broadened responsibilities have led to minor modifications in structure. In spite of these evolutionary changes, it continues to serve substantially the same purpose which inspired its founding fathers a half-century ago.



The first Carl J. Wiggers Award.

The 1941-42 Search for an APS Emblem

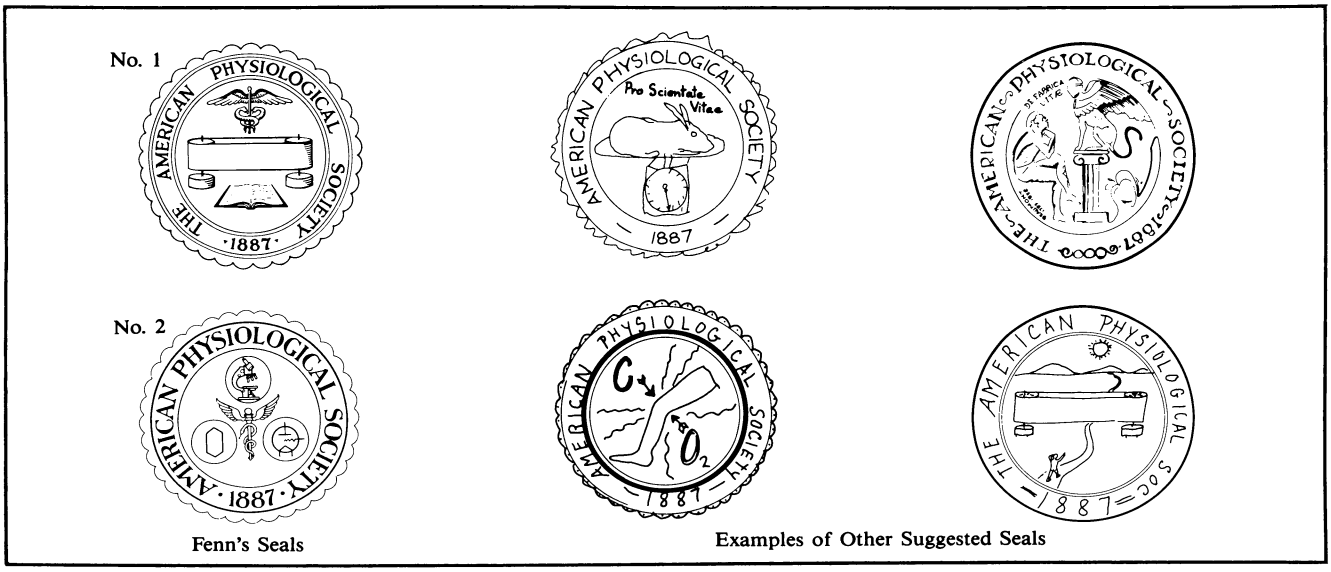
This issue of *The Physiologist* honors William F. Hamilton, designer of the simple and familiar APS seal that appears on all stationery, memoranda, and publications (see p. 64). In 1957, when Hamilton presented the seal at a meeting of Council, the Society, though it had no seal, was not actively seeking one. With little debate, the officers of APS gratefully accepted Hamilton's effort as one, but not the only, emblem of the Society (1). This was, however, not the first time the matter of a seal had been raised. Sixteen years earlier, the want of a seal had been brought to the attention of Council, and a concerted but ultimately failed effort to procure one was made. The amusing results of this search have been preserved in the Society's archives. In this long forgotten episode, Hamilton played a small but prescient part.

The minutes of the annual Council meeting in 1941 record that the President, Philip Bard, "raised the question of the existence and possible need of a seal of the Society" (2). The impetus appears to have come from Wallace Fenn, then a member of the Board of Publication Trustees, who had recently designed a seal for the Rochester Academy of Medicine and thought the Society might do well to have one also (3). Unsure whether a seal had ever been adopted, Council decided to have a search made of the articles of incorporation and to authorize the Secretary, Carl J. Wiggers, "to have a seal designed if it is established that one does not exist." Accordingly, when historical inquiry drew a blank, Wiggers wrote to Fenn in September 1941 for help. "Bard informs me that you have some ideas on the subject and might be willing to take on the job of designing it."

With considerable reluctance and repeated disclaimers as to his artistic ability, Fenn agreed to give the matter some thought, that is, if no one else could be found. Wiggers replied that he was "frankly somewhat disappointed" by this response. He wrote to Fenn: "I understand that you have considerable artistic talent, and hoped that we might count on you to take over the task of designing a seal. . . . May I not ask you to reconsider your decision and present a design at the Boston meetings? . . . Be a good fellow and help me out! S.O.S." Under "earnest protest," Fenn consented. In January, he reported to Wiggers that he was "frantically drawing concentric circles and erasing vigorously." He still doubted his talent and hoped that Council would decide to open a competition to all members of the Society for a seal to be presented in 1943.

At the Boston Federation meeting in March, 1942, Fenn laid three drawings before Council. They have regrettably not been saved in the archives. The minutes record that after "various criticisms and suggestions" were made, Fenn was requested to modify two of the sketches and send a copy to each of the members of Council for their comments (4). By late May Fenn had made the changes and circulated two professionally drawn designs (5). In comparison to Hamilton's simple insignia, Fenn's two emblems were complex, heavily symbolic, and dated. The first contained a caduceus, a kymograph, and an open book. This was the simplified version. In response to the comments at the Council meeting, Fenn had pleaded artistic license to remove detail from the kymograph and had omitted from the drum paper the Gothic lettering, "De Fabrica Naturae," deriving from Harvey, since, as he explained, "it was evident that in the reduced form it would become illegible." The second emblem incorporated no fewer than four symbols of science into the center circle: an Aesculapian staff, a microscope, a benzene ring, and an electron tube.

A great many additional pencil sketches of possible but improbable APS seals survive in a folder left by Fenn to the APS Archives. One set of designs featured the symbolic instantaneous transformation of oxygen to



Fenn's Seals

Examples of Other Suggested Seals

Toby Appel recently joined the staff of APS as Historian-Archivist. She holds a Ph.D. in history of science from Princeton University, and her publications have dealt with the history of biology and medicine. She has previously worked as an archivist at the National Archives, as a historical editor at the Charles Willson Peale Papers at the Smithsonian, and most recently as assistant editor of the Thomas A. Edison Papers at Rutgers. At present she is organizing the Society's archives and working on Centennial projects.

carbon dioxide. Several other seals showed a rabbit on a scale with the motto, "Pro Scientate Vitae." There was a seal representing the transformation of oxygen and carbon in the knee jerk, a seal with Galvani's frog preparation and Harvey's bandaged arm, a seal with a scholar monitoring a man on a treadmill, and a seal with a griffin perched on an Ionic column. Perhaps the most unusual showed a man (mankind?) traveling down a curved road into a distant horizon of mountains and shining sun. Across the golden pathway lay a giant kymograph on which the artist had written, and then after consideration erased, the words, "Per Experimentum ad Veritam."

The responses of Council members to Fenn's two final offerings supply revealing glimpses of how the leaders of APS in 1942 envisioned their discipline. Andrew C. Ivy, Carl J. Wiggers and his department at Western Reserve, and Hallowell Davis and his department at Harvard opted for Fenn's first drawing with kymograph, caduceus, and book. Davis wrote, "I prefer the kymograph, which is the obvious symbol for physiology as such, rather than the collection of symbols of other fields of activity which are used by physiology but are not the essence of physiology itself." Walter Garrey, Philip Bard, and Walter Meek preferred number two or some modification thereof. Meek thought the first drawing more attractive but voted for the second because it "represents more interests, biology, chemistry and physics." Bard, after showing the designs to members of his department at Johns Hopkins, reported that although the kymograph was the appropriate symbol of physiology, "nobody likes the general composition of number 1." The Hopkins physiologists advocated changing the second design by replacing the benzene ring by a retort (symbolizing synthesis) and the amplifier by a single kymograph. "It is thought the electron tube is not very appropriate just over the date 1887," Bard explained.

Newly elected to Council in April, William Hamilton wrote to Fenn on 26 May 1942:

> I am very much interested in the Seal and like the symbolism of No. 1 better than that of No. 2, literature, experiment and application, although the application is perhaps a little narrow since other fields than medicine may be considered important.
> The feeling of some of us here is that a portrait—say of Beaumont—drawn in the style of the Charles Thomas Seal or a simple motto might serve very well as a seal for our Society.

He recommended a broader canvassing of opinion before deciding. The harshest criticism came from members of Fenn's own department at Rochester. Some thought the seals lacking in dignity and "not worthy of the position they are to hold" while another suggested the kymograph "may be obsolete in its pictured form fifty years hence." Several agreed with Hamilton that a timeless abstract design was preferable to detailed and potentially dated symbols.

Faced with so many conflicting opinions, Fenn had no choice but to order the next year's supply of stationery without a seal on the letterhead and the matter was left hanging until the next annual meeting of the Society. Because of the war, no meeting was held in 1943 nor in 1944 or 1945. By the time the Society resumed normal activities, Fenn's seals were forgotten, and no further official consideration was given to the problem until Hamilton's seal of 1957. Fenn was not unhappy with the outcome of the Society's search for a seal. In his history of APS, he wrote, "The writer heartily agrees that the Hamilton Seal is far superior to the previous one proposed by Fenn but (fortunately) never accepted" (6).

References

1. Council Minutes, September 1-2, 1957, vol. 19, 1957.
2. Council Minutes, April 15, 1941, vol. 9, 1939-41.
3. Fenn to Wiggers, September 23, 1941. This and other letters mentioned are located in a folder on the seal in the APS Archives.
4. Council Minutes, March 31, 1942, vol. 10, 1941-43.
5. These designs as well as the many pencil sketches mentioned below are in the APS Archives.
6. Wallace O. Fenn, *History of the American Physiological Society: The Third Quarter Century, 1937-1962.* Washington, DC: Am. Physiol. Soc., 1963, p. 43.

Toby A. Appel

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Physiology Chairman's Objectives in Selecting Young Members for a Large Multidisciplinary State University

HARVEY V. SPARKS, JR.
Department of Physiology
Michigan State University
East Lansing, Michigan 48824-1101

The purpose of this presentation is to provide individuals interested in a career in physiology with information about the requisite characteristics of new faculty members in a large multifaceted state university department of physiology. It will be useful to describe the features of our Department in addition to the types of individuals we recruit for faculty positions. This will allow the reader to judge whether our needs can be extrapolated to other departments of physiology.

The Department of Physiology at Michigan State University serves five administrative units within the University. There are three colleges of medicine: Veterinary Medicine, Human Medicine, and Osteopathic Medicine. Our roles within these three colleges are very similar to those of most other medical school departments of physiology. In each case, we teach an introductory course in human physiology in the medical curriculum and participate to varying degrees in other courses which present correlations between clinical and basic sciences. We also welcome professional students into our laboratories both before and after they obtain their doctoral degrees. Our faculty members participate in the usual number of curriculum committees, admission committees, and other debating societies. In addition, each medical school dean expects a high level of research productivity by his basic science faculty. As a part of the College of Natural Science, we provide an undergraduate major in Physiology for approximately 200 students at any one time. The vast majority of these undergraduate majors in Physiology pursue a career in one of the biological sciences or go to medical school. Many of them spend at least some time working in one of our laboratories. Several members of our Department have partial appointments at the Agricultural Experiment Station. These faculty members are provided salary support to pursue research in areas of physiology related to agriculture.

Presented at the Symposium on Employment of Physiologists in Academic Departments, APS Fall Meeting, 14 October 1981, Cincinnati, OH. Other papers presented were published in *Physiologist* 25: 2, 1982.

All five of the above-mentioned administrative units play an important role in supporting the graduate program in our Department. The three Colleges of Medicine are especially helpful in providing a number of stipends for graduate students. Approximately 28 full-time equivalent faculty members share the responsibility for this diverse set of obligations. All of these positions are fully funded by University general fund or Agricultural Experiment Station dollars. Because of the relatively large number of faculty members, we have at least two individuals representing most of the subdisciplines including cardiovascular, endocrine/reproductive, renal, gastrointestinal, respiratory, neural, cell/biophysical, and comparative physiology.

Given the department described above, what type of individual do we have in mind when we recruit an assistant professor? First, we look for demonstrated research productivity. All of our faculty members participate in a research program to at least some degree, and almost all are funded by extramural sources and publish regularly in the physiological literature. We have approximately 30 graduate students and 25 postdoctoral scholars in our laboratories. There are weekly research seminars, journal clubs, and work-in-progress presentations by the graduate students. All of this is to say that we have a fairly large amount of research going on in the Department and we want every faculty member to contribute as an active investigator.

We use several measures to attempt to judge the likelihood that a recruit is capable of playing this role. First, we expect several publications in good journals and several years of postdoctoral experience. Although we usually have ideas about the subdiscipline that we would like the individual to represent, we are primarily interested in the quality of the person's work. We look forward to an outstanding research seminar when the individual visits the Department. We expect to hear a clear message concerning the importance of the work and why the individual is excited about continuing work in that field. We also look for evidence that it will be possible for us to support or enhance this person's research by collaborative efforts either within or outside of our Department and/or by supplying special equipment. We look for individuals with relatively broad training in research techniques and ideas because we feel a faculty member must be flexible and broadly trained if he expects to be productive over a long period of time. Letters of recommendation which come from a prospective

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faculty member's mentors and other associates are very important to us. These individuals are in the best position to know whether or not it is likely that the candidate is capable of the creativity and sustained and enthusiastic effort that is required if a person is to be successful in research.

We are also extremely interested in the candidate's interest in teaching. More than 300 medical students per year take two full introductory courses in human physiology and a similar course in veterinary physiology. We provide undergraduate courses for our 200 majors in Physiology as well as approximately 2,000 other undergraduate students each year. We teach several courses for our own graduate students, including cell and systems physiology and advanced seminars. Approximately 50 graduate students from other departments in the University also take our courses. Each faculty member gives an average of 40-50 lectures per year. In addition, he or she has several students at different stages of their development in the laboratory. In most courses, an instructor takes responsibility for the subdiscipline in which he/she does research. This means that although we give a comparatively large number of lectures each year, the subject matter for which each of us is responsible is relatively circumscribed and familiar. We do not feel overburdened with teaching, because we view teaching as an important part of our professional identity.

Because each of us has a relatively heavy teaching load, we want to be sure that a new faculty member will do his or her share with enthusiasm. We look for the following evidence that a person is likely to do well in the classroom. First, the research seminar provides an example of the candidate's skills as a teacher. Was the seminar well organized? Did the candidate communicate well with the audience? In our informal discussions we hope that the candidate will express an interest in teaching and his or her own ideas about how courses should be taught and students should be encouraged to learn. In this regard, we question the applicant very carefully about his interest in research training of graduate students as well as undergraduate and professional students. Finally, we are interested in knowing what experience the recruit has accumulated in teaching during graduate school and postdoctoral training. In some cases the letters of recommendation are helpful in assessing the quality of the applicant's teaching efforts.

A final part of our deliberation is whether or not we have an environment which can help the recruit to meet his or her own professional goals. Is the requisite equipment available or can we purchase it? Can we provide the amount and type of space the recruit needs for his research? Is the recruit likely to be happy in an atmosphere where team teaching and collaborative research projects are the norm? We have interviewed some very good applicants who may not be suited to the environment we can provide. On the other hand, there are others who are equally good and would thrive in our environment. We feel that it is our job to match our environment with the right recruit. This involves extremely frank discussions between the recruit and the incumbent faculty members. A two-day visit is usually sufficient to determine whether a particular recruit is at home in our environment, but if necessary we invite a candidate back for further discussion.

At the Careers Symposium in Cincinnati, more than one individual questioned whether it is possible for anyone to meet the lofty criteria enunciated by each of the speakers. I feel that it is possible and that it happens every time we have an open position and initiate the recruitment process. Perhaps it is unnecessary to state that we are not foolish enough to look for perfection. On the other hand, we have been able to find individuals who have great talent and enthusiasm for their chosen field and who look forward to the hard work required to sustain a productive career as a Physiologist.

Congressional Recess Schedule

The second session of the 98th Congress convened on January 23 for what is to be one of its shortest sessions in recent years. Aside from its usual recess periods the Congress will also be in recess for most of the summer for the nominating conventions and will adjourn on October 4 to campaign for reelection. The 1984 recess calendar:

	Senate	House
Easter	Apr 13–23	Apr 16–24
Memorial Day	May 25–30	May 25–30
Independence Day/Democratic Convention	Jun 29–Jul 23	Jul 2–23
Republican Convention	Aug 10–27	Aug 13–Sep 5*
Labor Day	Aug 31–Sep 5	
Adjournment	Oct 4	Oct 4

*Republican Convention and Labor Day.

Lab Animal Legislation by the Congress May Be Stopped by the Clock

Unless the Senate acts within the next several weeks—and with each passing day it seems more unlikely that it will act—the threat lessens that the Congress will approve new laboratory animal legislation this year.

The House, which passed its one bill (HR. 2350) involving laboratory animals, has been waiting since November for the Senate to act on similar legislation.

However, the two Senate bills concerned with laboratory animals continue to be tied up in committees, and the Senate has scheduled only 18 working days for the remainder of the year after it returns from the Easter recess on April 24. Adjournment of the 98th Congress is scheduled for the first week in October.

Of the two Senate bills, only one bill (S. 773) is similar to the House-passed bill: the legislative renewal of existing National Institutes of Health (NIH) authorizations. Amendments relating to the use of laboratory animals have been tacked onto both bills.

Added as amendments to the House version are provisions requiring NIH to establish a plan for the development of alternative methods; requirements that all NIH-funded grants involving the use of animals be monitored by an animal care committee; charging the Secretary of the US Department of Health and Human Services (HHS) to promulgate guidelines for the care and treatment of laboratory animals; and mandating an 18-month study on the use of animals in research by NIH grantees and the use of available alternative methods over the last five years.

The Senate's proposal for renewing NIH authorities has only one amendment concerning the use of animals, an 18-month study identical to the House bill but broadened to include all HHS-funded projects using animals. This bill, however, is stalled in the Committee on Labor and Human Resources because of concerns by Sen. Bob Packwood (R-OR) on another amendment restricting fetal research.

Indications now are that it could be several weeks before this bill is to be considered by the Committee if at all. Furthermore, it has been reported that Senate Majority Leader Howard Baker (R-TN) has told the Committee Chairman Orrin G. Hatch (R-UT) that there will be only three days for floor debate this year on all bills from his committee.

Because of the limited time the Congress plans to be in session this year and the restricted time for floor debate, there are indications that the Committee will not use its three days on the floor for discussion of renewal legislation but, rather, consider a continuing resolution for the renewal of NIH authorities. Continuing resolutions renew only the existing authorities and do not include amendments approved by either chamber.

The other Senate bill (S. 657) involving laboratory animals proposes amendments to the Animal Welfare Act. Hearings on the bill were held last summer by its sponsor Sen. Robert Dole (R-KS), but it has not been scheduled for consideration by the Committee on Agriculture, Nutrition, and Forestry.

Although Dole has agreed to modify his original bill including some of the recommendations made by the American Physiological Society at the hearings, the revised version has yet to be submitted to the Committee. Among the reasons stated for this are that the support in the Senate has ebbed and that no one in the House has expressed interest in sponsoring a companion bill. One basis for this reasoning is that this is an election year and no one wants to be embroiled in controversial legislation that can be put off until the 99th Congress.

Despite the fact that the clock may be running out on those who would promote new laboratory animal legislation this year, the proponents of such legislation are already making plans to renew their efforts when the next Congress convenes in January 1985.

Massachusetts Loses; Michigan Wins; Animal Welfare Bills Total 78

One state has passed legislation restricting the use of animals in research, and a total of 67 animal welfare bills are under consideration by general assemblies.

