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Cover: Carl J. Wiggers (*right*) at work in his laboratory. See Historical Articles, p. 407.

Correction to Author Index

Physiologist 25(4): 344, 1982

Names of the following participants in Poster Discussion Sessions (Tues. A.M.—Control of Breathing: Integration and Patterns; Tues. P.M.—Lung Fluid Balace; Wed. A.M.—Mechanics of Breathing: Airway Reactivity: Thurs. A.M.—Pulmonary Circulation: Vasomotor Responses; Thurs. P.M.—Metabolic Effects of Hypogravity, Hypokinesis and Exercise) were omitted from the Author Index and the Program for the 33rd APS Annual Fall Meeting.

The Meteoric Rise and Fall of William Townsend Porter, One of Carl J. Wiggers' "Old Guard"

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As the American Physiological Society approaches its centennial celebration, it is well to look back at some of the key figures who played prominent roles in the progress of the Society. One of these pioneer physiologists was Carl J. Wiggers (Fig. 1), in whose honor the Wiggers' Award Lecture is given each year. Another physiologist who contributed in many ways to the Society was William Townsend Porter, one of Wiggers' "Old Guard." Wiggers was deeply indebted to the four men shown in Fig. 2: in the upper left, William T. Lombard, Professor of Physiology at Michigan Medical School, Wiggers' Alma Mater; to his right, Arthur A. Cushny, Professor of Pharmacology at Michigan; at lower left, William H. Howell, who was Professor of Physiology at Michigan until 1892, the year after Wiggers entered Michigan Medical School; and finally, William Townsend Porter, the one outsider, Professor of Comparative Physiology at the Harvard Medical School.

In his autobiographical *Reminiscences and Adventures in Circulation Research* (1), Dr. Wiggers wrote of Dr. Porter in his role as editor of the *American Journal of Physiology*: "My first skirmish with an editor occurred in 1907 when I sent my second paper to W. T. Porter, during Lombard's absence in Europe. The paper was returned for two reasons: verbosity and redundancy and its lack of official approval from the head of the department. In kind (but resolute) language he pointed out that a meritorious discovery may fail to be appreciated because of faulty presentation and that by virtue of longer experience a departmental director is responsible for publications emanating from his laboratory. When the sting of criticism regarding its literary merits had ameliorated, I became grateful for the time Porter had devoted to the making of constructive suggestions, but I still resented his suggestion that papers required the approval of department heads before acceptance."

Presented at the Wiggers Award Dinner on 21 April 1982 at New Orleans. Excerpted quotes are published here by permission of the Harvard University Archives and the Harvard Medical Archives.

Wiggers then continued: "To an inexperienced author this suggested control of publications by the 'old guard' and an infringement on the prerogatives of youngsters to express their own views in their own ways. I even had the temerity to express these sentiments to Professor Porter. His reply was in no sense defensive; it was a bold crispy exposition of the many safeguards that such approval provided."

Wiggers also noted that Porter played several other important roles in the annals of American physiology: "He furthered the extension of laboratory instruction in physiologic science by making equipment available at low cost and, when the ventures finally proved profitable, he generously diverted accumulated proceeds to the establishment of a Research Fellowship. His pioneer researches on the coronary circulation, ventricular fibrillation, and the vasomotor center directed further research on circulation into practical channels. He set an example in presenting results of an investigation in a style that was both lucid and enjoyable. He showed faith in the development of physiologic research in America when he volunteered to assume financial responsibility for the first five volumes of the *American Journal of Physiology* and actually continued to do so for thirty-three volumes." Another link between the two physiologists developed in 1935 when Harold, Wiggers' son, was appointed a Porter Fellow to work with Hallowell Davis in the Department of Physiology at the Harvard Medical School.

W. T. Porter was born in Plymouth, Ohio, only a short distance from Cleveland, where Wiggers spend so many productive years. His father was also a physician who served in the Union Forces during the Civil War. Porter's mother died when he was 12 years old and he was orphaned at the age of 17. From then on, he had to

Figure 1
Carl J. Wiggers.

Figure 2
Wiggers' "Old Guard": Upper left, William T. Lombard; upper right, Arthur A. Cushny; lower left, William H. Howell; lower right, William T. Porter (1).

support himself at various jobs, and he did not enter medical school until he was 20 years of age. After three years of studies he received his M.D. degree in 1885 from St. Louis Medical College, now Washington University School of Medicine. During this period of study he apparently supported himself by working in the evenings. After two years service at the St. Louis Hospital and Medical College, he was appointed Assistant Professor of Physiology in 1887 and shortly thereafter went to Philadelphia for six months of study in physiological chemistry with Drs. Kemp and Marshall. On his return to St. Louis he taught laryngology and physical diagnosis, as well as physiology, and also maintained a private practice.