The one state where the general assembly has acted is Massachusetts, which now has one of the most stringent and broadest state controls on the use of animals in research as a result of a new law that goes into effect next October. The new law prohibits researchers from obtaining animals from pounds or outside the state, a restriction that is expected to increase at least five times the cost of using dogs for research, experimentation, and teaching.

While seven other states already have laws banning the release of pound animals from local shelters, Massachusetts is the only state that will close its borders to the import of animals from out of state.

The new law was pushed by a ProPet group, a coalition of animal welfare organizations, which stated that it preferred that lost or abandoned pets be destroyed rather than be used in research. Massachusetts reportedly destroys approximately 250,000 unclaimed dogs each year.

Although the animal rights advocates were successful in Massachusetts, the Jackson County, MI, County Commissioners denied by a 10-4 vote an appeal by animal rights activists to prohibit the release of pound animals to research institutions and educational facilities. However, the animal rights activists are proposing that the issue be placed on a referendum ballot in August.

Nationwide there have been at least 78 bills introduced so far this year at some level of government that would restrict the use of animals in research. This compares with 60 bills last year. Most of the proposed legislation has been focused on statehouses where 67 bills have been introduced.

William M. Samuels, CAE

Joint Meeting with the (British) Physiological Society, September 1985

The (British) Physiological Society has invited members of the American Physiological Society to be their guests at a joint meeting in Cambridge (UK) in September 1985. This will apparently be the first joint meeting of the two societies.

This is remarkable in view of the very close links which existed between the two societies in their early days and which, of course, have continued on an informal basis ever since. It is not generally appreciated that the first physiological journal in the English language had an editorial board composed of equal numbers of physiologists from Britain and the United States. This was the *Journal of Physiology,* which is now the chief journal of the (British) Physiological Society. The first volume appeared in 1878 following a letter from Professor Michael Foster in Cambridge to Henry P. Bowditch, Professor of Physiology at Harvard University suggesting a cooperative venture. The Editorial Board of the first volume consisted of three physiologists from England and three from the USA (Bowditch, Harvard; H. N. Martin, Johns Hopkins; and H. C. Wood, University of Pennsylvania). (Actually Martin was originally from the UK and returned to England later in life.) Foster was the Editor. In fact in 1890, R. H. Chittenden of Yale University replaced one of the English editors so that the Editorial Board was predominantly American. Naturally, when the *American Journal of Physiology* was started in 1898, the influence of the British-based journal waned.

The meetings of the (British) Physiological Society are rather different from those of the APS. Because the country is smaller, it is possible to have approximately eight meetings a year, most of these being in universities. Traditionally, Oxford and Cambridge host meetings during the summer. The meetings are generally only two days in length, with a dinner on the evening of the first day. Attendance at each meeting is on the order of 200-300 members.

The (British) Physiological Society has held a number of joint meetings with other national physiological societies, principally in Europe. Abstracts of papers delivered at these joint meetings are published in the *Journal of Physiology.* An interesting custom is that members of the Society who are present when the paper is delivered vote on whether the abstract should be published. Very occasionally the vote is negative; more often minor changes in the abstract are recommended.

A note on the name of the host society may be in order for APS members who plan to attend the meeting. The correct name is "The Physiological Society" and the absence of the name of the country has been variously viewed as an amiable eccentricity or a source of irritation. It will come as no surprise to stamp collectors because Britain is the only country in the world that does not indicate the origin of its postage stamps.

Although the meeting is 18 months away, it would be helpful to have some indication of the number of members who plan to attent the joint meeting. Please return the form below.

John B. West

REPLY TO: Physiological Society-APS Joint Meeting
c/o Dr. Orr E. Reynolds
9650 Rockville Pike
Bethesda, MD 20814

☐ I plan to attend the joint meeting in Cambridge in September 1985

☐ I plan to submit an abstract with a view to presenting a paper

Name _____

Address _____

_____

_____

City _____ State _____ Zip _____

APS Fall Meeting

August 26–31, 1984, Lexington, KY

The 35th Annual Fall Meeting of the American Physiological Society will be held August 26–31, 1984 in Lexington, KY. Registration will be located in the Lexington Center and will open at 2:00 P.M. on Sunday, August 26. Scientific Sessions—slide sessions, poster sessions, symposia, and tutorial lectures—will be scheduled in the Lexington Center and Hyatt Regency Hotel on Tuesday, August 28, through noon Friday, August 31. The APS Refresher Course will be held on Monday, August 27. The call for papers and general information will be mailed to members March 1, 1984.

Deadline for receipt of abstracts: May 14, 1984.

Symposia and Special Sessions (tentative titles)

- Loaded breathing: load compensation and respiratory sensation
- Current topics in neuroendocrine control of reproduction
- Quantitative approaches to the study of cardiovascular regulation
- Workshop: physiologist's approach to age-dependent changes in function
- Workshop: integrative approaches to physiology education
- Intrarenal hemodynamics
- Alteration in microcirculatory function during hypertension
- Vasoactive agents in control of the mesenteric circulation
- Neural control of renal function
- Chronophysiology and athletic performance
- Thermoregulation in the elderly

In addition to symposia, a series of tutorial lectures will be programmed. A special lecture titled, "Experiences of a blue grass physiologist in space," will be presented by Astronaut Story F. Musgrave.

Refresher Course

Determinants of oxygen uptake during exercise, organized by Daniel Richardson and Bryant Stanford

Bowditch Lecture

Glycoprotein hormone genes: hormonal regulation of expression, by William W. Chin

For further information: APS Fall Meeting Office, 9650 Rockville Pike, Bethesda, MD 20814. Telephone 301/530-7010.

Statistics on APS Membership
(As of February 1984)

Total Membership 6187

Distribution by Employment*

	No.	%
Medical Schools	3625	65
Physiology Departments	(1906)	(34)
Other Preclinical Departments	(455)	(8)
Clinical	(1209)	(22)
Administration	(52)	(1)
Hospitals and Clinics	241	4
Veterinary Schools	107	2
Dental Schools	50	1
Public Health and Graduate Schools	205	4
Undergraduate Schools	469	8
Commercial Companies	113	2
Government	342	6
Institutes and Foundations	217	4
Private Practice	46	1
Other Emeritus or Inactive	126	2

*5541 Respondents

Distribution by Earned Degree*

(Includes 668 individuals with multiple doctorate degrees)

	No.
Ph.D.	3735
M.D.	2159
D.V.M.	134
D.D.S. and other	28

*5388 Respondents

Principal Type of Work*

	%
Research	70
Teaching	16
Administration	7
Clinical	6
Other	1

*5544 Respondents

Distribution by Primary Specialty*

	%
Cardiovascular	21
Neurophysiology	13
Respiration	10
Endocrines	9
Renal	6
Electrolyte and Water Balance	5
Muscle and Exercise	5
Gastrointestinal, Food and Nutrition	4
Cellular and Tissue	4
Environmental	3
Blood	2
Comparative	2
Energy Metabolism and Temperature Regulation	2
Pharmacology	2
Reproduction	2
All Other Categories (None above 1%)	9

5432 Respondents

Distribution by Age*

	No.
70+	542
60–69	930
50–59	1572
40–49	1868
30–39	1120
20–29	76

*Optional personal data (numbers represent total respondents.)

Distribution by Sex*

Female	659
Male	5328

*Optional personal data (numbers represent total respondents.)

States in U.S. With More Than 100 Members*

California	661	Florida	156
New York	619	North Carolina	155
Texas	337	New Jersey	149
Pennsylvania	326	Missouri	140
Maryland	325	Virginia	125
Massachusetts	311	Connecticut	120
Illinois	287	Minnesota	115
Ohio	226	Wisconsin	108
Michigan	178	Tennessee	101

*50 States plus Puerto Rico and Virgin Islands.

Distribution by Racial Background and Heritage*

American Indian or Alaskan	7
Asian or Pacific Islander	239
Black	31
White	4215
Hispanic Heritage	81

*Optional personal data (numbers represent total respondents).

APS North American Membership

United States	5808
Canada	238
Mexico	10

Canadian Provinces With 5 or More Members

Ontario	93
Quebec	63
Alberta	22
British Columbia	21
Manitoba	19
Nova Scotia	10
Saskatchewan	7

Other provinces represented:
- New Brunswick
- Yukon Territory

APS Membership Outside North America

Countries with 5 or more members	
Japan	28
Germany, Federal Republic	23
United Kingdom	21
Switzerland	16
Australia	10
France	10
Sweden	10
Israel	9
Italy	9
Norway	6
Denmark	5
Venezuela	5
Belgium	5
Argentina	5
Spain and Canary Islands	5
Greece	5
Netherlands	5

Other countries represented

Austria	Panama
Brazil	Paraguay
British West Indies	Peoples Republic of China
Chile	Peru
Dominican Republic	Poland
Finland	Portugal
Hong Kong	South Korea
Hungary	Rhodesia
Iceland	Saudi Arabia
Indonesia	Singapore
Jamaica	South Africa
Kuwait	Taiwan
Lebanon	USSR
New Zealand	Yugoslavia
Nigeria	

ASSOCIATION OF CHAIRMEN OF DEPARTMENTS OF PHYSIOLOGY

ANALYSIS OF ANNUAL QUESTIONNAIRE - 1983/84

Type of Institution:

Physiology Dept. in a MEDICAL (89) or a NON-MEDICAL* (5) school. Total = 94

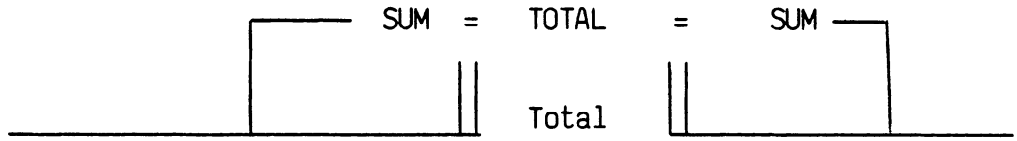
*Specify type of school: Veterinary (3); Institutional Res.(1); Land-Grant University(1)

Affiliation: PUBLIC (64) or PRIVATE (30).

Faculty Statistics:*

Bold numbers equal grand totals.
Numbers in light italic are
the means per department.

Numbers of faculty with academic appointments (regular or joint) in your department:



	Degrees Held				Number of Faculty	Tenured	Not Tenured
	Ph.D.	M.D.	Both	Other			
Entire salary through your department:							
Full time	998 *10.61*	92 *.97*	62 *.65*	50 *.53*	1213 *12.9*	756 *8.04*	423 *4.5*
Part time	33 *.35*	8 *.08*	3 *.03*	9 *.09*	51 *.54*	20 *.21*	33 *.35*
Part of salary through your department, and associated with:							
another basic sci. dept.	33 *.35*	8 *.08*	1 *.01*	2 *.02*	40 *.42*	18 *.19*	21 *.21*
a clinical dept.	31 *.32*	11 *.11*	4 *.04*	2 *.02*	47 *.50*	21 *.22*	23 *.24*
No salary through your department, and associated with:							
another basic sci. dept.	112 *1.19*	5 *.05*	8 *.08*	8 *.08*	119 *1.26*	58 *.61*	44 *.46*
a clinical dept.	173 *1.84*	135 *1.43*	24 *.25*	5 *.05*	333 *3.54*	144 *1.53*	141 *1.5*
Other (Emeritus, volunteers, etc.)	176 *1.87*	65 *.69*	21 *.22*	8 *.08*	260 *2.76*	50 *.53*	129 *1.37*

*In a correctly completed questionnaire, for each category of faculty listed on the left, the sum of the first four columns (Ph.D., M.D., Both, and Other) should equal the sum of the last two columns (Tenure and Non-tenure), and this number should be entered under "TOTAL". The combined data above are not internally consistent in this regard since we included all data received, even though a few questionnaires were completed incorrectly.

D. Unfilled Positions:

Please indicate the number of unfilled positions in each rank in your department:

Professor 20 (.21) Assistant Professor 55 (.58)

Associate Professor 13 (.13) Instructor 4 (.04)

How many of the unfilled positions are due to:

Retirement? 9 (.09) Failure to promote/tenure? 17 (.18) Death? 4 (.04)

Creation of new FTE's? 29 (.3) Others (resignations, etc.) 25 (.26)

Project number of junior positions expected to become vacant in the next 5 years due to retirement, new FTE's, etc.

yr. 1	yr.2	yr. 3	yr. 4	yr. 5
44 (.46)	49 (.52)	33 (.35)	28 (.29)	28 (.29)

E. Current Graduate Students and Postdoctoral Fellows:

Number of graduate students currently enrolled in Department Ph.D. program 991 (10.54)

Number of Postdoctoral Fellows currently in your Department 534 (5.68)

Number of vacant Postdoctoral positions 52 (.55)

F. Training Support:

Do you have a training grant that supports predoctoral trainees? YES (35) NO (58)

Do you have a training grant that supports postdoctoral trainees? YES (35) NO (57)

	Predoctoral	Postdoctoral
What is the average starting stipend for trainees?	$ 5,845	$ 14,689
What number of your predoctoral and postdoctoral trainees are supported by:	Mean (No. of Depts.)	
Training grants?	5.4 (35)	3.33 (30)
Individual federally funded awards?	3.36 (11)	2.23 (43)
Research grants?	4.55 (49)	4.19 (47)
State funds?	6.02 (42)	1.7 (10)
Private foundations?	1.77 (18)	3.11 (18)
Institutional awards?	4.02 (37)	1.38 (13)
Medical Scientist Training Programs?	2.75 (8)	1.25 (4)
Other? List. Foreign government (18); Military (3); Misc. other (3)	2.29 (20)	1.71 (7)

G. Numbers of trainees who have finished Doctoral or Postdoctoral work during the year ending June 30, 1983:

	Doctoral	Postdoctoral
Total number finishing:	153	132
Females	32	30
Blacks	2	1
Other Minorities	8	14
Position Needed	2	0
Research Area:		
Cardiovascular	52	36
Cell/Tissue	32	20
Compárative	5	1
Endocrine	49	29
Environmental	4	1
Gastrointestinal	5	4
General	29	8
Muscle/Exercise	9	5
Neural	31	33
Renal	8	10
Respiratory	8	7

Please assess the degree of satisfaction of your graduates in regard to their opportunities in the job market:

Very Pleased (6) Pleased (39) Neutral (21) Disappointed (4)

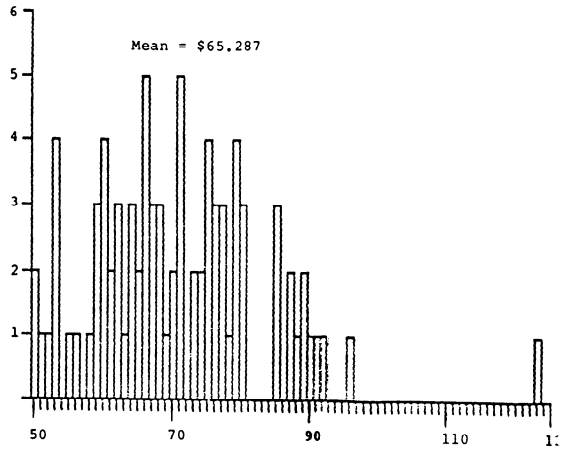
Very Disappointed (2)

How many postdoctoral students are presently taking additional training because they are unable to find a satisfactory position? 23

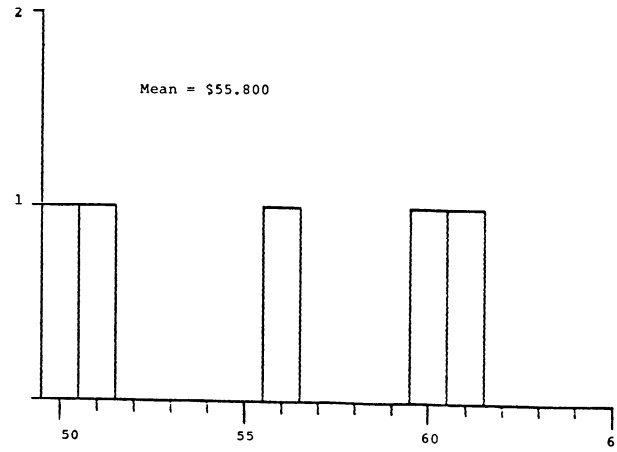
Years of service as chairman: Private Medical - 8.23 (30);

Public Medical - 8.03 (59); Non-medical - 4.19 (5)

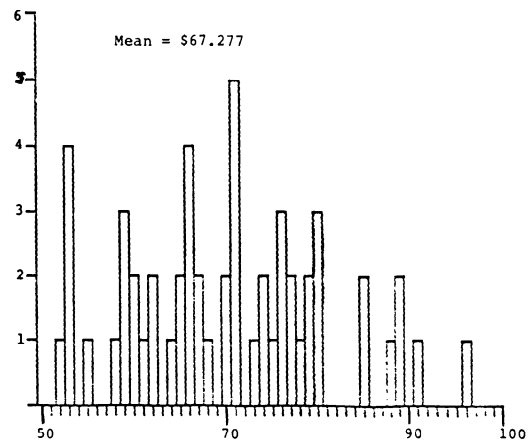
FACULTY SALARIES (in thousands)



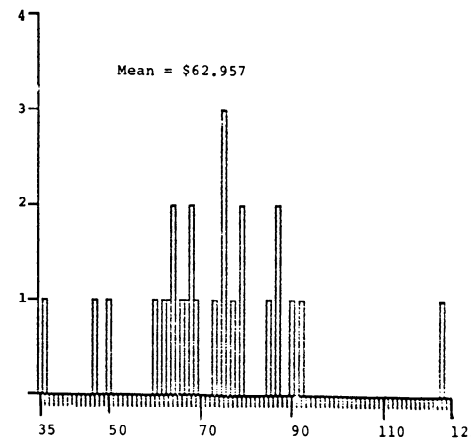
ALL SCHOOLS CHAIRMEN'S SALARIES



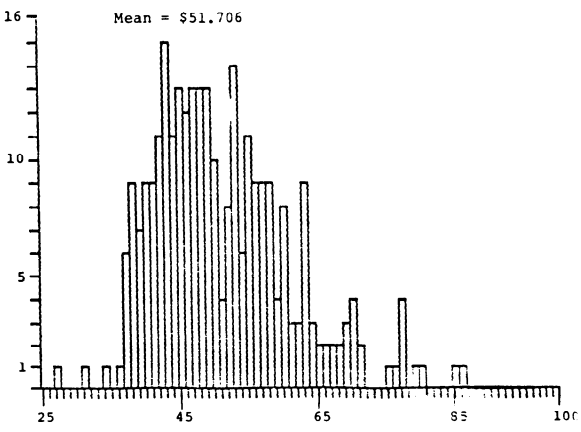
NON-MEDICAL CHAIRMEN'S SALARIES



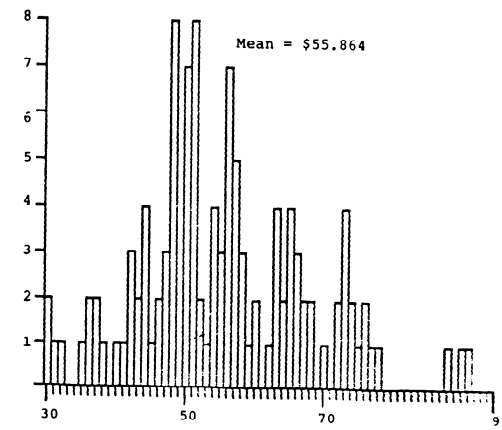
PUBLIC MEDICAL CHAIRMEN'S SALARIES



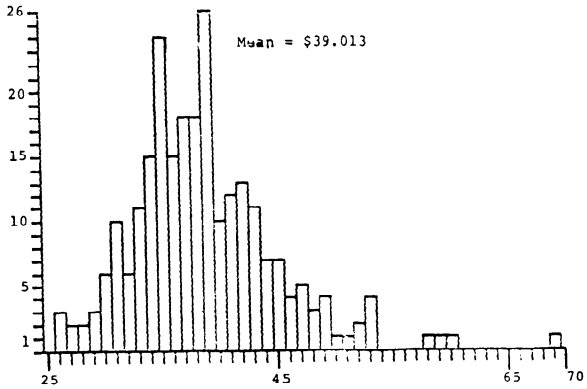
PRIVATE MEDICAL CHAIRMEN'S SALARIES



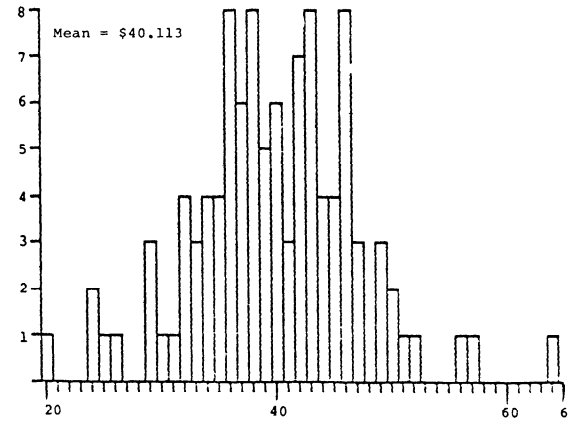
PUBLIC MEDICAL PROFESSOR'S SALARIES



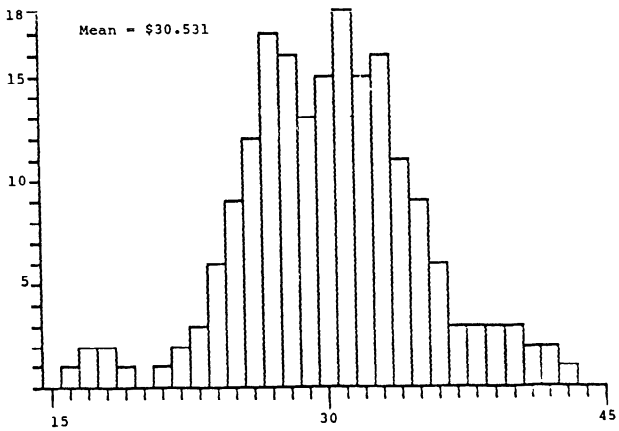
PRIVATE MEDICAL PROFESSOR'S SALARIES



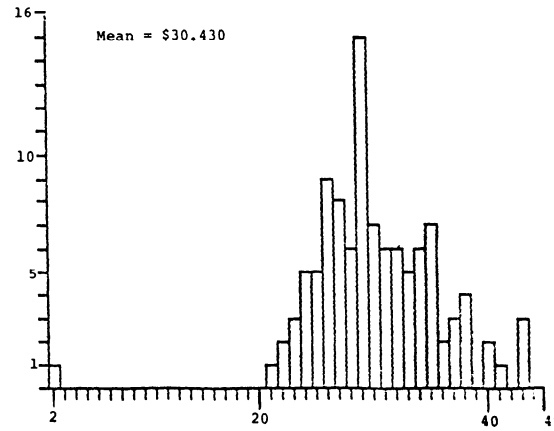
PUBLIC MEDICAL ASSOCIATE PROF. SALARIES



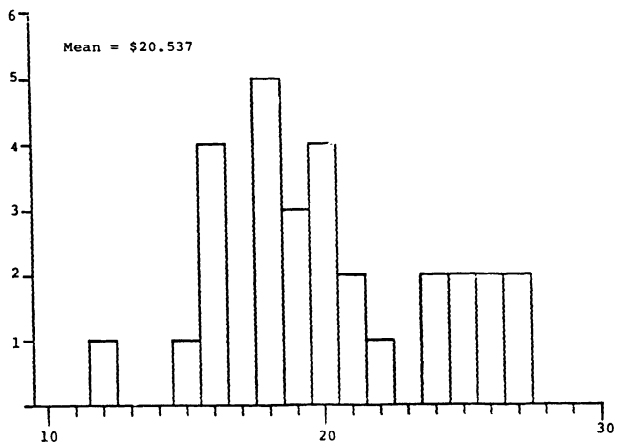
PRIVATE MEDICAL ASSOCIATE PROF. SALARIES



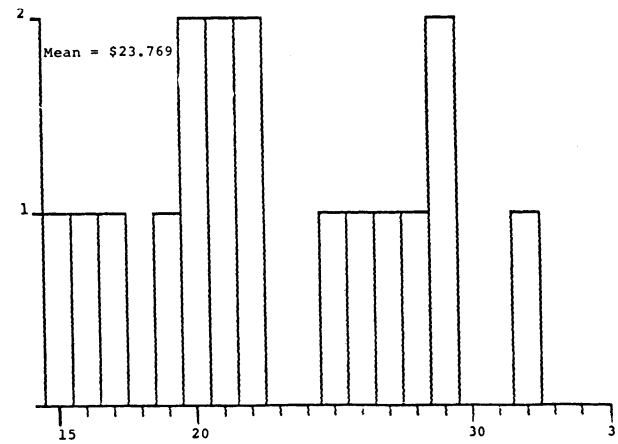
PUBLIC MEDICAL ASSISTANT PROF. SALARIES



PRIVATE MEDICAL ASSISTANT PROF. SALARIES



PUBLIC MEDICAL INSTRUCTORS' SALARIES



PRIVATE MEDICAL INSTRUCTORS' SALARIES

DEPARTMENTAL BUDGET*

	Institutional Sources	Outside Research Grants	Training Grants	Other Budget Support	Total
Private Med.	636,286 (29)	986,109 (28)	125,094 (15)	180,387 (16)	1,769,502 (29)
Low	95,500	47,800	2,956	5,500	95,500
High	2,326,700	3,236,600	538,734	1,048,381	5,648,400
Public Med.	742,656 (59)	894,037 (58)	116,457 (26)	160,444	1,610,300 (58)
Low	35,399	5,000	24,000	3,734	2,859
High	1,851,678	3,232,218	463,689	1,601,570	5,600,292
Non-Med.	892,087 (5)	1,029,102 (5)	164,947 (3)	589,675 (3)	2,373,963 (5)
Low	242,000	500,000	75,841	60,000	1,293,679
High	1,500,000	1,600,000	339,000	1,619,197	4,019,136
Combined	717,521 (93)	929,788 (91)	122,707 (44)	191,949 (51)	1.701,986 (92)

*Mean expenditures (in dollars) of schools reporting funding. Zero amounts were not included in computation of means or in range setting. The number in parentheses is the total number of departments reporting expenditures in that category.

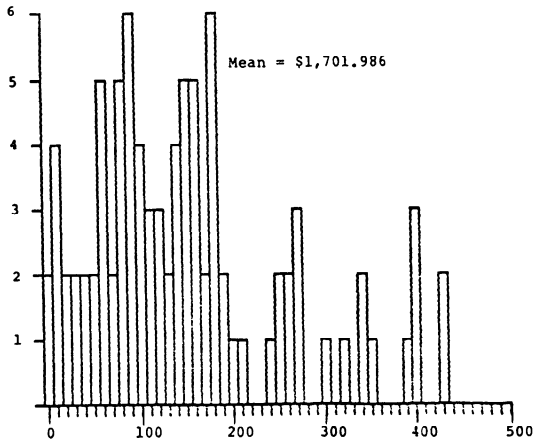
DEPARTMENTAL SPACE**

	Research	Teaching Labs	Other	Total	Mean No. of Full-Time Faculty
Private Medical	12,132 (30)	4,049 (30)	3,566 (30)	17,293 (30)	11.86
Public Medical	13,288 (56)	3,851 (56)	5,287 (56)	19,418 (56)	14.1
Non-Medical	14,683 (5)	6,233 (5)	7,832 (5)	27,181 (5)	13.39

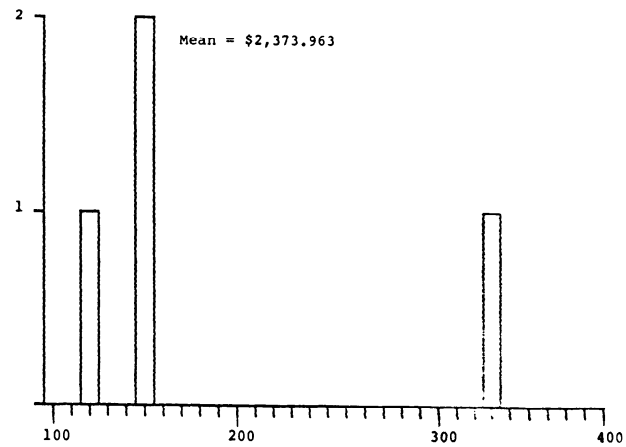
**Mean amount of space (in square feet) for schools reporting space data. Zero amounts were not included in computation of these means. The number in parentheses is the total number of departments reporting space in that category.

TOTAL DEPARTMENTAL BUDGETS

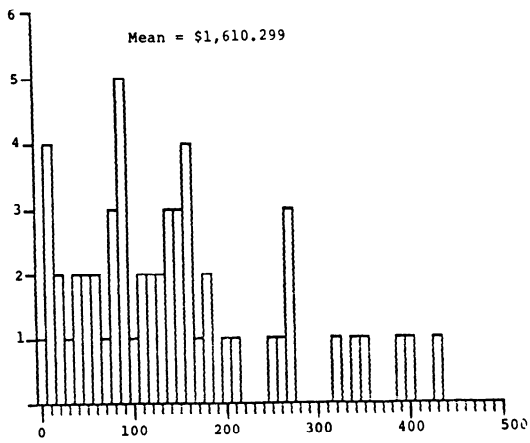
(in tens of thousands)



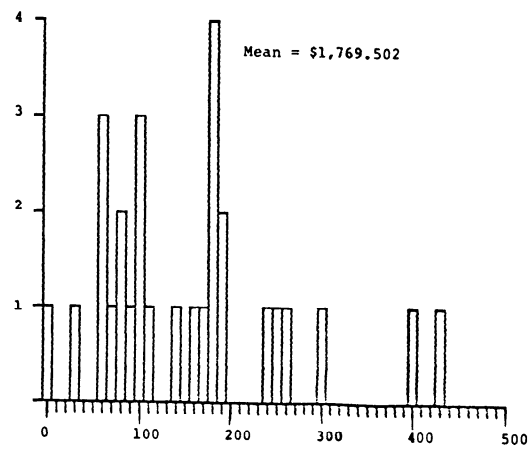
ALL SCHOOLS DEPT. BUDGETS TOTAL



NON-MEDICAL DEPT. BUDGETS TOTAL

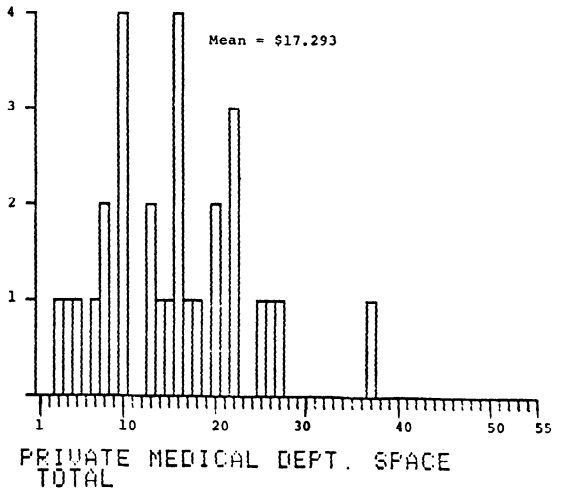


PUBLIC MEDICAL DEPT. BUDGETS TOTAL

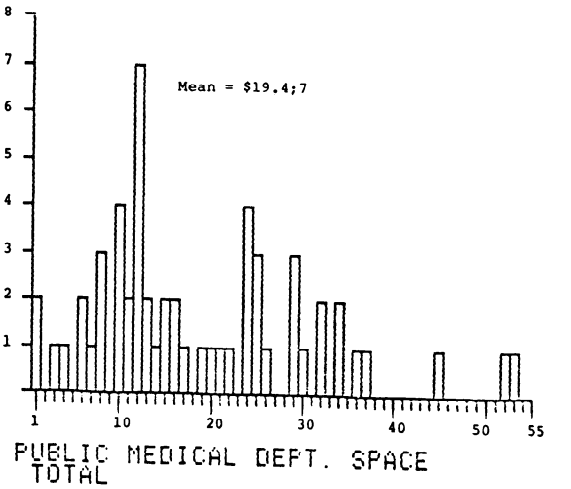


PRIVATE MEDICAL DEPT. BUDGETS TOTAL

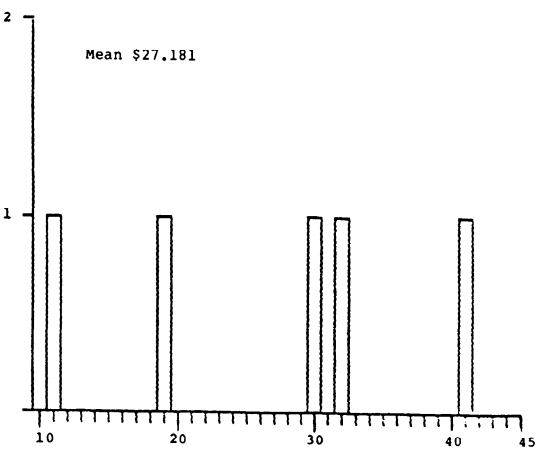
TOTAL DEPARTMENTAL SPACE
(in thousands of square feet)



PRIVATE MEDICAL DEPT. SPACE TOTAL



PUBLIC MEDICAL DEPT. SPACE TOTAL



NON-MEDICAL DEPT. SPACE TOTAL

1983/84 ACDP QUESTIONNAIRE
ADDENDUM

Comments

The data presented in the Table address the issue of the amount of time available to present the material in each type of course, broken down by type of instruction.

Course types beyond the first four were included in the "other" category by the respondents.

The distribution between "graduate" and "special graduate" was not clear, but the results of these two do not differ greatly. Probably most of the courses in each category are specialized in the sense that they are not comprehensive.

Some medical courses are actually presented over two semesters but they are listed here as a single comprehensive course.

The "special medical" category includes some courses for house staff.

There undoubtedly was some cross-over between "allied health" and "undergraduate", the latter of which appeared under the "other" category.

Note that the average teaching load per faculty member (in contact hours per year) is given as a separate number below the table.

			AVERAGE NUMBER OF HOURS DEVOTED TO THESE TYPES OF INSTRUCTION ON A PER COURSE BASI			
TYPES OF COURSE	N1*	N2*	AVG. # OF STUDENTS	LECTURE	WET LAB	COMPUTER BASED	OTHER
ALLIED HEALTH	65	88	109.9	65.07	13.94	1.06	7.39
DENTAL	21	22	100.22	71.54	15.09	3.09	16.95
GRADUATE	86	242	10.68	48.66	9.33	1.45	8.26
MEDICAL	76	76	138.07	108.56	37.28	2.25	29.38
NEUROPHYSIOLOGY	7	7	103.14	49.57	25.14	.14	10.14
PODIATRY	1	1	100	60	0	0	20
SPECIAL MEDICAL	13	18	34	39.94	8.05	2.77	40.44
UNDERGRADUATE	15	24	101.58	44.54	16.75	.04	5.95
VETERINARY	5	5	106	111.6	36	0	7
SPECIAL GRADUATE	4	17	10	43.52	0	0	0
OPTOMETRY	2	2	193	62.5	20	0	10

* N1= NUMBER OF SCHOOLS, N2= NUMBER OF COURSES

TOTAL NUMBER OF SCHOOLS INCLUDED IN ADDENDUM IS 81

THE AVERAGE TEACHING LOAD PER FULL TIME FACULTY IS 72.21 HRS./YR.

MEDICAL PHYSIOLOGY COURSE QUESTION TYPES:
SHORT ANSWER 92.6 %
ESSAY 7 %
ORAL .39 %

NUMBER OF INSTITUTIONS WHICH REQUIRE PASSING
PART I OF THE NATIONAL BOARD EXAMINATION: 47

NUMBER OF INSTITUTIONS WHICH USE THE PHYSIOLOGY SECTION
OF THE NATIONAL BOARD EXAM IN THEIR COURSE: 22

INSTRUCTIONS FOR APPLYING FOR APS MEMBERSHIP

CURRENT APPLICATION FORMS

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

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

GENERAL INSTRUCTIONS

FOR ALL CATEGORIES:

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

Alien Residents. Canadian residents should furnish a copy of "Landed Immigrant Status" form. Mexican residents should furnish a copy of their form FM-2.

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

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

DO NOT INCLUDE A CURRICULUM VITAE

Send no reprints.

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

QUALIFICATIONS (Except Students):

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

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

SPONSORS:

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

Each sponsor should write an independent confidential letter about the candidate using the five categories listed above to evaluate the candidate. Furnish an original and 7 copies to the Membership Secretary.

CHECK LIST:

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

Membership Secretary
American Physiological Society
9650 Rockville Pike
Bethesda, Maryland 20814

SPECIAL INFORMATION AND INSTRUCTIONS

FOR REGULAR MEMBERSHIP

Bylaws of the Society:

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

Duties and Privileges:

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

FOR CORRESPONDING MEMBERSHIP

Bylaws of the Society:

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

Duties and Privileges:

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

FOR ASSOCIATE MEMBERSHIP

Bylaws of the Society:

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

Duties and Privileges:

Same as for Regular Members except for the privilege of:

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

FOR STUDENT MEMBERSHIP

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

Bylaws of the Society:

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

Duties and Privileges:

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

Submit original and 7 copies of application and supporting documents.

APPLICANT'S LAST NAME _____

Date _____

THE AMERICAN PHYSIOLOGICAL SOCIETY
9650 Rockville Pike, Bethesda, MD 20814

MEMBERSHIP APPLICATION FOR:

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

CURRENT MEMBERSHIP CATEGORY; YEAR ELECTED _____

See Instructions

Name of Applicant: _____
First Middle Last

Mailing Address _____ Birth Date: _____

Citizenship: _____

Country of Permanent Residence:* _____

Telephone No.: _____

* Alien residents of Canada and Mexico see General Instructions. Alien residents of U.S. enter Alien Registration Receipt Card number _____.

1. EDUCATIONAL HISTORY

Dates	Degree	Institution	Major Field	Advisor

Doctoral Dissertation Title: (if any)

Postdoctoral Research Topic:

2. OCCUPATIONAL HISTORY

Present Position:

Prior Positions:

Dates	Title	Institution	Department	Supervisor

SPONSORS

#1. Name: _____ #2. Name: _____

Mailing Address: _____ Mailing Address: _____

Telephone No. Zip Code Telephone No. Zip Code

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

#1 Signature _____ #2 Signature _____

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

APPLICANT'S LAST NAME _____

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

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

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

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

List other scientific societies of which candidate is a member:

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

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

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

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

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

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

DO NOT INCLUDE A CURRICULUM VITAE

THE AMERICAN PHYSIOLOGICAL SOCIETY

9650 Rockville Pike, Bethesda, MD 20814

MEMBERSHIP RECORDS QUESTIONNAIRE

PLEASE MARK ALL ENTRIES IN RED.

CURRENT MAILING LABEL OR
PRINT NAME & ADDRESS

DATE _____

DATE OF BIRTH

Month Day Year

EMERITUS MEMBERS:
Check, if you would consider temporary or part time employment ☐

OPTIONAL PERSONAL DATA

SEX

☐ Female ☐ Male

A ☐ American Indian or Alaskan Native
B ☐ Asian or Pacific Islander
C ☐ Black
D ☐ White E ☐ Hispanic

POSITION TITLE CODE (SEE REVERSE) ☐

TYPE OF INSTITUTION Check one. (If retired, or unemployed check descriptors appropriate to last position held.)