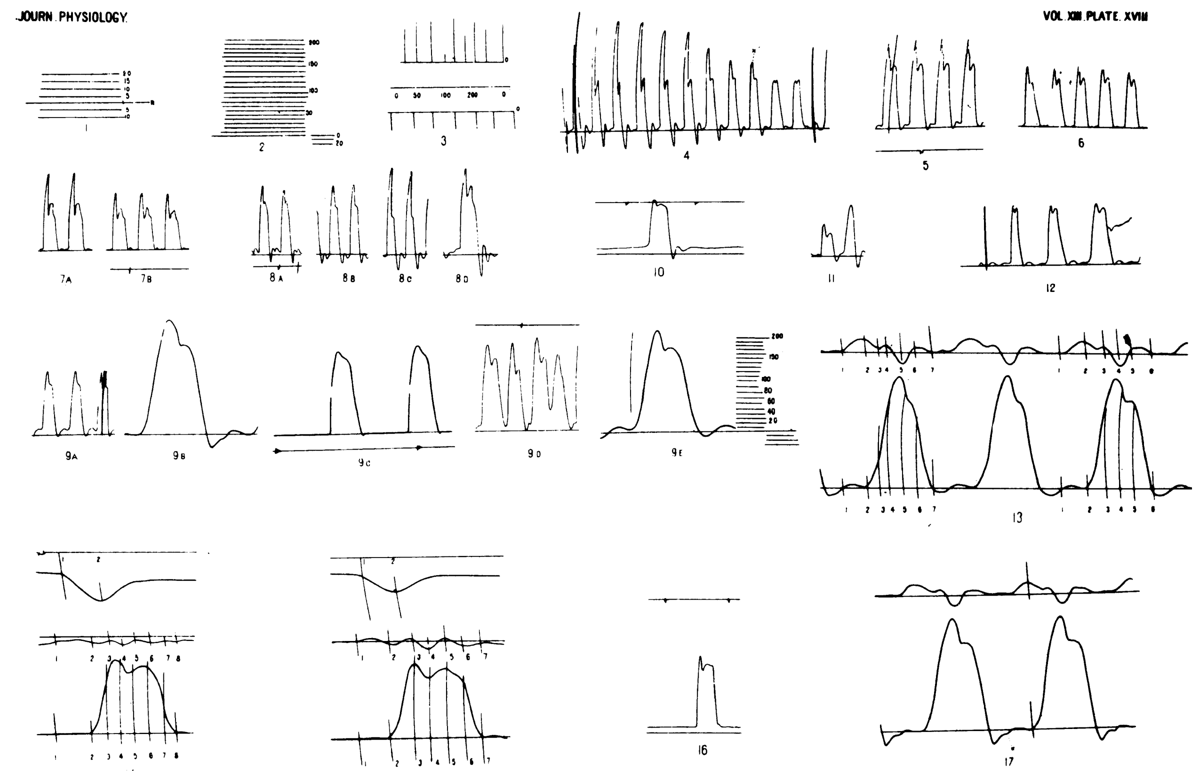
In 1888, only three years after graduation, Porter was promoted to Professor of Physiology at his alma mater, where he established the first physiology laboratory in the midwest. He was simultaneously chief surgeon at St. Louis Hospital. In June 1881 Porter sailed for Germany, where he worked with Flemming and Hansen in Kiel. He then went to Berlin to work with Gad for nine months before returning once more to St. Louis. In the following summers of 1891, 1892, 1893, and 1894, he again returned to Germany to do research. The summer of 1891 he spent with Hürthle in Heidenheim's laboratory. During the summers of 1892 and 1893 he worked with Drs. Gad and Schultz in Berlin and in 1984 with Züntz. Porter thus had a good and broad grounding in neurohistology and in respiratory and cardiovascular physiology. His postgraduate training abroad, marking a sharp contrast between the didactic teaching of physiology at St. Louis and the experimental student laboratory instruction in Germany, was instrumental in shaping Porter's future concepts of medical eduction.

We have no record as to what stimulated this young midwesterner, educated by the classic didactic method at a proprietary medical school, to turn to histologic and physiologic research. His first publication in 1890 came from Professor Flemming's Anatomical Institute at Kiel and was entitled "The Presence of Ranvier's Constrictions in the Spinal Cord of Vertebrates" (2). The first major physiological study, "Researches on the Filling of the Heart" was done in Heidenheim's Physiological Institute at Breslau under the tutelege of Hürthle, whose expertise in pressure measurements is illustrated in Fig. 3 (3). This study, which was published in the British *Journal of Physiology* in 1892, begins with the following statement: "The filling of the heart is the result of differences of pressure between the great veins, auricle and ventricle. I have sought to determine these differences and their relative importance, partly by the comparison of synchronous curves of intra-ventricular and intra- auriclar pressure, and partly by means of the differential manometer." The paper, published 90 years ago, has a surprisingly modern ring.

Porter's next publication (Fig. 4), "On the Results of Ligation of the Coronary Arteries," appeared in the *Journal of Physiology* in 1893 (4) and describes the results of experiments done in the Physiological Institute of the University of Berli in the laboratory of Professor Gad. Since only a handful of studies had been done on the effects of coronary occlusion on ventricular function, Porter was able to survey all of the world literature on the topic—from England, France, Germany, and Italy. In reviewing the literature he came to the following conclusion: "Seldom have results of physiological studies been more at variance. The attentive reader finds no statement that is not denied, no fact not in dispute. These controversies would alone compel an examination of the interesting phenomena in question and the necessity of further research is increased by the knowledge that changes in cardiac pressure following closure of the coronary artery have been inferred rather than determined, and have never been studied with the improved methods of the present day." From his exhaustive studies Porter was able to conclude that ligation of a small coronary artery did not lead to standstill of the heart, but that tying off of large arteries, particularly on the left side of the heart, led to a decrease in ventricular pressure, and then standstill of both ventricles, followed by ventricular fibrillation. The paper ended a century and a half of controversy on the effects of coronary ligation on ventricular function and also suggested that the coronary arteries were end arteries.

Porter's interests in medicine were extraordinarily broad. In addition to his studies on physiology of the circulation and respiration, Porter, like Henry Pickering Bowditch before him, became interested in the growth of children. He wrote a number of anthropometric papers including "The Physical Basis of Precocity and Dullness" (5) and "The Growth of St. Louis Children" (6). These growth studies of Porter were done as meticulously as his laboratory research. Tanner, in his *History of the Study of Human Growth* (7), called them the most important of the American studies of the time. What distinguished "Porter's St. Louis survey from other is the relating of body size to

Figure 3
Illustration of pressure tracings from Porter's first physiological paper published in 1892 (3).



apparent ability at School." He found that the pupils in the higher grades were heavier than the pupils of the same age in the lower grades. "Porter thought that physical strength, which he equated with height and weight, conditioned the amount of mental effort a child could make, and he was much concerned like all his contemporaries, with the question of school 'over-pressure'."

Porter's publications began to draw the attention of eminent scientists in Germany and England, as well as in America, and he numbered many of them as close friends. For example, when Charles Sherrington (Fig. 5), later to win the Nobel Prize, applied for prestigious chair in Oxford, he requested a letter in support from Porter, "the only one from the USA." It was therefore not surprising that Henry Pickering Bowditch (Fig. 6), Chairman of the Department of Physiology and Dean of the Harvard Medical School (and one of the founders of the APS), invited Porter to fill the vacancy created by Howell's assumption of the chair at Hopkins in 1893. Porter's (Fig. 7) task was to assume responsibility and reorganize the teaching of physiology at Harvard and, in particular, to introduce routine student laboratory experiments in the school on the corner of Boylston and Exeter Streets in the Back Bay of Boston (Fig. 8). His research laboratory immediately began to attract some of the best young people in physiology and as one examines the Dean's Reports from 1894 to 1900, it becomes apparent that Porter's laboratory was the most vigorous research facility at the Harvard Medical School.