MEDICAL SCHOOLS

33 _____ Physiology Departments
34 _____ Other Preclinical Departments
35 _____ Clinical
36 _____ Administration

OTHER

37 _____ Hospitals and Clinics
38 _____ Veterinary Schools
39 _____ Dental Schools
40 _____ Public Health and Graduate Schools
41 _____ College or University
42 _____ Commercial Companies
43 _____ Government (Inc. V.A.)
44 _____ Institutes and Foundations
45 _____ Private Practice
99 _____ Other (Specify)

EARNED DEGREE CODE (SEE REVERSE) NOT MORE THAN TWO ☐ ☐

MAJOR TYPE OF WORK (Check not more than one.)

04 _____ Research 05 _____ Teaching 06 _____ Administration 07 _____ Clinical

SECONDARY TYPE OF WORK (Check one only if it represents a significant portion of time and is different from your major type of work.)

04 _____ Research 05 _____ Teaching 06 _____ Administration 07 _____ Clinical

PRIMARY INTEREST AREA: (Enter the appropriate number from the list of interest area codes on the reverse also enter the letter under the area selected which best describes your specific interest.)

☐☐ MAJOR AREA ☐ SPECIFIC INTEREST

SECONDARY INTEREST AREA (If appropriate)

☐☐ MAJOR AREA ☐ SPECIFIC INTEREST

IF YOU HAVE SERVED ON A GROUP OR COMMITTEE WHICH IS ADVISORY TO THE GOVERNMENT CHECK AS APPROPRIATE.

A _____ Presidents Scientific Advisory
B _____ National Academy of Sciences
C _____ National Institutes of Health
D _____ Nat'l Aeronautical and Space
E _____ Dept. of Interior
F _____ Dept. of Defense (or Constituent Dept.)
G _____ Dept. of Agriculture
H _____ Congressional (Specify)

IF YOU HAVE EVER SERVED ON THE FOLLOWING APS GROUPS PLEASE CHECK AS APPROPRIATE.

A _____ Council
B _____ Education Committee
C _____ Finance Committee
D _____ Membership Committee
E _____ Program Committee
F _____ Publications Committee
G _____ Editorial Board (Specify)
H _____ Session Chairman
I _____ Symposia Speaker
J _____ Public Affairs
K _____ Public Information
L _____ Senior Physiologists
M _____ Porter Development
N _____ Animal Care & Experimentation
O _____ Committee on Committees
P _____ Centennial
Q _____ Financial Development
R _____ Career Opportunities in Phys.
S _____ Educational Materials Review Board

I AM A MEMBER OF THE FOLLOWING NATIONAL PROFESSIONAL SOCIETIES: Outside of FASEB:

A _____ American Association of Anatomists
B _____ American Institute of Biological Sciences
C _____ American Chemical Society
D _____ American Society for Cell Biology
E _____ American Society for Clinical Investigation
F _____ American Society of Mechanical Engineers
G _____ American Society of Microbiology
H _____ American Society for Neurochemistry
I _____ American Society of Plant Physiologsts
J _____ American Society of Zoologists (DCP&B)
K _____ Association of Chairmen of Departments of Physiology
L _____ Biomedical Engineering Society
M _____ Biophysical Society
N _____ Endocrine Society
O _____ Institute of Electrical and Electronic Engineers
P _____ Society of General Physiologists
Q _____ Society for Neuroscience
R _____ Canadian Phys. Society
S _____ American Medical Association
Z _____ Other (Specify)_____

POSITION TITLE CODES (use most closely related description)

A. Director or Deputy
B. Chairman
C. Professor
D. Research Associate
E. Sr. Research Associate
F. Associate Professor
G. Assistant Professor
H. Laboratory or Research Director
I. Institute Director
J. Dean or Associate Dean
K. Executive Secretary
L. Academician
M. Corresponding Academican
N. Private Practice or Consultant
0. Researcher
P. Medical Intern
Z. Other

EARNED DEGREE CODES

CODE	DESCRIPTION
01	PH.D. or Dr. Phil.
03	M.D. or Dr. Med.
05	D.V.M. or Dr. Vet.
06	ScD.
07	D.D.S., D. Odont or D.O.
10	ED.D or Dr. Ed.
25	Cand. Med.

INTEREST AREA CODES

01. Anesthesia

02. Anatomy and Embryology
A. Microscopic
B. General
C. Fetal physiology

03. Anthropology

04. Biochemistry
A. General
B. Clinical

05. Biophysics

06. Biomedical Engineering

07. Blood
A. General
B. Erythrocytes
C. Hematology
D. Cell formation
E. Volume
F. Coagulation
G. Platelets
H. Plasma proteins
I. Rheology

08. Cardiovascular
A. General
B. Heart
C. EKG
D. Cardiac output
E. Artificial heart
F. Coronary
G. Cardiac dynamics
H. Cardiology
I. Blood flow
J. Peripheral circulation
K. Hemodynamics
L. Hypertension
M. Blood pressure
N. Atherosclerosis
O. Hemorrhage
P. Blood capillaries
Q. Venous return
R. Shock
S. Pulmonary circulation
T. Splanchnic circulation
U. Control

09. Cellular and Tissue
A. Cytology
B. Mitochondria
C. Protoplasm
D. Cell membranes
E. Cell surface chemistry
F. Histochemistry
G. Electron microscopy
H. Tissue culture
I. Tissue metabolism
J. Tissue elasticity
K. Connective tissue

10. Comparative Physiology
A. General
B. Insects
C. Fish
D. Reptiles
E. Avian
F. Plants
G. Marine biology
H. Crustacean
I. Mammalian

11. Electrolytes and Water Balance
A. General
B. Active transport
C. Ion transport
D. Body fluids
E. Lymph
F. Salt and water balance

12. Endocrines
A. General
B. Neuroendocrines
C. Pituitary
D. Thyroid
E. Parathyroid
F. Insulin
G. Adrenal/Medulla
H. Adrenal cortex
I. Sex hormones

13. Energy Metabolism & Temperature Regulation
A. Energy metabolism
B. Calorimetry
C. Exercise
D. Fatigue
E. Temperature regulation

14. Environmental
A. Aviation
B. High Altitude
C. Space Medicine
D. Underwater
E. Bioclimatology
F. Hypothermia and cold
G. Hibernation
H. Shivering
I. Adaptation
J. Hyperthermia and heat
K. Sweating
L. Industrial health
M. Air pollution

15. Enzymes
A. General
B. Kenetics
C. Antienzymes
D. Digestive enzymes

16. Gastrointestinal
A. General
B. Deglutation
C. Gastric secretion
D. Gastric mucosa
E. Gastroenterology
F. Pancreatic juice
G. Absorption
H. Intestinal motility
I. Digestion
J. Gastrointestinal surgery
K. Salivary secretion
L. Intestinal secretion
M. Gastric Motility

17. General Physiology

18. Gerontology
A. Aging
B. Degenerative diseases
C. Geriatrics

19. Immunology

20. Liver and Bile

21. Lipids and Steroids
A. General
B. Fat metabolism
C. Cholesterol metabolism
D. Obesity
E. Fatty acids
F. Other (Specify)

22. Microbiology
A. General
B. Bacteria
C. Viruses
D. Yeasts
E. Cancer cells

23. Minerals, Bone and Teeth
A. General
B. Bone
C. Calcium metabolism
D. Calcification
E. Dental caries
F. Mineral metabolism

24. Muscle and Exercise
A. General
B. Muscle metabolism
C. Muscular contraction
D. Skeletal muscle
E. Heart muscle
F. Smooth muscle
G. Muscle cells
H. Muscle chemistry
I. Muscle enzymes
J. Muscle-physical processes

24. Muscle and Exercise (Cont'd)
K. Muscle-nerve
L. Exercise

25. Neurosciences
A. General
B. Brain
C. EEG
D. Cerebral cortex
E. Mid brain
F. Brain stem
G. Spinal cord
H. Autonomic regulation
I. Peripheral nerve
J. Nerve cells
K. Vision and optics
L. Hearing and acoustics
M. Taste
N. Speech
O. Other senses
P. Sleep
Q. Learning
R. Behavior
S. Conditioned responses
T. Comparative
U. Neurological diseases
V. Psychiatry
W. Psychology
X. Cerebellum
Y. Hypothalamus
Z. Pain
Reflexes

26. Nutrition and Food
A. General
B. Diet
C. Nutritional value of foods
D. Chemistry of foods
E. Vitamins
F. Digestion
G. Carbohydrate metabolism
H. Protein metabolism
I. Fat metabolism
J. Nutritional diseases

27. Pathology

28. Pharmacology
A. Pharmacodynamics
B. Evaluation of drugs
C. Autonomic drugs
D. Cardiac drugs
E. Anticonvulsant drugs
F. Analgesics
G. Toxicology
H. Therapeutics
I. Chemotherapy
J. Antibiotics
K. Neuropharmacology

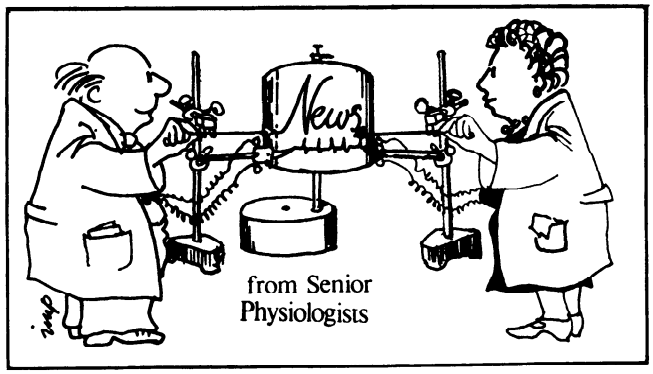
29. Radiology
A. Radiobiology
B. Ionizing radiation
C. Ultra-violet
D. Thermal burns
E. Cosmic rays

30. Renal
A. General
B. Tubular
C. Urinary tract
D. Renal disease
E. Comparative
F. Diuretics
G. Artificial Kidney

31. Reproduction
A. Fertilization
B. Pregnancy
C. Fetal physiology
D. Lactation
E. Obstetrics & Gynecology

32. Respiration
A. Pulmonary physiology
B. Respiration mechanics
C. Pulmonary diffusion
D. O_2 and CO_2 transport
E. Tissue respiration
F. Anoxia
G. O_2 poisoning
H. Asphyxia
I. Respiratory diseases
J. Chest diseases
K. Hypercapnia
L. Artifical lungs
M. Resuscitation
N. Control

99. Other
Z. Other



William C. Buchbinder to Edward Adolph:

It was very touching to have received from you, on behalf of the Society, congratulations on my 90th birthday. I thank you! I remember well having traveled with the gang from the University of Chicago—all my good friends, Carlson, Luckhardt, Ivy, and others—to a meeting in Rochester at the Strong Memorial Hospital, where I read a paper with solemn Lusk just in front of me who terrorized me with questioning. It was the day in 1927 when Cannon demonstrated his famous cat stripped of its sympathetic nervous system. Your Supplement on "Physiological Integrations in Action" I read with care and interest. If I may slightly alter a quote of Shelley, you remain "one of the trumpets which sing to battle."

1860 Berkeley Rd.
Highland Park, IL 60035

Arthur W. Martin to Bob Alexander:

Looking back I note that in 1977 it was *Nautilus* kidneys that enthralled me; then in 1979 I was reporting on spiders and worms, in addition to cephalopods. By 1981 the most promising, and least expensive, lines were water balance in slugs (which proved to be sensitive to ADH and to AVT-like neuropeptides) and metalloproteins in invertebrates. These proteins turned out to be transferrins, which we now think will be nearly ubiquitous in the invertebrate phyla, already clearly being present in both protostome and deuterostome lines. So now, in 1984, I am pleased to report that I am enjoying fairly good health, get to the laboratory almost every day, have been accepted into the laboratory of a colleague when I lost my own laboratory in 1981, and am having the greatest of fun with challenging modern concepts and the easier methods.

Slugs continue to be profitable study material, as indeed they should, being so high in the molluscan evolutionary tree. Where we tend to think of them as simple, they deceive us with eclat. Because they secrete mucus in slow motion, we have been able to isolate steps in mucus formation that we think may be surprisingly general. In vertebrates the steps are very rapid; nevertheless other investigators are finding very similar things, for example, in hagfishes. We hope the work will be useful. On the transferrin side, that of a simple ascidian turns out to be the so-far missing monosited protein. Probably a gene doubling led to the change in molecular weight from about 40,000 to about 80,000. As Williams has shown, this prevented the two-sited transferrin from being lost from filtration kidneys. A size increase was of no concern to ascidians, which have no identifiable kidneys, and may be true of other deuterostomes. In the protostome line, where filtration kidneys are common, transferrins may be of higher molecular weight, like that of a crab at 150,000. Nevertheless these proteins transfer iron to the receptors of rat reticulocytes.

I am now at the stage where a Ph.D. of my own training has retired, with another soon to follow. Though retired, the intellectual life has been so rewarding that I recommend it to my younger colleagues with all best wishes.

Dept. of Zoology
University of Washington
Seattle, WA 98105

H. Hugh Dukes to Bob:

About 1½ years ago I completed a "History of the Department of Physiology of the New York State College of Veterinary Medicine, the Middle Years: 1932–1960." This was distributed in Xerox form as it was too long for *The Physiologist*. I also coauthored, with William Hansel and Ellis Leonard, "A backward look far above Cayuga's water," which was published in *The Physiologist* in 1982. I recently gave archival material relating to my career to the Iowa Veterinary Medical Association at Des Moines. We travel very little now. My health, as well as that of my wife, is only fair, but we keep in contact with several universities.

2909 Woodland Ave., Apt. 501
Des Moines, IA 50312

L. Paul Dugal to Bob:

I am still alive and in excellent health. After 40 years of active duty as a professor, a researcher, and an administrator, I was craving for free time, for leisure, for freedom (!), and this I found in traveling, in practicing sports like golf and skiing, in reading, in attending concerts and plays, and in enjoying the beautiful view that we have from our house on the St. Lawrence. So life would not become monotonous, I have also participated as a scientific advisor in several capacities for Sherbrooke University, the University of Quebec, and the Quebec Council on Science Policy.

340 de la Corniche
St. Nicholas, Quebec G0S 2Z0

Robert S. Dow to Roy O. Greep:

I remain well and active, spending most of my time in private practice as a clinical neurologist. I have assumed a role in fund development at Good Samaritan Hospital and Medical Center, where we have been successful in raising almost three-quarters of a million dollars from local foundations and individuals for the Neurological Science Center. Willetta and I enjoyed two long trips during 1983, to Kenya and Egypt in January and to Southeast Asia in November. I was privileged to contribute to the symposium honoring my old friend Morris Bender in New York, also in November. We will celebrate our 50th wedding anniversity with a cruise to Alaska and a week's fishing there. I enjoy working at this leisurely pace and hope to continue thanks to seven very supportive neurological and neurosurgical partners.

The Neurological Clinic
2222 NW Lovejoy St.
Portland, OR 97210

Clinton N. Woolsey to Roy:

Thank you for your kind note and birthday greeting as I begin my 80th year on earth. I still keep busy and come to the laboratory practically every day. There is a good deal of material we have collected over the years, which has been reported at scientific meetings but still needs to be documented in detail. Currently I am working up data collected over a 10-year period on some nine chimpanzees in experiments in which 45 individuals took part. Each experiment continued around the clock for from three to eight days. This should come out as a monograph sometime in 1984.

In 1981 and '82 the material presented at the Dallas FASEB meeting symposium which I organized for the Neuroscience Committee appeared as a three volume work on "*Cortical Sensory Organization*." Volume 1 was on "*Multiple Somatic Areas,*" Vol. 2 on "*Multiple Visual Areas*," and Vol. 3 on "*Multiple Auditory Areas*." These were published by Humana Press, Clifton, NJ 07015. In addition I am completing a full account of the study in the 1930's with Phil Bard on the cortical control of placing and hopping reactions of monkeys and of a comparative study with Bob Goodwin on placing and hopping reactions in children. If I live as long as my two grandfathers, I have enough material to keep me busy for the next 10 years. At the 1982 Neuroscience meeting in Minneapolis, together with Jerzy Rose, I received the Ralph Gerard award from the society. My son Tom, now Professor of Anatomy and Neurobiology at Washington University in St. Louis, was designated to make the presentation—which was a great pleasure to me.

In recent years, beginning in 1978, I have participated in three IBRO Workshops at Bangkok (1978), Shanghai (1980), and Algiers (1981). I was the IBRO organizer for the latter two. In June 1983 I participated in a symposium in Stockholm, honoring the late Ingve Zotterman. I reviewed our work on cortical sensory organization. A monograph on the workshop is being edited by Dr. Ottosen of the Wenner-Gren Center and should appear during the coming year.

Greetings to all our friends in the Society.

Dept. of Neurophysiology
University of Wisconsin Medical School
Madison, WI 53706

Joseph Meites to Roy:

I reached 70 years of age on December 22, 1983, but shall continue full-time, with our departmental Chairman's approval, until the end of 1984. At present, I am still running a laboratory, presently with 2 postdoctorals, 2 graduate students, a half-time secretary, and a part-time animal caretaker. However, I am rapidly running out of funds and am seeking feverishly for means to continue operations for at least a few more years. Our principal research during the past several years has concentrated on the relation of the neuroendocrine system to aging processes, an appropriate enough subject for those in our age bracket. A book I edited on this subject, *Neuroendocrinology of Aging*, Plenum Publishing, New York, recently appeared (Oct. 1983). It contains almost all of the work done in this area, mainly in the last 10 years. Neuroendocrine intervention in old age does offer some hope, at least as indicated by experiments on old rats and mice.

My proudest achievement has been in seeing 37 graduate students through their Ph.D. degrees, plus 25 through M.S. degrees, and I have had about 35 postdoctoral fellows. I have derived a great deal of pleasure, stimulation, and education from my association with these young people during the 37 years I have been here and derive enjoyment in their achievements after they leave here. Together we have published about 500 full research papers, chapters, and reviews, and I have edited or co-edited 6 books.

I shall be the "honored guest" at the forthcoming *IV International Congress on Prolactin* on June 27–29, 1984, in Charlottesville, VA, and have received an official invitation from mainland China to present a series of lectures in October, 1984, at different medical schools. A few other trips are probable in 1984.

As far as advice to younger colleagues is concerned, I doubt that I have anything very original to say. I believe it is a good idea to be and to remain active physically and mentally, to form good health habits (stay away from strong drink, tobacco, and drugs), learn to appreciate nature and human companionship, and never "retire" in your older years if one can possibly avoid it.

Dept. of Physiology
Michigan State University
East Lansing, MI 48824-1101

Samuel E. Pond to Joseph P. Saunders

In view of my circumstances I suggest that you conclude the mailing of *The Physiologist* with Volume 26, 1983. Because of my failing vision and the limited storage space for science journals in our present residence, it will be better to discontinue it, although I am still interested in the field of physiology and read what I can as printed matter comes to hand. My thanks to you for continuing the subscription in my retirement; but there may be another who would profit more. I am considerably beyond the activity period of life, too long perhaps, and have to find a way out of snags as the years come and go. There is still a chance my experiences of the past may be useful to others, so I continue with our Cobbossee Watershed District work to improve the water and supply, but this is quite a way from teaching and research as formerly in human and general physiology. At nearly 95 I'm having fun in this area, a very comfortable camp (parts built in 1780, but now quite modernized). My wife and I take turns with others in the community jollying along and moving about in a very limited way. We catch glimpses of "Life" by radio and TV or *The Christian Science Monitor* (from Bostontown). We are both in fairly good health, and our family moves us on occasion to Cape Cod, MA, for other recreation. Best wishes to your success in the extension of a remarkable publication.