Porter's rising stature in physiology was evident when William H. Welch, the dean of the Johns Hopkins Medical School, invited him (8) to publish a paper in the first number of the *Journal of Experimental Medicine*,

ON THE RESULTS OF LIGATION OF THE CORONARY ARTERIES. BY W. TOWNSEND PORTER. (Pl. II.)

I. LITERATURE.*

THE experimental study of the influence of an interruption of the coronary circulation on the action of the heart may be said to have begun with Erichsen[6]. It is true that Chirac[4] had tied a coronary artery in a dog nearly one hundred and fifty years before, and had seen the heart soon after cease to beat, yet this isolated observation appears to have borne no fruit. Perhaps Chirac would have gone further had the physicians of his day taken much interest in the coronary arteries, but the frequency and serious consequences of the disease of these vessels were then and for many years thereafter quite unknown.

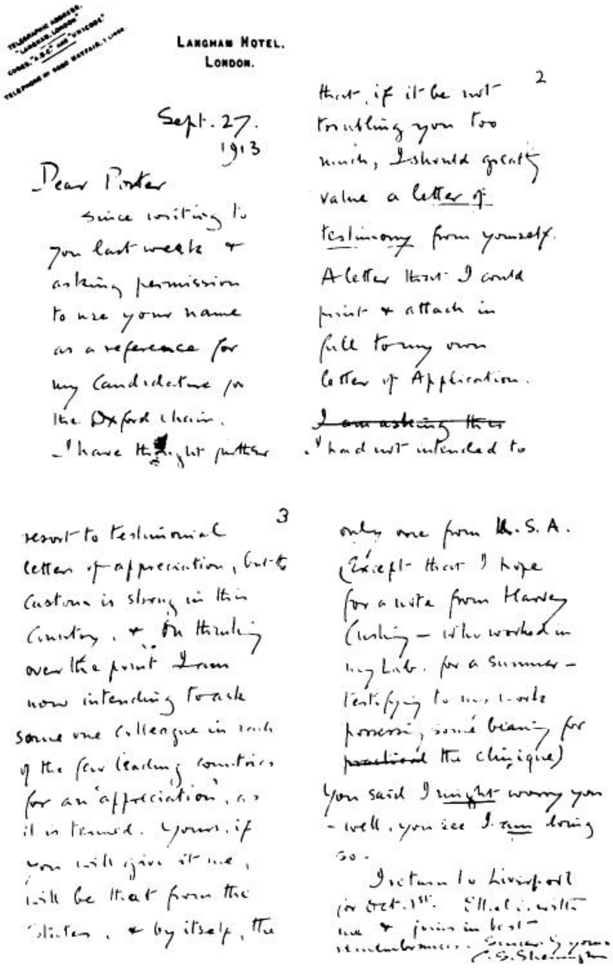
Chirac had long been dead when Morgagni[14], Thebesius[14] and Crell[14] observed calcification of the coronary arteries. It was near the end of the eighteenth century, before Jenner[11] and Parry[16] associated Angina pectoris, the new disease which Rougnon[18] and Heberden[9] had shortly established, with this calcification, and Jenner made his celebrated diagnosis of John Hunter's malady. The death of Hunter[10] in 1793 in a paroxysm of angina, and the discovery that his coronary arteries were indeed calcareous, as Jenner had predicted, was a great stimulus to the clinical and pathological study of these vessels. This interest, with some fluctuations, has continued to the present time and ha- been especially strong in the past ten years.

Erichsen, as we have said, was the first to make an experimental study of this theme. His research appears to have been incited by the opinion of Marshall Hall[8] that an interruption of the coronary circulation was a frequent cause of sudden death. His first experiment was as follows: "A moderately large dog, about two years of age, was pithed; artificial respiration was then set up by an assistant, the thorax opened, and the heart exposed as rapidly as possible. It was acting forcibly and

* The numbers after authors' names refer to list of cited works, p. 135 *et seq.*

PH. XV. 9

Figure 4
Title page of Porter's paper published in 1893 (4).



LANGHAM HOTEL,
LONDON.

Sept. 27.
1913

Dear Porter

Since writing to you last week & asking permission to use your name as a reference for my candidature for the Oxford chair, I have thought further

2

that, if it be not troubling you too much, I should greatly value a letter of testimony from yourself. A letter that I could print & attach in full to my own letter of Application. ~~I am asking this~~ I had not intended to

3

resort to testimonial letters of appreciation, but the custom is strong in this country, & on thinking over the point I am now intending to ask some one colleague in each of the few leading countries for an 'appreciation', as it is termed. Yours, if you will give it me, will be that from the States, & by itself, the

only one from U.S.A. (Except that I hope for a note from Harvey Cushing — who worked in my Lab. for a summer — testifying to my work possessing some bearing for ~~practical~~ the clinique) You said I might worry you — well, you see I am doing so.

I return to Liverpool on Oct. 1st. Ethel is with me & joins in best remembrances. Sincerely yours
C. S. Sherrington

Figure 5
Letter form Charles Sherrington to W. T. Porter, 1913.

which was scheduled to appear in January 1896. When Porter submitted a paper on the coronary circulation and another on a new method of measuring intraventricular pressure, Welch replied gratefully, "Your articles will be the chief ornament of our first number and I am greatly obliged to you for them" (9). Following their publication Welch again wrote to Porter in glowing terms that "Your articles in my opinion have been the best of the physiological ones which have appeared in the Journal" (10). As further acknowledgment of

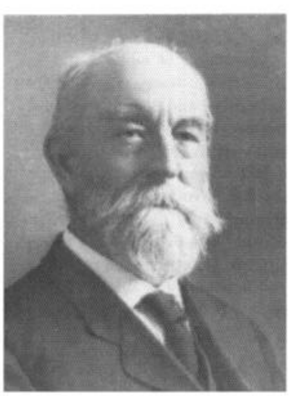


Figure 6
Henry P. Bowditch.

Figure 7
W. T. Porter in Boston.

Figure 8
Harvard Medical School, 1883-1906.

Porter's ability, W. H. Howell, the editor of the *American Textbook of Physiology*, invited him to write on the innervation of the heart, the nutrition of the heart, and the innervation of the blood vessels for the first edition of what was to become Howell's *Textbook of Physiology*.

Bowditch was serving a second term as President of the American Physiological Society at the time Porter arrived in Boston, and Porter, with prescient vision, emphasized to him the stimulus to physiology that an American journal devoted solely to this field would provide. As Eugene Landis (Fig. 9) has written, Porter played a key role in the founding of the *American Journal of Physiology*: "During his first years at Harvard, while sending to journals of physiology abroad results of his numerous studies on respiration and circulation, he repeatedly stressed, verbally and in writing, the urgent need for developing in this country a suitable medium for publishing results of physiological research. When the young American Physiological Society debated from 1894 to 1898 the feasibility of establishing its own journal, it was W. T. Porter who solved the problem by volunteering to undertake not only the managing editorship, but also full financial responsibility. To his activities as an investigator and teacher he added those of a zealous editor and astute business manager. A need for the journal can best be estimated by examining the contents of the first volume, which was published in 1898 and included papers by Porter, Howell, Lusk, Mendel, Cushny, Chittenden and A. N. Richards, together with Walter B. Cannon's paper on the use of X-rays to study gastric motility" (11). For many years Porter personally carried the debt of the new journal, but in 1914 he was able to turn over to the Society a journal finally in the black. The founding of the journal was only one of the important educational innovations fostered by Porter.

Another innovation of Porter's was the opening of his laboratory to female physiologists. Ida H. Hyde (Fig. 10), whose portrait recently appeared on the cover of *The Physiologist* (12), was the first woman to do research at the Harvard Medical School. Her paper on the effect of distention of the ventricle on the flow of blood through the walls of the heart (Fig. 11) also appeared in the first volume of the *American Journal of Physiology* (13). You will note that although the work was done in Dr. Porter's laboratory and under his close supervision, he did not appear as a coauthor of the paper.

Figure 9
Eugene M. Landis.

Porter was convinced from his German postgraduate experience that medical students must have first-hand laboratory knowledge of their subject if the standards of scientific education were to be raised, otherwise "much of the student's learning is mock physiology based on mock anatomy," for "nature can not be studied apart from nature" (14). In the early 1890s the medical students at Harvard were subjected to four hours of continuous lecturing five afternoons a week, from 2 to 6 o'clock. The boredom was broken only by occasional demonstrations, the details of which few students could see, and by an inordinate number of examinations. Porter emphasized in 1898, in words that bear repeating today, that "the force now making for reform is irresistible. It is nothing less than the conviction that the mass of knowledge in every department of medicine has grown so huge as to overwhelm both professor and student. The only refuge lay in the thorough mastery of the scientific method. The medical student must acquire power rather than information. Only thus will he be able to hold a steady course through the baffling winds and crosscurrents of the veritable sea of knowledge" (14).

Unfortunately, it was a gracious Harvard custom to allow each appointee to a chair in science to furnish his own laboratory appartus. Bowditch had brought back from Germany enough physiological equipment, at his father's own expense, to furnish two small laboratories. However, he generously opened the doors to all members of the faculty interested in the advancement of scientific medicine, thus starting the first laboratory of experimental medicine in the United States. But the response left space for only an occasional student, on an elective basis, to perform experiments there.

Figure 10
Ida H. Hyde, first woman member of the American Physiological Society (12).

THE EFFECT OF DISTENTION OF THE VENTRICLE ON THE FLOW OF BLOOD THROUGH THE WALLS OF THE HEART.

BY IDA H. HYDE, PH. D.

[*From the Laboratory of Physiology in the Harvard Medical School.*]

IN the course of the experiments "On the relation of the volume of the coronary circulation to the frequency and force of the ventricular contraction in the isolated heart of the cat," made in this Laboratory in 1896,[1] it was incidentally observed that distention of the left side of the isolated heart lessened the volume of the circulation through the coronary vessels, notwithstanding the maintenance of a constant pressure in the aorta. As distention of the heart is a state frequently observed in mountain climbers, athletes, hod-carriers, and many other classes, being indeed almost inseparable from violent, prolonged muscular efforts, and as it constitutes, in its severer forms, a disease of great clinical interest, a systematic pursuit of the clew which Magrath and Kennedy gave is well worth making.

The problem seemed a simple one. The coronary vessels of the isolated heart of the cat should be supplied with defibrinated cat's blood by maintaining a uniform blood-pressure in the aorta, and the outflow from the coronary veins, or, in other words, the volume of the coronary circulation, should be recorded by a suitable apparatus. The effect of the artificial distention of the left side of the heart upon this outflow would then be visible.

The apparatus for accomplishing these ends consisted of a reservoir in which the defibrinated blood could be kept at the temperature of the body; a pressure flask, by which the blood could be driven from the feeding reservoir into the aorta; a mercury manometer, for recording the blood-pressure in the aorta, so that the experimenter could be sure that the driving force remained the same throughout the observation; a membrane manometer, of the Hürthle type, for recording the changes of pressure in the left ventricle; a Mariotte flask, by which the intraventricular pressure could be raised to any height desired; a drop counter, for registering the

[1] MAGRATH, J. B., and H. KENNEDY: Journal of exper. medicine, 1897. ii. p. 13.

Figure 11
Title page of Ida H. Hyde's paper, 1898 (13).

This was the situation when Porter arrived in Boston in 1893. He later wrote: "All the first-year subjects were then taught side by side. The dissecting room and the chemical laboratory were first class. Physiology was almost exclusively talk and text-book. Almost all the students put off any real work in Physiology until the sixth week before the final examination (at the end of the year). Then the students bought the stenographic notes of Dr. Bowditch's admirable lectures, and crammed for the examination--and almost all of them passed.