Box 6720, RR #2
East Winthrop, ME 04364

ANNOUNCEMENTS

1985-86 Advanced Research Fellowships in India

The Indo-US Subcommission on Education and Culture is offering twelve long-term (6–10 months) and nine short-term (2–3 months) awards, without restriction as to field, for 1985-86 research in India. Applicants must be US citizens at the postdoctoral or equivalent professional level. The fellowship program seeks to open new channels of communication between academic and professional groups in the United States and India and to encourage a wider range of research activity between the two countries than now exists. Therefore, scholars and professionals with limited or no experience in India are especially encouraged to apply. *Application deadline:* 15 June 1984. *Information:* Council for International Exchange of Scholars, Attention: Indo-American Fellowships Program, Eleven Dupont Circle, Suite 300, Washington, DC 20036. Phone 202/833-4985.

William N. Creasy 1984–85 Visiting Professorships in Clinical Pharmacology

The Burroughs Wellcome Fund is offering the tenth series of Creasy Visiting Professorships of Clinical Pharmacology for the 1984–85 academic year. The Visiting Professorships honor the late William N. Creasy, former President and Chairman of The Burroughs Wellcome Fund, and are intended to strengthen the discipline of Clinical Pharmacology by promoting increasing teaching, training, and research activities. Individuals proposed should have scientific interests relevant to, but not necessarily restricted to, Clinical Pharmacology. Each Professor will spend a week at the selected medical school engaged in teaching students, faculty, and house staff and will deliver a Creasy Memorial Lecture on a subject pertinent to Clinical Pharmacology. *Application deadline*: 15 May 1984. *Information*: The Burroughs Wellcome Fund, 3030 Cornwallis Rd., Research Triangle Park, NC 27709. Phone: 919/248-3000.

Future Meetings

1984	
APS "Fall" Meeting	Aug. 26-31, Lexington
1985	
FASEB Annual Meeting	April 21-26, Anaheim
Joint APS/The (British) Physiological Soc Mtg	Sept. 12-14, Cambridge (UK)
APS Fall Meeting	October, Buffalo
1986	
FASEB Annual Meeting	Apr. 13-18, St. Louis
IUPS Congress	July 12-20, Vancouver, Canada

Courses on Genetic and Biochemical Engineering

BRE Systems is offering two intensive short courses "Genetic Engineering: A Short Course" (2-4 May 1984) and "Biochemical Engineering Fundamentals" (18-20 June 1984) at the Hyatt Regency O'Hare, Chicago (course fee of $700, enrollment limited). *Information:* BRE Systems, 1665 E. Mountain St., Pasadena, CA 91104. Phone: 213/356-4116.

MIT Course in Design and Analysis of Scientific Experiments

Massachusetts Institute of Technology will offer a one-week elementary course in Design and Analysis of Scientific Experiments, 9-14 July 1984. Applications will be made to the physical, chemical, biological, medical, engineering, and industrial sciences and to experimentation in phychology and economics. The course will be taught by Professors Harold Freeman and Paul Berger. *Information:* Director of Summer Session, Room E19-356, Massachusetts Institute of Technology, Cambridge, MA 02139.

Meeting of North American Chapter of International Society of Lymphology

The 1984 meeting of the North American Chapter of the International Society of Lymphology will be held November 9 and 10 at the Texas Medical Center sponsored by the University of Houston and Baylor College of Medicine. The meeting will host three symposia: *1*) Cardiac Lymph; *2*) NMR Imaging; and *3*) Regulation of Macromolecular Permeability. Volunteer communications are welcome. *Abstract deadline*: 15th May. *Information*: Dr. Lloyd Michael, Dept. of Medicine, Baylor College of Medicine, Houston, Texas 77030 (713/790-3146) or Dr. George Grega, Dept. of Pharmacology, U. of Houston, Houston, Texas 77004 (713/749-4107).

Pharmacology of Thermoregulation Sixth International Symposium

The Pharmacology of Thermoregulation, sixth in a series of International Symposia, will be held 26-31 August 1985 at Jasper Park Lodge, Jasper, Alberta, Canada. *Information:* Dr. Peter Lomax, Dept. of Pharmacology, UCLA School of Medicine, Los Angeles, CA 90024; Professor E. Schönbaum, Peelkensweg 4, 5428 NM Venhorst, The Netherlands; or Dr. Warren Veale, Dept. of Medical Physiology, Faculty of Medicine, University of Calgary, Calgary, Alberta, T2N 1N4, Canada.

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Science Software Quarterly New Publication

The Center for Environmental Studies, Arizona State University, announces a new quarterly publication, devoted to computer software for natural science applications. *Science Software Quarterly* will include reviews of commercial software with scientific applications; an open forum for advertisement of "custom" software designed by working scientists for specialized scientific uses; articles on choice, operation, and maintenance of scientific software libraries; tips on hardware (compatibility, portability, adaptation of software for different systems, peripheral use, etc.); classified ads for sale or exchange of used computer hardware and peripherals; and listings of learning/training resources (books, seminars, tutorials). *Science Software Quarterly* will cover software for microcomputers, minicomputers, and mainframes. We are presently looking for reviewers of software and documentation, contributors of articles and ideas, and software designed for use in any natural science field (ecology, agriculture, botany, zoology, environmental science, museum science, etc.). *Information:* Dr. Diana J. Gabaldon, Center for Environmental Studies, Arizona State University, Tempe, AZ 85287. Phone 602/965-3051.

Optical Methods in Cell Physiology

A symposium on Optical Methods in Cell Physiology, organized by the Society of General Physiologists, will be held 6-9 September 1984 at the Marine Biological Laboratory, Woods Hole, MA. Keynote address by Professor Sir Andrew Huxley, PRS. The conference will feature invited lecturers who will discuss image enhancement techniques, optical measurements of membrane potential, intracellular pH, and intracellular [Ca], and photobleaching and photoactivation techniques, as well as workshops and laboratory demonstrations. Open poster sessions will also be held. *Call for abstracts*: deadline 1 June 1984. *Information*: Dr. Paul De Weer, Dept. of Physiology and Biophysics, Washington University School of Medicine, St. Louis, MO 63110.

American Society for Cell Biology Annual Meeting

The 24th Annual Meeting of the American Society for Cell Biology will be held in Kansas City, MO, 12-16 November 1984. *Deadline for receipt of abstracts:* 22 June 1984. *Information:* ASCB National Office, 9650 Rockville Pike, Bethesda, MD 20814. Phone: 301/530-7153.

Society for Industrial Microbiology Annual Meeting

The Annual Meeting of the Society for Industrial Microbiology will be held 12-17 August 1984 at Colorado State University, Ft. Collins, CO. *Information:* Ann Kulback, SIM, c/o AIBS, 1401 Wilson Blvd., Arlington, VA 22209. Phone: 703/256-0337.

Comparative Respiratory Society

The Comparative Respiratory Society was established in 1982 for the purpose of promoting the exchange of knowledge of the respiratory system between basic and clinical sciences. Membership is open to veterinarians, physicians, and other allied health professional and scientists who share a special interest in the understanding of respiratory systems from a comparative aspect. *Information:* J. R. Gillespie, Veterinary Medicine Teaching Hospital, 1008 West Hazelwood Drive, Urbana, IL 61801.

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Renal Regulation of Acid-Base Balance: Ammonia Excretion

GEORGE A. TANNER
Department of Physiology and Biophysics
Indiana University School of Medicine
Indianapolis, Indiana 46223

The kidneys play a major role in regulating acid-base balance in humans and other mammals. Under normal conditions, the kidneys eliminate the nonvolatile ("fixed") acids produced by the metabolism of foodstuffs in the body. Under conditions of excess acid intake or production, they increase excretion of hydrogen ions in the urine. An important part of the renal compensation for acidosis is the enhanced production and excretion of ammonia. When alkaline loads are imposed, the kidneys increase the output of bicarbonate (a base) in the urine. By these adjustments, the kidneys help to maintain arterial blood pH at a normal value of 7.35–7.45.

Trivial amounts of free hydrogen ions are excreted in the urine; most of the hydrogen ions eliminated in the urine are combined with urinary buffers. The major urinary buffer in persons with normal renal function is ammonia. A normal person on a mixed diet will produce about 40-80 meq of strong acid in a day. About 30-50 meq of hydrogen ions are excreted combined with ammonia. In an acid urine, almost all of the ammonia is present as ammonium ions; the equilibrium between free base (NH_3) and ammonium ion (NH_4^+), $NH_4^+ + H_2O \rightleftharpoons NH_3 + H_3O^+$, lies far to the left. About 10-30 meq of hydrogen ions are excreted as titratable acid. Titratable acid includes urinary buffers other than ammonia, such as phosphate (7).

The major purpose of this experiment is to demonstrate the changes in ammonia excretion and urine pH that occur in response to metabolic acidosis (induced by ammonium chloride ingestion) or metabolic alkalosis (produced by sodium bicarbonate ingestion). Rats are provided with solutions of ammonium chloride (NH_4Cl), ammonium bicarbonate (NH_4HCO_3), sodium chloride (NaCl), or sodium bicarbonate ($NaHCO_3$) to drink for 1 day. The next day they are placed in metabolism cages, and measurements of urine pH and urinary ammonia excretion are made. The measurements are simple, and dramatic differences between the NH_4Cl-treated rats and other treatment groups are observed. The experiment suggests that the enhanced ammonia excretion observed after NH_4Cl ingestion is not directly due to the ingested ammonia but, rather, should be viewed as a physiological response to the induced acidosis.

Methods

The following equipment is needed: regular and metabolism cages for rats, animal balances, balances for weighing urine collection vials (accurate to 0.1 g), spectrophotometers, pH meters, water bath (37°C), test tubes, and pipettes.

The day before their laboratory section meets, the students report to the laboratory early in the morning (before their first class), and each group of four students weighs four rats and provides each rat with about 200 ml 0.2 M NH_4Cl, 0.2 M NH_4HCO_3, 0.2 M NaCl, or 0.2 M $NaHCO_3$ to drink. Each solution contains 10% sucrose (cane sugar) to encourage fluid intake by the rats. Each drinking bottle and cage is labeled with the students' names and the solution provided. The bottles should be tightly stoppered to prevent dripping. The rats at this point are in their regular cages and should have food.

The next morning (before their first class), the students weigh the rats and drinking bottles again. If any rat has lost more than 10 g body wt or has failed to consume at least 30 ml of fluid, the animal should not be used. The rat should be given some ether to sniff (use a nose cone), and gentle suprapubic pressure should be applied; this will cause the rat to empty its urinary bladder. The time should be noted, since this is the start of the urine collection period. When ether is used, of course, adequate ventilation must be provided and smoking prohibited. Each rat is next placed in an individual metabolism cage without food and with 10% sucrose to drink. This solution should not contain any of the salts, since accidental spillage into the metabolism cage will falsify the results. An Erlenmeyer flask, weighed to the nearest 0.1 g, is placed under the spout of the metabolism cage for collecting the urine. The students return to the laboratory about 4 h later and give the rats another

whiff of ether. This time the rats should urinate into the metabolism cages. The time should be noted (end of urine collection period). The urine collection flask is weighed again, and from the urine volume (assume a density for all solutions of 1 g/ml) and collection time, the average urine flow rate (ml/h) is calculated.

The urine pH should be measured as soon as possible with a pH meter. For the measurement of ammonia, an aliquot of urine should be diluted 250-fold with distilled water. The colorimetric method used depends on the reaction of ammonia with phenol and sodium hypochlorite in the presence of sodium nitroprusside catalyst to form indophenol. Indophenol exhibits a stable blue color, the intensity of which is directly proportional to the ammonia concentration (8).

The students should set up and label six 20-ml test tubes. Into the first, they pipette 1.00 ml distilled water; into the second, 1.00 ml ammonia standard solution (0.214 μmol/ml ammonium sulfate); and into tubes 3–6, 1.00 ml of diluted urine from each rat. To each tube, 1.0 ml phenol color reagent (Sigma Chemical catalog no. 640-1) and 1.0 ml alkaline-hypochlorite reagent (Sigma Chemical catalog no. 640-3) are added in the order specified, and the contents are promptly mixed by inverting against a piece of Parafilm. Since phenol and alkaline-hypochlorite reagents are caustic poisons, they must not be pipetted by mouth and contact with the skin should be avoided. All tubes are incubated for 15 min in a 37°C water bath (or at room temperature for 30 min). Eight milliliters of distilled water are then added to each tube, and the contents are mixed thoroughly. Absorbances (A) are read in a spectrophotometer at a wavelength of 630 nm. The spectrophotometer is set to zero absorbance with distilled water in the cuvette. The reagent blank (tube 1) absorbance should not exceed 0.10 with a 1-cm cuvette; high values suggest contamination of the distilled water or reagents with ammonia or that the reagents have deteriorated. The urinary ammonia concentration is calculated from the following equation

$$\text{urinary ammonia concn} = \frac{0.214\ \mu\text{mol/ml}}{A_{\text{standard}} - A_{\text{blank}}} (A_{\text{sample}} - A_{\text{blank}}) \times 250$$

Urinary ammonia excretion is calculated as the product of urine ammonia concentration and urine flow rate and is normalized to 100 g rat body wt.

Results and Discussion

Table 1 shows representative data from rats provided with different drinking solutions for 24 h. The most striking difference is the greatly increased ammonia excretion in the rats provided with an NH_4Cl solution to drink. By contrast, rats provided with NH_4HCO_3 did not show a higher rate of ammonia excretion than control (NaCl) rats. The amount of ammonium salt ingested did not differ significantly in the NH_4Cl- and NH_4HCO_3-treated rats (Table 1). The differing rates of ammonia excretion should be viewed in terms of the effects of ingestion of the ammonium salts on acid-base balance. Ingested ammonium salts are converted in the liver to urea. The biochemical pathway involved, the ornithine cycle, was first described by Krebs and Henseleit in 1932 (4). For simplicity, we can consider that NH_4Cl is converted to urea, water, and hydrochloric acid, according to the following reaction

$$2NH_4Cl + CO_2 \rightarrow H_2N\text{-}\underset{\underset{O}{\|}}{C}\text{-}NH_2 + H_2O + 2HCl$$

The hydrochloric acid, a strong acid, is neutralized by body bicarbonate stores, and a metabolic acidosis is produced. Ingested NH_4HCO_3 is converted to urea, water, and carbonic acid, according to the following simplified reaction

$$2NH_4HCO_3 \rightarrow H_2N\text{-}\underset{\underset{O}{\|}}{C}\text{-}NH_2 + 2H_2O + H_2CO_3$$

In this instance, H_2CO_3, a weak acid, is formed and is excreted by the lungs as CO_2. No acidosis results. In fact, a slight tendency toward a metabolic alkalosis may result from NH_4HCO_3 ingestion, because an aqueous solution of the salt is slightly alkaline (pH 7.7) and becomes progressively more alkaline as NH_3 and CO_2 are formed and the CO_2 is lost to the air.

The enhanced urinary ammonia excretion resulting from ingestion of NH_4Cl is not directly due to the ingested ammonia but rather is a consequence of the acidosis which this salt produces. In response to metabolic acidosis, the kidneys increase the excretion of ammonia due to *1*) enhanced trapping of ammonia in the urine as ammonium ions and *2*) increased production of ammonia by the kidney tubule cells. The urinary ammonia is derived primarily from the deamidation and deamination of the amino acid glutamine (1, 3, 7). Although urinary ammonia excretion does not achieve maximal rates until 2-4 days after induction of acidosis, increased renal ammonia synthesis does contribute to the enhanced excretion after 1 day of acidosis (6). The enhanced ammonia excretion by the kidneys allows the animal to dispose of large amounts of hydrogen ions and is a major element in the renal defense of acid-base homeostasis.

The urine pH values (Table 1) are consistent with the changes expected with acidosis (low urine pH in NH_4Cl-treated rats) and alkalosis (alkaline urine pH in $NaHCO_3$-treated rats). A problem with this determination, however, is that loss of CO_2 from the urine samples, which cannot be prevented in the metabolism cages, results in an alkaline shift in pH (5).

The same rats may be used for several laboratory sessions, since the animals will recover completely from the imposed acid-base disturbances after 2 days. Students like the experiment because it is straightforward and because meaningful physiological data are collected in intact animals. If the instructor wishes to substantiate the fact that NH_4Cl ingestion does, in fact, produce a metabolic acidosis and that $NaHCO_3$ ingestion leads to a metabolic alkalosis, arterial blood samples may be collected from the rats, and blood pH and P_{CO_2} measurements may be done. For economy, we generally do not do these measurements but, instead, provide the students with a table of blood acid-base values from identically treated rats (Table 2). Major differences and trends are usually obvious from inspection of the data. For instructors wishing to use statistical methods, the comparisons to be made should be specified before the study (i.e., a priori). We consider the following four comparisons to be of primary interest: *1*) NH_4Cl vs. NH_4HCO_3 treatment;

Table 1
Effects of Drinking Various Solutions for 1 Day

	NH_4Cl	NH_4HCO_3	NaCl	$NaHCO_3$
Rat body wt, g	275 ± 20	271 ± 13	273 ± 14	271 ± 13
Increase in rat body wt, g/day	1 ± 3	3 ± 8	10 ± 8	7 ± 7
Fluid consumption, ml/day	54 ± 10*	73 ± 14	95 ± 18	90 ± 17
Urine pH	6.1 ± 0.3*	7.5 ± 0.5†	7.7 ± 0.3	8.1 ± 0.4
Urine flow rate, ml/h	4.2 ± 3.2	4.6 ± 1.8	3.7 ± 1.8	5.6 ± 0.5
Urine ammonia concn, μmol/ml	51.9 ± 25.6*	4.3 ± 2.8†	5.3 ± 2.4	1.6 ± 1.1*
Urine ammonia excretion, $\mu mol \cdot h^{-1} \cdot 100\ g\ body\ wt^{-1}$	55 ± 9*	5.8 ± 1.9†	6.4 ± 3.4	3.3 ± 2.6

Values are means ± SD for 6 rats in each group. Drinking solutions consisted of 0.2 M salt + 100 g sucrose per liter tap water.
*Significantly different ($P < 0.05$) from NaCl group.
†Significantly different from NH_4Cl group.

Table 2
Effects of Drinking Various Solutions on Arterial Blood Acid-Base Values

	NH_4Cl	NH_4HCO_3	NaCl	$NaHCO_3$
pH	7.26 ± 0.07*	7.44 ± 0.03†	7.39 ± 0.04	7.45 ± 0.02
P_{CO_2}, mmHg	45 ± 6	51 ± 6	48 ± 8	53 ± 4
Plasma HCO_3^- concn, meq/liter	20 ± 5*	33 ± 2†	28 ± 2	36 ± 2*
Base excess, meq/liter	−7.0 ± 5.8	7.6 ± 0.4†*	2.6 ± 1.6	10.7 ± 1.7*
P_{O_2}, mmHg	88 ± 8	75 ± 11	85 ± 10	73 ± 7

Values are means ± SD for 5 rats in each group. Blood was collected anaerobically from abdominal aorta in barbiturate-anesthetized rats.
*Significantly different ($P < 0.05$) from NaCl group.
†Significantly different from NH_4Cl group.

2) NH_4Cl vs. NaCl (control) treatment; *3)* NH_4HCO_3 vs. NaCl treatment; and *4)* $NaHCO_3$ vs. NaCl treatment. We use the F_{max} test for testing for homogeneity of variances. If homogeneity can be assumed, we use a single classification analysis of variance and the Dunn-Šidák method for multiple comparisons. If homogeneity of variances cannot be assumed, we use a t' test and the Dunn-Šidák method (9).

The following questions may provide a framework for a discussion of the data and the kidneys' role in acid-base regulation.

1. Compare the rates of ammonia excretion in the NH_4Cl-, NH_4HCO_3-, and $NaHCO_3$-treated rats vs. the NaCl group. Did both groups of rats ingesting the ammonium salts have similar rates of urinary ammonia excretion? What happens to the ingested NH_4Cl? Why does NH_4Cl ingestion produce a metabolic acidosis?
2. What is the source of urinary ammonia? The increased excretion of ammonia by the kidneys in chronic acidosis has been described as a "life-saving adaptation." Explain. What are some current theories that explain the increased rate of renal ammonia synthesis in acidotic animals? (See Refs. 1, 3.)
3. What fraction of the total ammonia is present as the free base NH_3 in a urine sample of pH 6.3? (The pK_a of the ammonium ion is about 9.3.) Which form of ammonia, NH_3 or NH_4^+, penetrates cell membranes more readily and why?
4. What urinary buffers contribute to titratable acid? How is titratable acid measured in the clinical laboratory? What factors affect the amount of H^+ excreted as titratable acid?
5. Compare the urine pH of the four groups of rats. Why is urine pH alone an inadequate measure of renal acid excretion? Why does exposure of the urine samples to air lead to an alkaline shift in pH? How do the kidneys form an acid or alkaline urine?
6. Summarize and explain the renal compensations for the four types of acid-base disturbance: metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis. (See Refs. 2, 7.)
7. Characterize the acid-base status of the animals in Table 2 (see Ref. 2). What effect does barbiturate anesthesia have on respiration? What is the respiratory compensation for a metabolic acidosis or alkalosis? What is the physiological basis for the respiratory response? Why is respiratory compensation incomplete?

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Nutrition as a Modulator of the Aging Process

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The first evidence strongly indicating that nutrition can influence aging was published in 1935 by McCay and his colleagues (13). In that study, it was shown that with weanling rats severe levels of food restriction, which markedly reduced skeletal growth and delayed sexual maturation, resulted in a remarkably long life for rats able to survive the first year of this dietary regimen. This finding has been repeated many times (21), and it has also been shown that levels of restriction that do not markedly influence skeletal growth and sexual development are also effective (3). It should be noted, however, that severe restriction increases life-span much more than moderate restriction; e.g., when Ross (16) restricted male rats to 30% of the ad libitum food intake, some animals survived for more than 1,800 days, which is to be compared with the more than 1,400 days obtained by Yu et al. (22) when male rats were restricted to 60% of the ad libitum food intake. Food restriction has been shown to have a similar effect in several other species as well (2).

Sacher (17) pointed out that increasing the length of life, in and of itself, does not necessarily mean that an intervention influences the aging process. However, food restriction does much more than influence the length of life. Its general actions can be summarized as follows: *1*) it extends the life-span; *2*) it retards age-related physiological deterioration; and *3*) it retards age-related disease processes. Although no one of these effects alone provides unequivocal evidence that food restriction slows the aging process, the simultaneous occurrence of all three is strong evidence that such is the case.

In our investigations, all three of these effects have been studied simultaneously, and for this reason the results of our studies will be the main focus of the ensuing discussion. The first of our studies involved two groups of male Fischer 344 rats: *group A* fed a standard semisynthetic diet ad libitum and *group R* fed 60% of the mean food intake of the *group A* rats from 6 wk of age on. The caloric composition of the standard diet was 21% protein, 57% carbohydrate, and 22% fat. The second of our studies also used male Fischer 344 rats and involved the following five dietary groups: *group 1* was a repeat of *group A* and *group 2* a repeat of *group R*; *group 3* was restricted to 60% of the food intake of *group 1* from 6 wk to 6 mo of age and then fed ad libitum for the rest of life; *group 4* was fed ad libitum until 6 mo of age and then restricted to 60% of the food intake of *group 1*; *group 5* was fed ad libitum, but instead of the standard diet the caloric composition of the food was changed to 12.6% protein, 65.4% carbohydrate, and 22% fat. In both studies, the rats were maintained in a specific pathogen-free environment by means of a barrier facility.

Extension of Life-Span

Survival curves (22) from our first study are presented in Figure 1. As would be expected with a population of highly protected rats, the survival curve of the 115 rats of *group A* is quite rectangular. It is interesting that the survival curve of the *group R* rats is less rectangular; however, it is clear that food restriction markedly increased the life-span, since when the last rat in *group A* died about 70% of the *group R* rats were still living. This finding should be compared with the effects of technology and medicine on the human survival curve; these interventions did not influence the human life-span but did rectangularize the survival curve (i.e., they resulted in a marked increase in the median length of life).

The longevity aspect of our second study involved only 40 rats per group rather than 115 rats per group as in our first study. This number proved to be adequate, since the use of an inbred strain of rats, a barrier system, and defined diets resulted in excellent reproducibility of survival curves. For example, the survival curve of *group 1* rats (n = 40) almost perfectly replicated that of the *group A* rats (n = 115), and the survival curve of *group 2* rats (n = 40) similarly replicated that of *group R* rats (n = 115).

Group 1 rats had a median length of life of 701 days and a maximum length of life of 941 days compared with a median length of life of 1,046 days and maximum length of life of 1,296 days for the rats of *group 2*. The rats of *group 3* had a median length of life of 808 days and a maximum length of life of 1,040 days; i.e., food restriction limited to early life resulted in a small but significant increase in both median and maximum length of life. The rats in *group 4* had a median length of life of 941 days and a maximum length of life of 1,299 days; i.e., food restriction started in adult life was less effective than near-lifelong food restriction in increasing the median length of life but just as effective in extending the maximum length of life. In line with this finding is the work of Weindruch and Walford (20) with mice showing that even at the advanced age of 12–13 mo food restriction significantly extends life-span, though not as effectively as when started early in life. The rats in *group 5* had a median length of life of 810 days and a maximum length of life of 969 days; i.e., protein restriction without caloric restriction resulted in a small but significant increase in median length of life but did not significantly influence the maximum length of life.

Retardation of Age-Related Physiological Deterioration

Although not comprehensively studied, there is a sizable body of data showing that food restriction retards age-related physiological change (most such change appears to reflect a deterioration of the physiological system). The data in Figure 2 are typical of these findings (10). At young ages, there is little difference between the food-restricted and ad libitum-fed rats (e.g., in Figure 2 at 6 and 12 mo of age, *group 1* and *2* rats had similarly low serum cholesterol concentrations). However, with increasing age, the ad libitum-fed rats showed a change (e.g., in Figure 2, the serum cholesterol concentration of

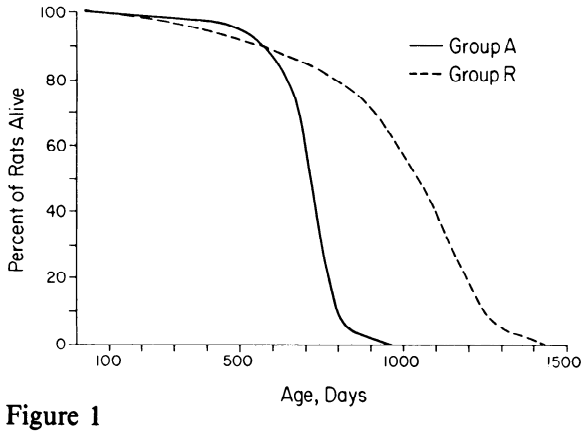

Figure 1

Survival curves of *group A* (ad libitum-fed) and *group R* (restricted to 60% of ad libitum food intake) rats. [From Yu et al. (22)].

group 1 rats markedly increased with age), whereas this age-related change was delayed and less marked in food-restricted rats (as is evident in Figure 2 for the serum cholesterol concentration of *group 2* rats). In our laboratory (12), this general pattern has been observed for many functions: *1*) the age-related increase in the serum concentration of certain hormones (calcitonin and parathyroid hormone); *2*) the response of cells to hormones (the lipolytic response of adipocytes to epinephrine); *3*) the loss of skeletal muscle mass; *4*) the loss of bone mass; and *5*) the loss in mechanical response of skeletal muscle. Levin et al. (8) have obtained similar findings in rats in regard to the age-related loss of corpus striatal dopamine receptors. There is also an extensive literature on the ability of food restriction to delay age-related deterioration of the immune system in mice (6, 19). In all of the cases where it has been tested in rats and mice, food restriction started in adult life was found to be as effective in delaying physiological deterioration as food restriction started in early life.

The effects of food restriction on the response of fat cells to the lipolytic action of glucagon (12) has certain unique characteristics (Figure 3). In ad libitum-fed rats (*group A*), the response of fat cells to the lipolytic action of glucagon was totally lost during early life (between 6 wk and 6 mo of age). Food restriction prevented this; indeed, the response of fat cells from 1-yr-old restricted rats (*group R*) was as great as that of cells from 6-wk-old rats. Moreover, at no age was there an absence of response of fat cells from restricted rats to the lipolytic action of glucagon. This is not an acute action of food restriction, since restricting 6-mo-old *group A* rats for 1 mo did not significantly restore the lipolytic response to glucagon.

Retardation of Age-Related Disease Processes

Chronic nephropathy is a commonly occurring age-related disease process in rats (5). In many aspects, it has characteristics similar to atherosclerosis in humans. The lesions progress in severity with increasing age, and almost all rats have these lesions, although the severity varies from individual to individual. Clinical expression of the disease in terms of elevated blood urea nitrogen (BUN), elevated serum creatinine concentration, parathyroid hyperplasia, osteodystrophy, and metastatic calcification only occurs late in life with many rats never exhibiting these clinical findings. Chronic nephropathy is graded 1, 2, 3, 4, and E in order of severity of histopathology. Rats with grade 1, 2, and 3 lesions have normal BUN and serum creatinine levels. Rats with grade 4 lesions have moderately elevated BUN and serum creatinine levels, whereas rats with grade E lesions have markedly elevated BUN and serum creatinine levels often accompanied by the other clinical findings noted above. On the basis of cross-sectional sacrifice of rats, it was shown that group 1 rats had a rapid progression of these lesions with most 27-mo-old rats having grade 4 or grade E lesions. The progression of these lesions in *group 2* and *4* rats was much less rapid; e.g., at 30 mo of age, almost all rats had only grade 1 and 2 lesions. The rate of progression of these lesions in *group 3* and *5* rats was less than for *group 1* rats but greater than for *group 2* and *4* rats. Thus, food restriction that includes adult life was the most effective dietary manipulation in retarding this age-related disease. However, this does not mean that protein restriction (*group 5*) was ineffective; e.g., 51% of the *group 1* rats have grade E lesions at death, but only 10% of the *group 5* have such lesions. It is striking that protein restriction so markedly retarded the development of chronic renal failure without mark-

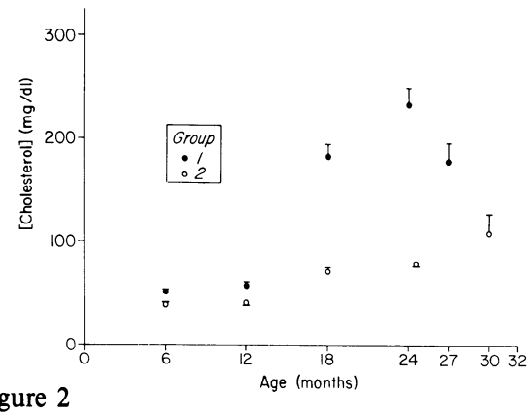

Figure 2

Changes in serum cholesterol concentrations with age in *group 1* (ad libitum-fed) and *group 2* (restricted to 60% of ad libitum food intake) rats. [Modified from Masoro et al. (10)].

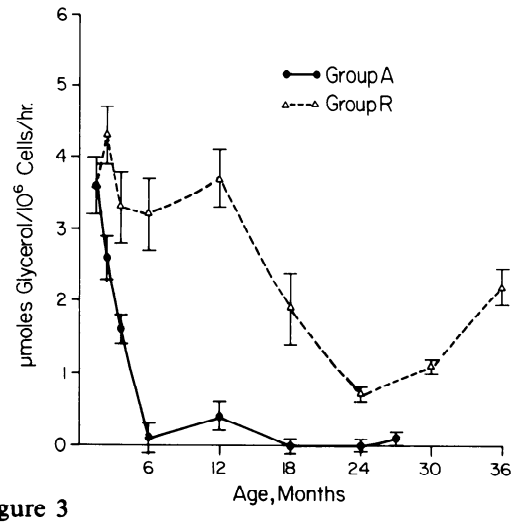

Figure 3

Changes in lipolytic response of fat cells to glucagon in *group A* (ad libitum-fed) and *group R* (restricted to 60% of ad libitum food intake) rats. [From Masoro et al. (12)].

edly increasing the length of life. This strongly indicates that food restriction prolongs life by mechanisms in addition to its action on chronic renal disease.

Cardiomyopathy is also a commonly occurring age-related disease in rats (5). Its progression was also retarded most by adult food restriction (*groups 2* and *4*). However, food restriction limited to early life (*group 3*) and protein restriction (*group 5*) have some but a lesser ability to retard its development.

The data on the rats killed at various ages showed the appearance of neoplastic disease to be delayed in the rats of *groups 2* and *4* (another example of the marked beneficial effects of adult life food restriction). However, the rats of *groups 2* and *4* that died spontaneously had a higher percentage of tumors than rats of *groups 1, 3,* and *5* that died spontaneously. Of course, rats in *groups 2* and *4* that died spontaneously were much older than the rats that died spontaneously in the other groups. Thus, adult life food restriction delays the occurrence of neoplastic disease but does not prevent it from becoming the major clinical problem related to the death of *group 2* and *4* rats.

Hypotheses

During these past 50 years, four major hypotheses (shown in Table 1) have dominated thought about the mechanisms by which food restriction slows the aging process.

The first hypothesis was the reason that McCay et al. initiated their studies on food restriction. They postulated that aging is a postmaturational process, and therefore if maturation could be prevented, aging would not occur. They tried to prevent maturation by food restriction but were only able to delay it. They concluded that food restriction slowed the aging process because it delayed maturation and felt that their data supported this conclusion. However, our finding that food restriction started at 6 mo of age (*group 4*) is as effective as food restriction started at 6 wk of age (*group 2*) in extending life-span makes it unlikely that this hypothesis is valid.

There has been a considerable amount of data from studies with mice and rats showing that length of life correlates inversely with the rate of growth and directly with the duration of growth. Those findings were recently reviewed by Goodrick (7). Since food restriction started at weaning or soon thereafter both slows growth and prolongs its duration, it was reasonable to hypothesize that it extended the length of life by this mechanism. Our findings that *group 4* rats, which grew rapidly until 6 mo of age, had the same life-span as *group 2* rats, which grew slowly for an extended period, makes it unlikely that the hypothesis provides insight into the basic mechanism by which food restriction slows the aging process. The findings of Weindruch and Walford (20) on effects of food restriciton on extending the life-span of mice when started at 12–13 mo of age provide further support for this conclusion.

Table 1
Major Hypotheses on Mechanisms by Which Food Restriction Retards Aging Process

1) It acts by delaying maturation
2) It acts by slowing the rate of growth and prolonging its duration
3) It acts by reducing body fat
4) It acts by reducing the metabolic rate per unit body mass

Many nutritionists feel that food restriction slows the aging process by reducing body fat. This stems from the widely held view that in humans even a small increase in body fat over the so-called ideal level leads to a decreased longevity, a view that has recently been challenged (1). Moreover, the hypothesis that reducing body fat is the mechanism by which food restriction prolongs life is not supported by the data of our first study (4) in which the fat content of rats was measured longitudinally. In this study, there was no correlation in *group A* (ad libitum-fed rats) between maximum body fat content, which ranged from 12 to 25% of body weight, and length of life of the rat. However, in the case of the *group R* (food-restricted) rats with a maximum body fat content ranging from 7 to 14% of body weight, there was a positive correlation, i.e., the fatter the rat, the longer the length of life.

The hypothesis that food restriction prolongs life and slows the aging process by reducing the metabolic rate per unit body mass was proposed in 1977 by the late George Sacher (17). He based his hypothesis on his analysis of data published by Ross (15) on rats fed five different dietary regimens. The caloric intake differed among the five groups, ranging from 18 to 75 kcal per rat per day. The average survival time also differed among the five groups, ranging from 780 to 970 days. Moreover, the average survival time inversely correlated with the daily caloric intake per rat. However, the total caloric intake per gram body weight during the life-span was found to average 102 kcal for all groups, with no particular group differing from that value by more than 4.5%. Therefore, Sacher concluded that food restriction prolongs life by increasing the time required for the rat to reach this 102 kcal per gram body weight per lifetime total; i.e., he concluded that food restriction increases longevity by reducing the rate of fuel utilization per gram body weight. This view is in accord with the concept of Rubner, first stated at the turn of the century. Also, it was on this general basis that the "Rate of Living Theory of Aging" was formally proposed in 1928 by Pearl (14).

However, data recently reported from our laboratory (11) make it unlikely that this "metabolic rate" hypothesis provides insight on the basic mechanism by which food restriction slows the aging process. The rats in our first study fed the restricted diet (*group R*) consumed the same number of kilocalories per day per gram lean body mass as did the ad libitum-fed rats (*group A*). The *group R* rats had a lifetime caloric intake per gram body weight of 134 kcal compared with 92 kcal for the *group A* rats; i.e., the restricted rats consumed more calories per gram body weight per lifetime and lived longer than the ad libitum-fed rats.

There are several possible reasons for the differences between our findings and those reported by Sacher. First, Sacher had to make assumptions concerning the use of Ross' data, since he only had the published data available to him. Different assumptions could have yielded results similar to ours. Since raw data were used, no such assumptions were needed in making our calculations. Second, Ross used the male Sprague-Dawley strain, which gets obese with age, whereas we used the male Fischer 344 strain, which remains lean throughout life; a large mass of adipose tissue in the ad libitum-fed compared with the restricted Sprague-Dawley rats could

well have compromised the accuracy of Sacher's calculation, since he used body mass rather than lean body mass. Finally, Ross used severe food restriction, whereas a moderate level of restriction was used in our study.

The bottom line is that none of the hypotheses that have been seriously proposed appears to provide valid insight into the mechanism by which food restriction slows the aging process. Is there another and perhaps more productive way to view the interaction of food restriction with the aging process? My colleague, Dr. Byung P. Yu, and I feel that the general scheme for the action of food restriction diagrammed in Figure 4 (9) provides the basic framework for the further experimental exploration of this interaction. This scheme proposes that food restriction acts to slow the aging process or processes. It further postulates that a specific metabolic mechanism or mechanisms couple food restriction to its action on the aging process. In this scheme, the retardation of physiological deterioration, immune deterioration, and age-related diseases are viewed as secondary events (i.e., as inevitable results of the slowing of the aging process) and the increase in life-span is viewed as a tertiary event (i.e., the result of retardation of physiological deterioration, immune deterioration, and age-related disease).

Although logic makes it almost inevitable that food restriction is coupled to the aging process by a metabolic mechanism, there are few clues to what this may be. An obvious possibility is that food restriction acts by slowing the rate of general cell metabolism; data from our laboratory (11) discussed above make this unlikely. In considering specific metabolic mechanisms, several come to mind on the basis of the scant data in the literature and theoretical concepts about aging. An intriguing possibility is that food restriction modulates aging by decreasing free radical damage either by reducing the rate of free radical generation or by influencing the biochemical machinery that protects the animal from free radical damage. Another possibility is that food restriction slows the aging process by modulating either the circadian concentration pattern or the daily mean level of circulating fuels or hormones or both. In support of such a view is the suggestion (18) that the premature aging of some insulin-dependent diabetics is caused by abnormal circadian levels of plasma glucose because insulin levels do not change in an appropriate way to meet the variations in metabolic needs. Another possibility is that food restriction slows the age-related decline in the rate of turnover of proteins and related biological structures. Since renewing the molecular structure of cells is necessary to prevent rapid aging, such an action of food restriction would be expected to markedly retard the rate of aging.