"It was easy to say that Physiology should be taught by experiments performed by the students themselves. The Harvard Medical School in 1899 had over 200 students in Physiology. Working in pairs they would use over 100 kymographs. These were, at that date, made one at a time, chiefly in Leipzig. They cost $200.00 each, delivered in America, and there was a delay of five or six months. Obviously the richest university could not equip 200 students at such prices.

"This Gordian knot was cut by inventing new apparatus and by simplifying old models, so that all the essential apparatus could be made by quantity production, then a new idea. The student was to learn Physiology by his own laboratory observations during four continous months. The talk and the text-book were to follow his observation of the living tissue.

"This plan was a double success. (1) It gave the Harvard Medical student real Physiology. (2) Quantity production left surplus apparatus to be used by other schools.

"An effort was made to have the apparatus manufactured by a commercial firm. That effort failed. So, in its first years, the apparatus was made by 'The Mechanics of the Harvard Physiological Laboratory'. But that could not be allowed on non-taxed property. Hence the Harvard Apparatus Company was formed. The original capital was raised by President Eliot. The contributors were Francis Blake, celebrated telephone inventor; Augustus Hemenway, a Boston philanthropist; and three eminent professors in the Harvard Medical School" (15).

With such an auspicious start, why was Porter so soon forgotten? At the turn of the century Porter essentially ran the Department of Physiology at Harvard Medical School as Bowditch, approaching retirement, turned over more and more of the duties to him. The instruction in the department was Porter's responsibility, and he planned "a more extended course than medical students have ever been given" (16). To help him organize the new teaching program, Porter recommended the appointment of Walter Bradford Cannon (Fig. 12) as instructor. In a letter to President Eliot of Harvard, Porter wrote: "Cannon has worked in this laboratory and is familiar with the new plans. He has published investigations of value. He is a strong, well-balanced man, older than his years, and certain to be a credit to the University. Dr. Bowditch some time ago promised Cannon he should be recommended for an instructor's place, with $1200 salary" (16).

Two years later Porter wrote yet another letter in Cannon's behalf to President Eliot: "Your interest in attaching clever young men to the University has been so often shown that I feel you will welcome a brief mention of Dr. Cannon's present position? Dr. Cannon's unusual ability is already known to you. He is an independent investigator, an excellent administrator, and

Figure 12
Walter B. Cannon as a student at Harvard Medical School.

a man of tact, now well advanced in a career of distinction. . . Dr. Cannon this year does the work usually done by an Assistant Professor. . . .

"Dr. Cannon has not of course asked me to write you nor complained in any way. He is devoted to Harvard. I write because the demand for physiologists outruns the supply. Men inferior to Dr. Cannon are offered much larger salaries. Should Dr. Cannon leave us, his place could not be filled at present" (17).

Ten months later, in 1902, Porter again pressed Eliot: "This will be the third year in which Dr. Cannon has done a professor's work. His training and experience would secure him an assistant professorship in any other university. There is no better man for the place" (18). Porter's fears of losing Cannon were well founded. Early in 1903 he sent another letter to Eliot: "Dr. Cannon has been asked to be Professor of Physiology in the Medical Department of the Western Reserve University (a chair later filled by Carl J. Wiggers). His loss to us would for the present be irreparable. There is no young physiologist of his capacity in the country, and even if there were he could not readily be trained to do Dr. Cannon's work in this school. Dr. Cannon now receives two thousand dollars. Should he decline the Western Reserve offer and others reasonably certain to be made him I hope that his salary may be increased beginning next September" (19).

While Porter was pleading for Cannon, his own position began to deteriorate. The 1960s was only one of many eras of student unrest at Harvard. In 1904 a group of students sought an audience with the Dean of the Harvard Medical School to protest the large number of failures in Physiology. Porter, on his arrival at Harvard in 1893, had complained that almost all students were passed, with too little regard for standards of excellence; now the students were complaining that a third of the class was failing. Perhaps, in his missionary zeal, Porter had pressed too fast to raise the standards of scientific education, for Harvard, unlike Hopkins, still did not require a college degree for admission for all students, and 38% of those without college degrees had failed to pass physiology in the years 1902 to 1904. On the other hand, the students were outspoken in their praise of Cannon as a teacher, and President Eliot had come to rely heavily on the young man's advice in university matters. Thus, when Cannon received a call from Cornell Medical School in 1906, Eliot decided to resolve the dilemma in the following manner: 1. Cannon would succeed Bowditch as Higginson Professor and Chairman of the Department. 2. Porter would become Professor of Comparative Physiology. He was thus shunted aside from the mainstream of the Medical School.

Relations between Cannon and Porter were strained for years thereafter. Cannon used the front stairs; Porter walked down the rear ones. Little was heard of Porter. However, as the American Physiological Society approached its Fiftieth Anniversary in 1937, there appeared to be "an awakening consciousness of the unassuming but inspiring role of William Townsend Porter in the annals of American physiology. It was an agreeable and appealing surprise, therefore, when President Mann, acting with the approval of Council, nominated Doctor Porter Honorary President of the Society for the semicentennial celebration. This nomination was supported by Dr. A. J. Carlson, Dr. W. B. Cannon, Dr. Chas. W. Greene, and other, and was carried." (20, p.170-171).

At the anniversary celebration in Baltimore in 1938, President Walter E. Garrey introduced the Honorary President and Toastmaster, Dr. Porter, with warm words of praise. The ovation which ensued deeply touched Dr. Porter, who responded: "Your generous applause moves almost to tears this aged man and poor. It is the more welcome because for many years I have not enjoyed the pleasure and the great benefit of these meetings. My relation to the Society has been that of a flying buttress—I have helped from the outside in my small way.

"I am pleased, too, because you escape the error of all my earlier life. I used to put the head above the heart. You are more wise. You applaud, not the intellect, but the wish to be of service." (21, p.193).

In 1929, after his retirement from Harvard, Porter offered the Harvard Apparatus Company as a gift to the American Physiological Society. On December 28, 1929, the Council of the Society resolved: "It is the opinion of the Council of the American Physiological Society that it would not be practicable for the said Society to undertake or to supervise the management of the Harvard Apparatus Company. At the same time the Council wishes to place itself on recond in believing that there is no one agency, during recent years, which has contributed more to the development of sound teaching and experimental physiology in this country than the Harvard Apparatus Company." Rebuffed by Council, Porter then set up a nonprofit foundation to run the Harvard Apparatus Company.

In closing, I should like to refer back to Dr. Carl J. Wiggers once more. In his *Reminiscences* (1) Wiggers wrote that "Porter's last act of generosity was the presentation to the Society in 1922 of all unsold copies of the first 33 volumes." Had Dr. Wiggers lived on he would have been pleased to know that Dr. Porter's generosity did not end there but continues today in the financing of the Porter Development Program of the American Physiological Society. All of the funds for this program for minority students in physiology—Black, American Indians, Hispanics—have come from the Foundation established by William Townsend Porter, the Harvard Apparatus Foundation. Thus, as long as the American Physiological Society will exist we shall be the beneficiaries of Dr. Porter's generosity and his desire" to encourage and assist young men and women of promise in their study of physiology."

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Departmental Histories

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Uniformed Services University of the Health Sciences
Bethesda, Maryland 20814

The Uniformed Services University of the Health Sciences, in Bethesda, MD, was established in 1972 by an act of the United States Congress. The school was founded to teach the unique aspects of military medicine as well as a regular medical curriculum to a stable cadre of military physicians who would be the career medical corps of the future. The University, an agency of the Department of Defense, began operations in 1976 with its first medical student class of thirty-two students; class size has increased to one hundred and fifty-six students as of 1981. All students admitted to the medical program are commissioned as Lieutenants in the United States Army or Air Force or as Ensigns in the Navy or Public Health Service.

The Department of Physiology, the first Basic Science Department of USUHS, was organized in 1976 by Dr. Francis J. Haddy, who was appointed to recruit a faculty and to develop the department. Dr. Haddy came from Michigan State University, where he had served for ten years as Chairman to their Physiology Department. Prior to that time, he had served as Chairman to the Physiology Department at the University of Oklahoma. He brought to USUHS a group of colleagues from Michigan to serve as a core teaching staff and to continue research in several areas.

The department was first housed in the Forest Glen Annex of Walter Reed Army Medical Center in Silver Spring, MD, in Laboratories previously occupied by Dr. Donald Gregg and his colleagues. In that first year, medical lectures and laboratories were conducted in the museum section of the Armed Forces Institute of Pathology at Walter Reed Army Medical Center in Washington, DC. The opening day classes for the medical students were in Medical Physiology. The course was discipline based, taught by systems through lectures, supplemented with frequent laboratory exercises, and the department also participated in the presentation of an Applied Physiology course.

In the second year of USUHS, the department moved into the partially completed permanent site of the University on the grounds of the National Naval Medical Center in Bethesda, MD. The temporary quarters of the department at this site were in an area that was part of a long-range plan for expansion of medical student Multi-Discipline Laboratories. These temporary quarters were occupied for two years, and then in 1979 the department was moved to its present and permanent area in the school.

The graduate program of the University began with admission of the first graduate student to the Department of Physiology in 1977; and he was the first University Ph.D. awardee. By Fall of 1981 the graduate student population in Physiology had grown to eighteen students, ten male and eight female. In addition to research training, the following Physiology graduate courses are offered: Medical Physiology (taken with first-year medical students), Cardiovascular, Endocrinology, Hematology, Experimental Neurophysiology, Membrane Transport, Gastro- Intestinal, Sensory, and Renal. The Department also developed a postdoctoral fellowship program very quickly. There were eight fellows in training in the year 1981.

The department's faculty and consequently its teaching and research orientation are well balanced with respect to organ systems, basic science, and clinical expertise. The faculty consists of two Armed Forces members, and the balance are civilians. The Department benefits from the proximity of government and university research laboratories. Many local scientists serve as adjunct faculty and regularly contribute to the teaching program. Collaborative research is a common occurrence between departmental scientists and those of nearby institutions.

A list of faculty, graduate students, and postdoctoral fellows for the period 1976-1982 has been deposited in the archives of the APS.

F. J. Haddy

Department of Physiology
Medical College of Ohio
Toledo, Ohio 43699

The Ohio State legislature chartered the establishment of the fourth medical school in Ohio as the Toledo State College of Medicine in 1964. During 1966, President Glidden L. Brooks appointed the first three chairmen for the departments of anatomy, physiology, and psychiatry and also the librarian. In this year, Leonard Nelson resigned a Career Development Award at Emory University and set out to organize the Department of Physiology of the renamed Medical College of Ohio. He spent 1967 as Program Director, Developmental Biology, at the National Science Foundation, from which vantage point in Washington, DC, he began to recruit faculty from around the world, Calcutta to St. Louis, Baltimore to Seoul, London to Rochester, and Columbus to Ljubljana, and to arrange for a site for the department. Physiology was provided some space in the Biology-Chemistry Building at the University of Toledo, the Maumee Valley Hospital basement, and the Research Institute of Toledo Hospital. In exchange for the former, we participated in the development and accreditation of the graduate program of the Biology Department. The first biology Ph.D. degree was awarded to A. V. McGrady, now Associate Professor of Physiology at MCO.

Teaching formally began in Fall 1969, with 32 students in the first class. The MCO president described the physiologists as part of the MCO "community of scholars" tempered with students teamed against faculty playing Frisbee on the side lawn. The first few years made teaching a real challenge—new students, new faculty with different philosophies of education recruited from all over the world, with recurrent questions about the "relevance" of basic science. Slogans became the order of the day. We were part of a "community of scholars" whose goal was to turn out "undifferentiated physicians" from a three-year "integrated curriculm," which was soon heavily weighted on the side of the applied physiologist of clinical persuasion.

Building I, the Health Science Building on the new "west campus," was dedicated in 1973 by Robert Berne, George Palade, Elizabeth Russell, and Charles Huggins. (In his exuberance at finding us in the middle of the Toledo Mental Health Center cornfield, adjacent to potter's field, Charley Huggins led the local reporters covering this momentous occasion on a merry chase over the undeveloped campus!) Our anticipation of the gleaming facilities was somewhat dampened by the discovery that each laboratory had only two electrical outlets and no distilled water; this was rectified in time for the dedication ceremony.