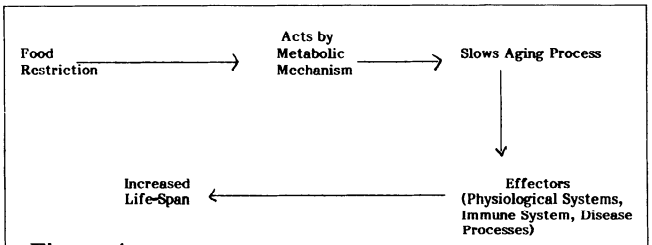

Figure 4

A general scheme for action of food restriction. [From Masoro (9)].

Clearly, searching for this metabolic mechanism has "needle in the haystack" characteristics. Nevertheless, because knowledge of this mechanism is of such great importance, both in regard to learning about the basic nature of aging and in regard to practical interventions aimed at modulating the undesirable characteristics of aging, this area should be a major focus of future gerontological research.

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Effects of Aging on the Respiratory System

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Growth and development of the human respiratory system is essentially complete by about 18–20 years of age (36, 43). Most indices of pulmonary function have been demonstrated to reach their maximum levels between the 20th and 25th year and then decline progressively with age in normal healthy adults (34). This discussion will attempt to relate the alterations in the function of the respiratory system that occur with aging to what is known about changes in respiratory system structure during the course of life.

Studies of effects of aging on the respiratory system may be difficult to interpret for several reasons (38). Chronic exposure to environmental pollutants, repeated pulmonary infections, smoking, and differences in lifestyle, working conditions, and socioeconomic factors may cause alterations in the respiratory system that are not easy to distinguish from changes due to aging alone. Therefore, different criteria applied in the selection of "normal" elderly subjects may make studies of the effects of aging on pulmonary function hard to compare. Many pulmonary function tests require cooperation and active participation by subjects, which may be difficult to obtain from elderly people. Obviously, direct comparisons of pulmonary function data from animals with those from humans are not possible in tests that require active participation of the subject. There may also be differences in the techniques employed in obtaining pulmonary function data in different laboratories. Finally, almost all of the information concerning changes in pulmonary function with age has come from *cross-sectional studies* (those in which groups of people of different ages are compared with each other at the same time) rather than from *longitudinal studies* (those in which a group of people is tested repeatedly as they age).

Changes in Human Respiratory System Function with Age

Standard Lung Volumes and Capacities

The changes that occur in the standard lung volumes and capacities with aging are shown in Figure 1. The *total lung capacity* (TLC), which is the volume of gas in the lungs after a maximal inspiratory effort, is normally determined by two opposing forces: the strength of the inspiratory muscles and the inward elastic recoil of both the lungs and chest wall (9). Although the TLC has been demonstrated in several studies to decrease with age, if the TLC data are normalized for the decrease in height that is seen in the elderly, then there is no change in the total lung capacity with age, as shown in Figure 1 (3). The decreased height of elderly subjects is a result of a decrease in the size of the intervertebral spaces, as well as the fact that in cross-sectional studies subjects from younger generations are taller than those from older generations were at the same age, probably as a result of better nutrition (19).

The *residual volume* (RV) is the volume of gas remaining in the lungs after a maximal forced expiration. It is determined by the strength of the expiratory muscles, which act in opposition to the outward recoil of the chest wall at low thoracic volumes, and the tendency for small airways to collapse and trap gas in alveoli during a forced expiration (9). Numerous studies have shown that the RV increases with age, as does the ratio of the RV to the TLC (34, 38).

The *vital capacity* (VC) is the volume of gas expired in a maximal expiration starting after a maximal inspiration. The VC is therefore equal to TLC − RV. Because the TLC is unchanged by aging (if normalized for height changes) and the RV increases, the vital capacity decreases with age (34, 38).

The *functional residual capacity* (FRC) is the volume of gas in the lungs at the end of the normal tidal expira-

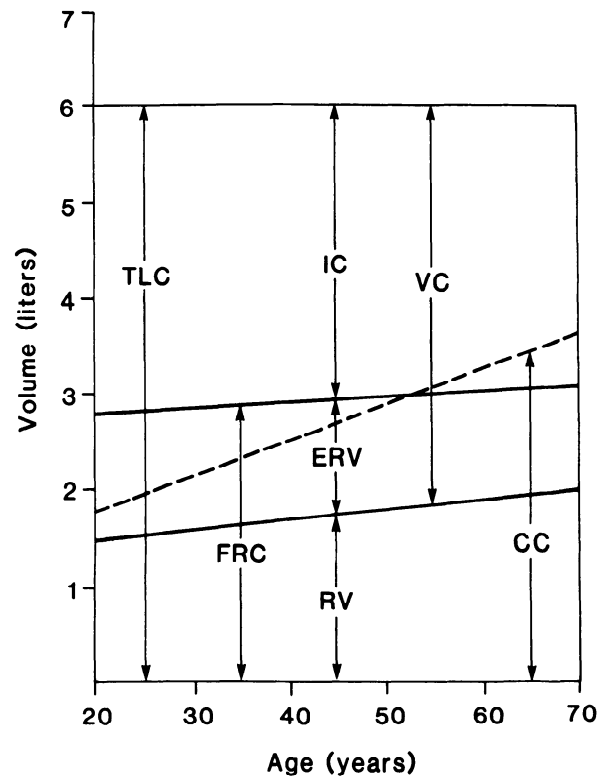

Figure 1
Schematic representation of the alterations in the standard lung volumes and capacities occurring with age. TLC, total lung capacity; FRC, functional residual capacity; ERV, expiratory reserve volume; RV, residual volume; IC, inspiratory capacity; VC, vital capacity; CC, closing capacity.

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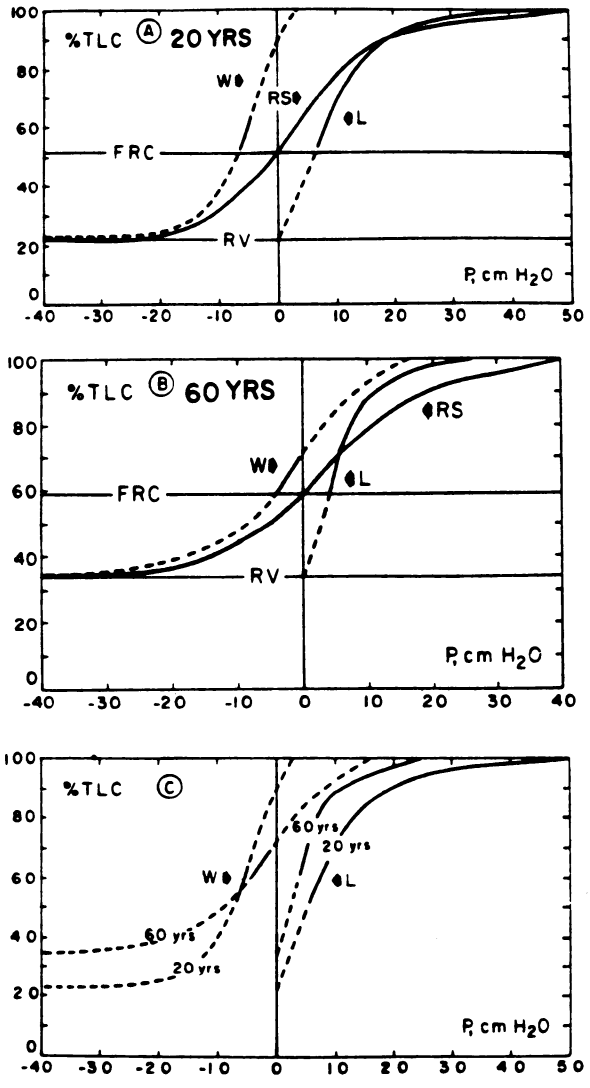

Figure 2

Representative relaxation pressure curves showing static pressure-volume relationships of the lungs (L), chest wall (W), and total respiratory system (RS) for a 20 year old (*A*), a 60 year old (*B*), and both on the same graph (*C*). These curves are obtained by having trained subjects breathe to lung volumes above and below functional residual capacity (FRC) and then relax their respiratory muscles while the airway is occluded at the mouth. The recoil pressure (P) of the whole respiratory system is determined by measuring the pressure at the mouth, proximal to the occlusion. The separate contributions of the lung and chest wall can be determined by measuring intrapleural pressure. TLC, total lung capacity; RV, residual volume. [From Turner, Mead, and Wohl (56).]

tion. Because this is a time in the respiratory cycle when all of the muscles of respiration are relaxed, the FRC represents the balance point between the inward elastic recoil of the lungs and the outward elastic recoil of the chest wall (47). Studies on the effects of aging on the FRC have yielded variable results: some have shown no change in the FRC (3); others have demonstrated that FRC and FRC/TLC increase but not as much as RV and RV/TLC, respectively (38, 56). These different findings may reflect differences in the way the FRC was determined in different studies. The helium-dilution and nitrogen-washout techniques do not include gas trapped behind closed airways, whereas the body plethysmograph technique does (8). Thus, some methods of determining the FRC may underestimate it if there is appreciable gas trapping at this lung volume, which may be the case in elderly people. Most recent studies have shown that the FRC increases with age (34).

The *expiratory reserve volume* (ERV) is the volume of gas expired during a maximal expiration starting at the end of a normal tidal expiration. It is therefore equal to FRC − RV. Because even those studies that have shown an increasing FRC with age have shown greater increases in RV, the ERV decreases with age. The *inspiratory capacity* (IC) decreases with age in those studies showing an increasing FRC.

Respiratory Mechanics

The changes that occur in the mechanics of breathing with aging are summarized in Table 1. The *elastic recoil of the lungs* decreases with age, especially at higher lung volumes (56). This is seen as a leftward shift of the lung recoil pressure curve. *Static pulmonary compliance,* which is the inverse of the elastic recoil, increases with age, as is shown in Figure 2 (37, 56). The pulmonary compliance is equal to the ratio of the change in volume to the change in pressure and is therefore the slope of the lung recoil pressure curve. The steeper slope in the elderly individual indicates greater pulmonary compliance.

Dynamic pulmonary compliance has been shown to decrease (6) and become more frequency dependent with age (7). This change probably reflects increased resistance to airflow in small airways more than it does decreased compliance of alveolar units (46), especially since static lung compliance increases. In fact, the increased resistance to airflow in small airways is probably in part a result of decreased alveolar elastic recoil leading to decreased support of small airways, as will be discussed shortly.

The *compliance of the chest wall* decreases with age, as is also shown in Figure 2 (37, 56). The chest wall recoil pressure curve is shifted to the right and is less steep, indicating a greater inward recoil pressure and less compliance of the chest wall. The chest wall curve crosses the zero recoil pressure line at a much lower lung volume, so that chest wall elastic recoil shifts from outward to inward at a much lower lung volume. The FRC and RV are increased.

The *closing volume or closing capacity* (CC), which is the lung volume at which small airways begin to close during a forced expiration, increases from about 30% of TLC at age 20 to about 55% of TLC at age 70, as shown in Figure 1 (1, 5). The closing volume may exceed the FRC in elderly people (32), which suggests that they may have airway closure and poorly ventilated or unventilated alveoli at resting lung volumes (57).

Airway closure usually begins to occur in the lower regions of the lung of a normal young person who is standing or sitting in an upright posture (59). This is mainly a result of the finding that there is a gradient of intrapleural pressure in the thorax, so that intrapleural pressure is more negative in upper regions of the chest than it is in lower regions. This gradient, which is mainly caused by the effects of gravity, results in alveoli in upper lung regions having larger volumes than those in lower regions of the lung. This is because they are subjected to greater distending pressures. At the end of the normal tidal expiration the pressure inside the alveoli is probably 0 cmH_2O (atmospheric) throughout the lung.

The pressure outside the upper lung regions is more negative than it is outside the lower lung regions, so that the alveoli in upper parts of the lung are subject to greater mechanical stresses. If it is assumed that alveoli throughout the lungs have similar compliance characteristics, those in upper parts of the lung should therefore be at larger volumes.

Small airways in lower regions of the lung are more likely to collapse than those in upper lung regions, because alveoli there are at lower volumes and therefore have less elastic recoil helping to hold small airways open (60) and because intrapleural pressure is higher (less negative at the FRC and more positive during a forced expiration) than it is in upper regions of the lung (59).

The gradient of intrapleural pressure is also responsible for regional differences in alveolar ventilation (59). The alveoli in lower regions of the lung of a young person in the upright posture are better *ventilated* than those in upper regions. The alveoli in upper lung regions are at higher volumes than those in lower lung regions, as already stated. Because of this, they are at less steep portions of their individual pressure-volume curves. That is, they are less compliant because they are at a higher volume. They therefore have a smaller change in volume per change in distending pressure during each breath than alveoli in lower lung regions, which are at steeper portions of their pressure-volume curves. Thus, because alveoli in lower lung regions are more compliant, they are better ventilated than those in upper parts of the lung.

The point of this discussion is that if elderly people have airway closure in lower lung regions, the pattern of greater ventilation in lower lung regions seen in normal young subjects will not occur (14). As we will see, this may result in less efficient matching of ventilation and perfusion in the lung (24) and may contribute to the decreasing arterial oxygen tension (Po_2) seen with aging.

Table 1 also shows that most *dynamic measurements of lung volume* decrease with age (27, 28). The maximal expiratory flow rate (the peak airflow generated during a forced vital capacity, FVC), the maximal midexpiratory flow rate (the airflow during the midpoint of FVC), the forced expiratory volume in 1 s (FEV_1), and the ratio of the FEV_1 to FVC all decrease with age. This is probably a result of decreasing strength of the expiratory muscles, decreasing chest wall compliance, and an increasing tendency for airways to close during forced expiratory efforts, causing gas trapping in the lungs (57). The maximum voluntary ventilation (MVV), which is the maximum volume of air that can be breathed in and out in 12 or 15 s (expressed in liters per minute), also decreases with age (19). However, this is a rather nonspecific test, reflecting lung and chest wall mechanics, the strength of the respiratory muscles, the status of the controllers of breathing, and motivational aspects.

Pulmonary Gas Exchange

Table 1 summarizes the changes in pulmonary gas exchange that occur with age. The arterial Po_2 decreases progressively and linearly, falling from approximately 95 Torr at age 20 to about 75 Torr at age 70 (38, 52). Because the alveolar Po_2 does not change (at least in the well-ventilated alveoli), the *alveolar-arterial oxygen gradient*, or (A-a)Do_2, increases progressively with age by the same amount (25, 38, 48). The factors that determine the (A-a)Do_2 include the physiologic shunt, which increases slightly from less than 5% at age 20 to approximately 15% at age 70 (10), the matching of ventilation and perfusion, and the diffusing capacity.

Table 1
Relationship of Changes in Structure to Changes in Function

Alteration	References
Loss of alveolar elastic recoil:	29, 41, 42, 60
Increased static pulmonary compliance	56
Decreased pulmonary elastic recoil pressure	56
Increased functional residual capacity	38, 56
Decreased support of small airways	60
Greater effect of dynamic compression	6, 60
Decreased dynamic lung volumes	6, 27, 28
Increased residual volume	3
Increased closing volume, gas trapping	1, 5, 10, 32
Decreased dynamic pulmonary compliance	6, 7
Less uniform alveolar ventilation	14, 17, 24
Ventilation-perfusion mismatch	24
Decreased response to hypoxia and hypercapnia	23, 30, 39
Alterations in chest wall structure and decreased respiratory muscle strength:	40, 49
Decreased chest wall compliance	37, 56
Increased residual volume	3
Decreased vital capacity, dynamic lung volumes	27, 28
Decreased maximum voluntary ventilation	19
Decreased response to hypoxia and hypercapnia	23, 30, 39
Loss of alveolar surface area and changes in the pulmonary circulation:	50, 54
Ventilation-perfusion mismatch	24
Increased alveolar dead space	16, 48, 53
Decreased diffusing capacity	13, 18, 20
Decreased arterial Po_2	52
Increased (A-a)Do_2	25, 48

The *physiologic shunt* includes the effects of ventilation-perfusion mismatch, as well as the anatomic shunt. *Ventilation and perfusion* are not matched as well in the lungs of the elderly as they are in the lungs of younger subjects (24). Alveolar ventilation becomes less uniform with age, as indicated by such tests as nitrogen washout or lung clearance index (14, 17). This is probably attributable to airway closure in lower lung regions causing more ventilation of upper lung regions, as was discussed previously. As is well known, there is normally greater perfusion of lower lung regions in young healthy adults (59). Although a few studies have shown slightly increased perfusion of upper lung regions in the elderly (2, 31), it is reasonable to assume that preferential ventilation of upper lung regions without decreasing blood flow to lower regions and increasing blood flow to upper regions will result in disturbed ventilation-perfusion relationships. The *alveolar dead space* (alveoli that are ventilated but not perfused) increases in the elderly, probably because of a decreased cardiac index, leading to unrecruited pulmonary capillaries (16, 53). It is also possible that structural alterations of pulmonary vessels may occur with aging and attenuate the strength of the hypoxic pulmonary vasoconstriction (57).

The *pulmonary diffusing capacity* (DLCO) decreases progressively and linearly with age, falling approximately 20% over the course of adult life (13, 20). This decrease is probably a result of decreased alveolar surface area, as well as a decrease in the pulmonary capillary blood volume, both of which are known to occur with aging (18). The decrease in diffusing capacity

may not have as great an effect on the (A-a)Do_2 as does the less well matched ventilation and perfusion.

Arterial carbon dioxide tension does not change consistently with age, despite the decreased arterial Po_2 and the increased (A-a)Do_2 (57). Possible explanations for this include the greater diffusivity of carbon dioxide through the alveolar-capillary barrier and the differences in the oxygen and carbon dioxide dissociation curves.

Control of Breathing

The *ventilatory responses to both hypoxia and hypercapnia* have been shown to decrease with age (23, 30). These decreased responses could be a result of any combination of several alterations in the respiratory system that occur with age (57). It is possible that the sensors for hypoxia, the arterial chemoreceptors, and for hypercapnia, both the central and arterial chemoreceptors, become less sensitive with aging. Changes may also occur in the central respiratory controller. However, it seems more likely that the attenuated responses to hypoxia and hypercapnia reflect decreased strength of the respiratory muscles and alterations in the mechanics of the lung and the chest wall, including decreased chest wall compliance and the greater tendency for dynamic compression and airway closure to occur during forced expiration (39). The occurrence of snoring and obstructive sleep apnea also increase with aging (4, 55).

Exercise Capacity

The ability to exercise, as indicated by the *maximal oxygen uptake* ($\dot{V}o_{2\,max}$), decreases progressively and linearly with age, falling about 35% between the ages of 20 and 70 (11, 26, 38). Although changes in lung and chest wall mechanics, the pulmonary diffusing capacity, ventilation-perfusion relationships, and the control of breathing contribute to this decrement, the main cause of the decreased ability to exercise is probably a decreased ability to increase the cardiac output (38).

Pulmonary Defense Mechanisms

The elderly have fewer cilia lining their airways than are seen in the lungs of younger individuals, which probably leads to a decreased efficiency of the *mucociliary escalator* (44). Elderly people also show decreased *reflex responses* to mechanical or chemical stimulation of the upper airways or tracheobronchial tree. For example, coughing is less efficient in terms of volume, force, and flow rate, probably as a result of decreased respiratory muscle strength and the altered mechanics of the lung and chest wall (57).

Changes in Human Respiratory System Structure with Age

Alveoli and Alveolar Ducts

After about age 40, alveolar ducts and respiratory bronchioles enlarge with age at the expense of the surrounding alveoli (50, 58). This results in a larger fraction of the lung volume occupied by alveolar ducts and a smaller volume of the lung represented by alveoli. The alveolar surface area decreases with age (54), although it is not clear whether this reflects an actual decrease in the number of alveolar septa or changes in their configuration (50).