We then received notice that a nursing program was beginning at MCO and physiology was to be an intregal part of the curriculum. Currently the Physiology Department participates in several different programs: undergraduate and graduate medical and nursing, residency, Ph.D., M.S., physical therapy, and eventually industrial hygiene. The nursing program was the first in the "consortium" between Medical College of Ohio-University of Toledo-Bowling Green State University. A small fleet of yellow school buses appeared and was used to transport the nursing students the 30-mile distance between campuses. The Physiology Department has had a major role in development and implementation of the nursing curriculum.

The charter class consisted of thiry-two medical students, four more than originally planned. We now enroll one hundred fifty medical students, one hundred thirty baccalaureate nursing students, ten masters of science in nursing, forty-five graduate students (Ph.D. in the Medical Sciences), and twenty-four students in physical therapy, all of whom receive instruction in human physiology under the aegis of the Physiology Department.

The Physiology faculty are involved in a variety of extradepartmental activities: J. R. Claybrook has been President of the Academic Senate and is now serving as Associate Dean for Research; J. N. Ross has also served as Senate President and MCO Representative to the Advisory Committee of the Ohio Board of Regents; B. Richardson is Director of Minority Affairs; A. V. McGrady has organized and serves as Staff Physiologist of the Behavioral Science Clinic as well as Basic Science Coordinator of the School of Nursing; L. Nelson has recently been appointed to the Associate Deanship of the Graduate School; J. Chakraborty organizes and is the Director of the Clinical Correlations program; P. Brand is Secretary of the Senate and Chief Lepidopterist.

Since 1967, members of the Medical College faculty have served as Ph.D. and M.S. advisors and members of graduate committees at both the Univesity of Toledo and Bowling Green State University. Our own graduate program at MCO commenced in the fall of 1115. Among the first Ph.D. degrees awarded in the Graduate School at MCO one was to P. Metting, now Assistant Professor at MCO (cardio-pulmonary). Her Ph.D. advisor was Associate Professor J. N. Ross (cardiovascular). J. N. Ross is now Professor and Chairman of Medicine at Tufts University, School of Veterinary Medicine.

In 1980, the curriculum was transformed to a four-year schedule with discipline-organized teaching, which is coordinated so that the physiology of the organ systems is presented concurrently with the anatomy and biochemistry of the same systems. This restructuring of the curriculum permitted 25% of the first-year medical students to participate in ongoing research activities of various faculty members primarily during the summer. Some of the summer-stipended students have continued their research participation in subsequent years.

Physiology department research activities are widely varied. They include monoclonal antibody studies of human and mouse sperm antigens; sex differentiation in gerbil brain; chemical contraceptive reduction of wild mustang populations; liver cell culture and homograft transplant; cardiovascular prosthetic materials and device development; receptor regulation of cardiopulmonary circulation; organic anion transport in isolated perfused garter snake and rabbit kidney tubules; membrane potentials in mature bull sperm and mouse spermatids; cholinergic regulation of calcium transport in sea urchin and bull sperm; calcium modulation in pancreatic secretion; in vitro fertilization in mice; benign prostatic hyperplasia in guinea pigs and prostate malignancies in man; insulin localization in ectopic sites; steroid hormone receptor function in the uterus; physiological basis of acupuncture pain control; and calcium and prostaglandin control of aldosterone production.

Since its formation, the department has enjoyed a fairly high degree of stability: one conferral of emeritus status, two deaths, one resignation to transfer to a professorship- chairmanship in a veterinary college, one resignation to a private practice, one resignation to private enterprise; and one resignation to return to native country. The full-time faculty has been augmented in its teaching responsibilities with about six members with joint appointments in other departments (including obstetrics and gynecology, neurosciences, surgery, pharmacology, medicine, and anesthesiology) and several adjunct appointments from the University of Toledo, Departments of Biology and Physical Education.

Even though the Medical College of Ohio is a free-standing institution, it participates in some research and teaching activities at the graduate level with University of Toledo and Bowling Green State University and through Sigma Xi with the Research and Engineering Divisions of the Owens-Illinois Company.

During the first years of building the department, the chairman utilized operating budget funds to design and equip laboratories for recruits before their actual appearance on the scene. Needless to say, he was severely reprimanded (but happily not further punished) for using operating funds for the purchase of capital equipment. This inadvertence helped considerably in permitting early development of the departmental research activity which continues with support from various federal and private funding agencies.

We owe a great debt of gratitude to a number of visiting professors who came to our aid during our years of painful growth. These included E. B. Brown, R. Berne, M. Levy, R. C. Little, A. Olszowka, G. Gurtner, and A. J. Vander among others.

A list of faculty for the period 1967-1982 has been deposited in the archives of the APS.

A. V. McGrady

Department of Physiology and Biophysics Temple University School of Dentistry Philadelphia, Pennsylvania 19140 1863–1982

Temple University is a state-related institution that is part of the Commonwealth of Pennsylvania System of Higher Education. The Health Sciences Center, one of the University's five main divisions, is located along Broad Street in North Philadelphia, about one mile north of the main campus. The Health Sciences Center is composed of University Hospital, the College of Allied Health Professions, and the Schools of Medicine, Dentistry, and Pharmacy.

Since its inception, the Department of Physiology and Biophysics has been an organic entity of the School of Dentistry. The Department is responsible for teaching the required courses in Physiology and Biophysics to students in the Schools of Dentistry and Pharmacy, and the College of Allied Health Professions. In addition to a full predoctoral teaching program, the Physiology and Biophysics Department also presents an accredited Doctor of Philosophy program.

The present teaching staff is composed of eight full-time members, all with the earned doctorate from respected institutions: John A. Drees, Associate Professor, Ph.D., Indiana University; Frank J. Hohenleitner, Associate Professor, Ph.D., Hahnemann Medical College; Lyle W. Horn, Associate Professor, Ph.D., Johns Hopkins University; Francis M. Kendall, Associate Professor, Ph.D., Temple University; John S. Martin, Associate Professor, Ph.D., Jefferson Medical College; Claudio A. Nicolini, Professor, Ph.D., University of Padua; Martin F. Tansy, Professor and Chairman, Ph.D., Jefferson Medical College; Jacob Zabara, Associate Professor, Ph.D., University of Pennsylvania.