The number and size of the interalveolar fenestrae increase with age (45), with a concomitant degeneration of the adjacent elastic fibers which provide structural support of the alveoli (60). This loss of elastin fibers in the walls of alveoli and alveolar ducts occurs despite an increase in the total pulmonary elastin content, as a result of increased elastin in the pleura, septa, bronchi, and blood vessels (41). Thus, the ratio of relatively indistensible collagen to more distensible elastin is 2:3 in the young adult but appears to decrease with age, because the total elastin content increases while the collagen content remains relatively constant (42). There are also increases in cross-linking between collagen fibers, elastin fibers, and each other (29). Although the exact relationship between these alterations in structure and the changes in lung mechanics is not well established, the structural changes do appear to be the source of the increased lung compliance and decreased pulmonary elastic recoil. There may also be age-related changes in the composition and turnover of pulmonary surfactant, but as yet there is not information on the effect of aging on pulmonary surfactant (26).

Pulmonary Vasculature

There is an increase in the thickness of the larger pulmonary arteries with age, especially of the intimal and medial layers (21, 51). Resting mean pulmonary arterial pressure and pulmonary vascular resistance show little change with age, but the vasculature becomes less distensible and there may be fewer unopened capillaries to recruit (12, 15). Therefore, during exercise mean pulmonary arterial pressure may increase more and pulmonary vascular resistance may decrease less than they do in younger individuals (15). As already noted, there is a decrease in the pulmonary capillary blood volume with age, resulting from either loss of or changes in the configuration of alveoli and alveolar septa, as well as the decreased cardiac index of the elderly.

Larger Airways

There is an increase in the number of bronchial mucous glands in the elderly (22). Bronchial cartilage shows a tendency to calcify in the aged, which is probably the main cause of the slight increase in dead space seen in older people (23).

Thoracic Structure

As mentioned previously, important changes in thoracic structure occur with aging. *Costal cartilages* calcify, resulting in decreased mobility and compliance of the rib cage (49). The spaces between *spinal vertebrae* decrease and the degree of kyphotic spinal curvature increases, leading to a shorter thorax with an increased anteroposterior diameter (40). A greater deposition of abdominal and thoracic adipose tissue may also contribute to the decreased chest wall compliance of the elderly. Finally, the strength of the muscles of breathing decreases with age (49).

Summary: Relationship of Changes in Structure to Changes in Function

The main structural alterations that occur as a result of aging are *1*) a loss of alveolar elastic recoil, *2*) alterations in chest wall structure and decreased respiratory muscle strength, and *3*) a loss of alveolar surface area and changes in the pulmonary circulation. The effects of these structural changes on respiratory system function are summarized in Table 1.

Loss of Alveolar Elastic Recoil

The loss of alveolar elastic recoil results in *increased static pulmonary compliance* and *decreased pulmonary elastic recoil pressures*, especially at higher lung volumes. Because the functional residual capacity represents the balance point of the inward elastic recoil of the lungs and the outward elastic recoil of the chest wall (which increases), an *increased FRC* is expected, but this has not been seen in all studies. A major consequence of the loss of alveolar elastic recoil is a *loss of support of small airways* by "traction" or "tethering." This results in a greater effect of *dynamic compression* of airways during forced expiratory efforts, as indicated by *decreased dynamic lung volumes* and airflows, such as the maximal expiratory flow rate, maximal mid-expiratory flow rate, forced expiratory volume in one second, and less specific measurements like the maximum voluntary ventilation and dynamic pulmonary compliance. The loss of alveolar elastic support of small airways also results in *airway closure at higher lung volumes* and contributes to the *increased residual volume.* Airway closure at or near normal lung volumes causes *less uniform alveolar ventilation,* especially in lower lung regions, which contributes to *ventilation-perfusion mismatch.*

Alterations in Chest Wall Structure and Decreased Respiratory Muscle Strength

Alterations in chest wall structure causing decreased compliance of the chest wall and the decreased strength of the respiratory muscles also contribute to the increased residual volume and *decreased dynamic lung volumes,* as well as the less specific *maximum voluntary ventilation.*

Loss of Alveolar Surface Area and Changes in the Pulmonary Circulation

Loss of alveolar surface area and changes in the pulmonary circulation lead to decreased pulmonary capillary blood volume and a decreased surface area for alveolar-capillary gas diffusion. This results in a *decreased diffusing capacity,* which along with a slight increase in the physiologic shunt and a *less efficient matching of ventilation and perfusion,* contributes to a *progressive decrease in arterial* Po_2 and a *progressive increase in the alveolar-arterial oxygen difference* with aging.

All of these structural alterations, plus others in the respiratory and cardiovascular systems, may act together to attenuate less specific indices of cardiopulmonary function, such as the ability to perform muscular exercise, as indicated by the maximal oxygen uptake, or the responses to hypoxia and hypercapnia.

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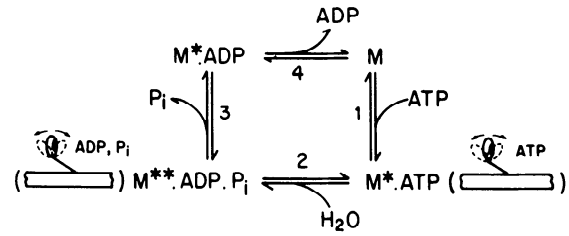

Simplified mechanism of myosin ATPase. Numbers refer to sequential steps.

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Book Reviews

Beneficial Effects of Endotoxins.
Alois Nowothy (Editor)
New York: Plenum, 1983, 581 pp., illus., index, $69.50.

Endotoxins are constituents of the cell wall of bacteria that cause a "fascinating variety of biological effects, unparalleled by any other natural products." Nowothy has assembled contributions from investigators actively interested in the effects of endotoxins on host defense and immunology in an attempt to produce a book that reviews "from every available angle" the known beneficial effects of endotoxins. Included in this category are *1*) enhancement of the immune response by stimulating DNA synthesis in B lymphocytes or by acting as an immune adjuvant, *2*) stimulation of synthesis and release of interleukin-1, interferon, and other biologically active proteins, *3*) protection against the harmful effects of radiation, and *4*) induction of antitumor activity.

The book is primarily descriptive; various biological activities of endotoxins thought to be beneficial are outlined. As many of the authors have noted, the mechanisms behind the protective effects of endotoxins are still unknown. Intermingled among these chapters are some well-written reviews not specifically related to the main theme of the text (e.g., induction of endotoxin tolerance by Greisman, protection against Gram-negative bacteremia by Braude and Ziegler, etc.).

The effects of endotoxins are so widespread that it is virtually impossible to cover all that are known and speculated to be beneficial. Nevertheless, I (armed with my own biases) was surprised by the narrowness of coverage in this book. One of the major effects of endotoxins is the production of interleukin-1. Recent evidence supports the hypothesis that interleukin-1 is closely related, if not identical to, endogenous pyrogen and leukocyte endogenous mediator. The effects of interleukin-1 on the immune system were reviewed by Lachman, Nakano, and Uchiyama, Gollahon et al., and others, but no mention was made about the potentially beneficial effects of endogenous pyrogen or leukocyte endogenous mediator. In fact, in the introductory chapter, Nowothy lists fever as the best known of the *toxic* effects of endotoxin. There have been recent reviews in *Microbiological Review* by Roberts, in *Reviews of Infectious Diseases* by Mackowiak, and numerous individual reports in *Science, Nature,* and other widely read journals indicating that moderate fevers are actually beneficial. I was surprised that this book did not even have one chapter (out of 28) that dealt with this area. No mention was made of the potentially beneficial effect of reductions in plasma iron or zinc, elevations in plasma copper and acute phase proteins, or other responses to the endotoxin-induced release of interleukin-1/endogenous pyrogen/leukocyte endogenous mediator. Again, there have been numerous reviews (e.g., by Weinberg in *Science* and in *Microbiological Reviews* on iron) and short articles on these subjects, indicating that these changes are beneficial and therefore should have been reviewed in a text purporting to cover the entire field.

As in most edited texts, the writing styles vary considerably. Most, but not all, chapters have summaries or conclusions. No consistent attempt has been made to point out in these summaries the specific beneficial effects of endotoxins. Some authors have relied considerably on abbreviations, which although defined in the text, are not listed in an appendix. This can lead to considerable confusion. For example, on one page the following abbreviations were used: LPS, C3H/HeJ, LAP, HPBL, and EP. This might seem a trivial criticism; however, to those investigators most familiar with one of the major effects of endotoxins, the development of fever, EP refers to "endogenous pyrogen." In this book, EP generally refers to "endotoxin protein."

There is an extremely interesting discussion of the conceptual structure of biology in Ernst Mayr's "The Growth of Biological Thought" (Belknap Press of Harvard Univ. Press, 1982). Biology can be divided into *proximate* and *ultimate* causes. Briefly, proximate causes deal with the functioning of an organism. Questions relating to proximate causes are those concerned with, for example, "*What* are the mechanisms by which blood pressure remains relatively constant in the face of moderate hemorrhage?" or "*How* is substance x transported . . .?" Ultimate causes are related to evolutionary events. An ultimate question will often be in the form of "*Why* is blood flow to the brain maintained relatively constant, despite changes in mean arterial pressure?" As stated by Mayr, "proximate causes have to do with the decoding of the program of a given individual; evolutionary (ultimate) causes have to do with the changes of genetic programs through time, and with the reasons for these changes." It seems to me that a book attempting to describe the biological role of endotoxins, one that makes statements about the beneficial aspects of these biologically ubiquitous substances, should have devoted considerable space to ultimate causes. There is, however, virtually no discussion about the evolution of host response to endotoxins. Why have there evolved so many beneficial (and in some cases harmful) effects to endotoxins? The only contributor that even asked this question was Jacobs ("What is the biological role of responses of the cells of the immune system to LPS?"). Endotoxins presumably have been around for hundreds of millions of years. All organisms have had to learn to live with these ubiquitous substances. How do lower animals respond to endotoxins? Are there known beneficial effects of endotoxins in insects or other invertebrates? Does injection of endotoxin into lower vertebrates lead to protection against radiation, tumors, and viral or bacterial infections? The most widely used assay for the detection of endotoxin relies on proteins released from amebocytes of the horseshoe crab. Could we understand more about the evolution of host response to endotoxin (both beneficial and harmful) by looking more closely at the responses of these lower animals? I believe that this book would have been greatly strengthened by the addition of chapters attempting to address the questions relating to the evolution of these numerous host responses to endotoxins.

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Cardiovascular Physiology IV
A. C. Guyton and J. E. Hall (Editors)

Baltimore, MD: University Park, 1982, 371 pp., illus., index, $49.95 (Int. Rev. Physiol. Ser.)

Guyton, in his "Consultant Editor's Notes," has provided us with some of the criteria we should use in evaluating the success of this volume in the International Review of the Physiology series. He writes ". . . we hope and believe (our policies) will add important qualities often missing in reviews, especially integration of physiological mechanisms and instructiveness." He goes on to say that these reviews are not to consist of an "annotated list of references" and expresses the hope of presenting to the reader ". . . a series of treatises that they will use not merely as a reference but also as an exercise in refreshing and modernizing their whole store of physiological knowledge."

This volume, the fourth in the cardiovascular series, is definitely a success when evaluated by those criteria.

There are eight review articles here. They cover a moderately wide range of topics: atherogenesis, hypertension, contraction of cardiac muscle, resetting of baroreceptors, formation of lymph, the role of vasopressin, renal hemodynamics, and the response to volume expansion. Four of the papers deal with pathophysiology in some form, two discuss more basic mechanisms, and four consider regulation as a central theme.

While there are plenty of references for the bibliophile (from as "few" as 75 to as many as 272), the authors have in general adhered to Dr. Guyton's charge to integrate and instruct. The topics are succinctly put into their appropriate context, and current data and concepts are presented. Many of the papers are well illustrated, often with data taken directly from the original literature or assembled by the author(s) of the review. There are a good number of summarizing or integrating figures that in capsule form give the reader a useful visual image with which to organize his or her thinking about the topic at hand.

This volume should be of use to workers in the cardiovascular and related fields; as is usually the case, the utility of each individual article is likely to be directly related to how far the topic is removed from the individual's own fields of expertise. Teachers of physiology will find this volume of great use in updating their thinking about important and timely topics in cardiovascular physiology. Students, particularly graduate students, will find this a valuable source of current information (and references) from the frontiers of cardiovascular research.

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Molluscan Neuro-Endocrinology
J. Lever and H. H. Boer (Editors)

New York: North-Holland, 1983, 268 pp., illus., $32.00

This book well illustrates a salient aspect of modern comparative endocrinology: animal groups which once received little attention by endocrinologists and about which the limited information available was considered only of peripheral interest, are now yielding large bodies of knowledge, no longer esoteric but, rather, contributing to conceptual advances based on sophisticated methods, thorough analysis, and well-controlled experimention. Annelid, coelenterate, echinoderm, and turnicate endocrinology are authentic subdisciplines, and so, as this book fully illustrates, is gastropod endocrinology. This volume does not really treat molluscan endocrinology (there is only one paper on the pelecypod and only two papers on a cephalopod); in fact, it is in good part a collection of papers on one pulmonate gastropod, *Lymnaea stagnalis,* which has become an almost "classical" experimental animal for neuroendocrinological studies owing to the detailed analysis conducted in recent years by investigators at the Free University of Amsterdam. The sustained research efforts of Joosse, Boer, Roubos, Geraerts, de Vlieger, ter Maat, and others have been varied and productive. *Aplysia* and other gastropods also receive attention, and it is interesting to note that *Aplysia,* an animal of choice for electroneurophysiologists for some years now, emerges as another animal of choice for neuroendocrinologists. However, the work on *Lymnaea,* a rather unprepossessing pond snail of small size, remains uniquely impressive in the breadth and depth of information available.

The book is a collection of research papers and some interesting overview presentations (notably by Boer and Schot on the phylogeny of peptidergic systems, by Ram on gastropod egg-laying hormones, and by Price on phenylalanyl-methionyl-arginyl-phenylalanine-amide peptide [FMRF-amide] and related peptides) from a minisymposium organized by the Amsterdam group in August 1982.

Notable aspects discussed in this volume include the presence of vertebrate neuropeptides or their relatives in gastropods (neurotensin, TRH, somatostatin, etc.), the egg-laying hormones of *Aplysia* and *Lymnaea* and the control of their biosynthesis and secretion, the electrophysiology and ultrastructure of neurosecretory neurons and their connections, and factors regulating vascular functions and hydromineral and carbohydrate metabolism. Again, one is impressed by the spectrum of techniques that are today being employed to delineate the neuroendocrine biology of mollusks.

For the comparative physiologist, this book is a useful and information-laden volume. For the alert graduate student and postdoctoral fellow, the symposium makes clear the potential for further meaningful neuroendocrinological research on the phylum Mollusca of both general and evolutionary significance.

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Multiple Choice Questions in Physiology. S. Jennet and O. Holmes

Baltimore, MD: Urban & Schwartzenberg, 1983, 118 pp., illus., index, $7.50

This book is one in a series of useful pocket-sized revision books recently introduced by Pitman Medical. The series comprises multiple choice question (MCQ) books and pocket examiners devoted to basic medical sciences and clinical topics. The authors of this particular text are enthusiastic teachers, active in developing teaching methods and new materials for student use, and I feel this becomes apparent as one goes through the book.

There are obvious limitations to the use of MCQs in assessing students, as they do not allow the candidates to express ideas in their own words nor to develop logical or original arguments. An additional criticism often aimed at MCQs is that they only test the ability to recall facts. However, the questions in this book are also designed to test ability to solve numerical problems and to make valid inferences from data presented. To this end diagrams are included in some of the questions. There are an increasing number of books available on MCQs in Physiology, but few include diagrams or figures. Inclusion of such material adds to the value of the book as a teaching aid, although most students are unlikely to meet this type of question at examination. Another way in which this text differs from most others is in the inclusion of an index.

The introduction to the book has a useful section on common pitfalls in the construction of questions. One pitfall not mentioned is to set a stem that could be followed by any one of several hundred items, e.g., question 6-32 "With reference to endocrine function," which is duplicated in question 6-39 "With reference to endocrine function in general." This particular example illustrates a rather tedious shortcoming of the book: too many questions begin "With reference to" or "Concerning." The questions have not been divided according to organ systems but, rather, in terms of function, which is useful conceptually, although the sections are rather unequal in length, the questions in each ranging from 8 to 56 in number. The answer code together with short explanatory notes is given in the second part of the book. As the questions and answers are of a similar length, it might have been possible to put the answers on the page following the questions, which would have been easier for the reader.

The authors state in the introduction that "comments on remaining imperfections will be welcomed." I hope my comments are of help. They are meant in no way to detract from what is a valuable little book of a generally very high standard which should be of use to both teacher and student.

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Physiology of the Kidney (2nd ed.) L. P. Sullivan and J. J. Grantham (Editors)

Philadelphia: Lea & Febiger, 1982, 236 pp., illus., index; $17.50 (Canada)

Handbook of Renal Therapeutics M. Martinez-Maldonado (Editor)

New York: Plenum, 1983, 568 pp., illus., index, $49.50

A Guide of Water Electrolyte and Acid-Base Metabolism. R. D. Eastham

Littleton, MA: Wright PSG, 1983, 230 pp., illus., index, $15.00

The above texts approach renal disease from different aspects. The most enjoyable book for me to read was *Physiology of the Kidney* by Sullivan and Grantham. In the preface to the book the text is described as a manual to teach the principles of renal physiology to medical students and physicians. This book more than adequately meets the intended goal of the authors. Having read this text in its first edition, I find the second edition to be a dramatic improvement. As a young student of medicine, I was very impressed by Dr. Sullivan's writings, and the improvements made in this edition are remarkable. The book goes concisely through various aspects of renal physiology. It is not intended to be the latest in physiological research but instead tries to give an overview of current concepts, with an understanding of a very complex and always changing science. The text seems to read much better than the first edition. Most of the chapters have been rewritten, and newer information has been added. The new figures used in the text are also easier to understand and are very eye-catching. The bibliography has been updated to include the most recent references in the areas discussed. References are given individually at the end of each chapter and can be used to look up more specific information on individual topics.

The Handbook of Renal Therapeutics is edited by Martinez-Maldonado. It has multiple contributing authors, and this unfortunately is the weakness of the book. It purports by title to be a handbook of renal therapeutics, but in no way can it cover many of the topics that are discussed in the short amount of space provided. Many of the therapeutic approaches discussed represent the bias of the individual chapter authors. An example of this appears in the discussion of uremic pericarditis where the approach of the Minnesota group is presented. Although the approach to the problem is certainly valid, the discussion makes it seem that this is the only way uremic pericarditis should be handled, whereas, in fact, the use of intrapericardial steroids still remains controversial. At the end of the chapters are suggested readings on the subjects discussed in the text; however, the items mentioned in the text are not footnoted and again leave open for question the personal approach of the writer of each chapter. Most of the topics covered are excellently presented. The charts and diagrams used are easy to read and flow very nicely. The text has obviously avoided the complicated overwhelming tables that are found in the classic textbooks of nephrology. In the preface to the book, the editor states that the original intent of this text was to be a manual; however, due to the vast amount of material that became included, the manual turned into a handbook.

The third text presented for review is that of Eastham, *A Guide to Water Electrolyte and Acid-Base Metabolism.* This book is divided into five sections. There is a guide to the use of each section after the table of contents. The reviews are very brief but extremely poignant. Many clinically useful points are brought up in the text, and it makes for quick and easy reference. No detailed explanations, however, are given on many of the topics, but the book was not designed to include this information. It would certainly be useful for residents when a quick review of a specific topic is needed, and it adequately performs its function as a pocket book guide for young physicians. The text would benefit from a short bibliography so that the student could quickly find additional material for review.

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