Of the eight full-time resident faculty members, five hold memberships in the American Physiological Society, three hold memberships in the Biophysical Society, and one is a member of both plus the Institute of Electrical and Electronic Engineers. To date, the Department of Physiology and Biophysics has succeeded in retaining a broad range of research interests. This broad base enables the department to achieve the flexibility which is necessary to mount the extensive efforts which are needed today to attract extra-mural funding.

The history of the Department of Physiology and Biophysics is traceable to the founding of the second oldest dental school in continuous existence in the United States. In fact, the founder of this institution was a physiologist, Doctor John Hugh McQuillen.

In 1845, several progressive Philadelphia dentists, encouraged by the success of the Baltimore College of Dental Surgery, decided to make an effort to form a dental college in Philadelphia. They believed that Philadelphia, then the recognized center of medical education in the United States, would be able to support a dental school. Among this group were Drs. John D. White, Elisha Townsend, E. B. Gardette, Samuel Mintzer, Louis Roper, Eli Parry, and Robert Arthur. The first institution established in Pennsylvania for the purpose of imparting knowledge in the science and art of dentistry was organized by them in 1852 as the Philadelphia College of Dental Surgery. After a productive but brief span of four years, it yielded to the throes of internal dissension and ceased to exist.

In the fall of 1862, Dr. John H. McQuillen, holding the chair of Operative Dentistry and Physiology in the Pennsylvania College, retired from the faculty of that institution. In 1863, he joined with other members of the profession in the city and state and, after expending much effort and overcoming great opposition (for charters were not readily obtained in those days), they succeeded in procuring a charter from the Legislature of Pennsylvania for a new institution under the name of the Philadelphia Dental College.

After securing a competent faculty and Board of Trustees, the new institution opened its first term in November of 1863. The faculty consisted to five members. Dr. John H. McQuillen, Professor of Anatomy, Physiology and Hygiene, was elected Dean, and he held that office continually until his death in 1879.

John H. McQuillen, a native son of Philadelphia born February 12, 1826 was the son of Captain Hugh McQuillen who served under Decatur in the War of 1812. At 26, McQuillen graduated from Jefferson Medical College. One year later he received the honorary degree of D.D.S. from the Philadelphia College of Dental Surgery at its first commencement, on February 28, 1853. Everyone was greatly impressed by Dr. McQuillen's earnestness and his enthusiasm as a teacher and as an investigator. His activities during this period, justly qualify him as one of the pioneers in the scientific development of dentistry in the United States.

He was one of a few men who entered the profession at a time when everything was practiced strictly on an empirical basis. He applied a scientific method to the elucidation of many of the problems which confronted him, and helped place the profession and the modes of practice on a contemporary scientific plane. He maintained close contact with the best in science and art and acquainted himself with the most noted scientists. Keyed to excellence and innovation, he was able to appreciate, to select, and to put to practical use the work of many experts in the profession. He contended that a dentist should have a well-rounded education; in his own words, "a spherical education." For this, he was ridiculed by many who were unable to appreciate his idea. He was a leader in broadening the dental curriculum so that it embraced much more than "making plates" and "plugging teeth."

Doctor Thomas C. Stellwagen succeeded Dr. McQuillen in the Chair of Physiology. Thomas C. Stellwagen, M.A.,M.D.,D.D.S. was born in Philadelphia (July 24, 1841). He received his D.D.S. in 1861 and his M.D. from the University of Pennsylvania in 1869. In 1870 he was given the Chair of Operative Dentistry and Dental Pathology in the Philadelphia Dental College. In 1879 upon the death of his friend Professor McQuillen, the professorship of Physiology thus sadly vacated was conferred upon him by the Board of Trustees, at the recommendation of the Faculty. Professor Stellwagen occupied the Chair of Physiology until his retirement in 1906.

Doctor Stellwagen's successor was Dr. John C. Scott (Pharmacy Degree, Philadelphia College of Pharmacy, 1900, M.D., Medico-Chirugical College, 1906). Dr. Scott served in this capacity until he retired in 1944. In 1907, the Philadelphia Dental College and the Garretson Hospital of Oral Surgery were acquired by Temple University by mutual agreement. Included in the University's acquisition were the faculty, equipment, buildings, and grounds of the College and Hospital. Neither the college nor the personnel of the faculty were greatly affected by the change until 1918, when an almost complete reorganization took place. Despite drastic changes Doctor Scott remained.

In 1944, Temple University appointed Dr. Evert J. Larson (B.A. Biology, Yale University, 1931; A. M. Physiology, Clark University, 1933; Ph.D., Physiology, Yale University, 1938) as Professor and Chairman of the Department of Physiology of the School of Dentistry. He retired in 1964. During his tenure the School of Dentistry moved to its present location which it shared with the School of Pharmacy. The Department now began to furnish instruction in Physiology to Pharmacy students and consequently the traditional one-man department expanded to a two-man operation with one full-time Chairman. During this 20-year period, the Department served as a training ground for Ph.D. candidates from various medical schools in Philadelphia. The roster includes Edwin Polish (1950), H. Parker Stamford (1950), Domenic A. DeBias (1951, 1955-56), Fred DeMartinis (1951-54), Jack Levitt (1952-53), R. E. Seckendorff (1955-56], Frank Liu (1957-60], Henry Haven (1957-59), Joseph Shanfield (1957-59), R. McCreesh (1960), Frank J. Hohenleitner (1960-62), Martin F. Tansy (1961-64), Merle Kilmore (1963), Theodore J. O'Tanyi (1963-64), and Mahmood Tabatabai (1963-64). Upon completing their degree requirements these people eventually established careers in science, academia and academic administration (five Department Chairmen and one Associate Dean).

In 1965, Dr. Martin F. Tansy (A.B., Biology, Wilkes College, 1960; M.S. Physiology, Jefferson Medical College, 1961; Ph.D., Physiology, Jefferson Medical College, 1964) was appointed Chairman of a two-man department whose other member was Roland W. Austin, Ph.D. Dr. Austin left the department in 1966 and was replaced by two Jefferson Medical College graduate assistants, Dominick Cinti and Zalmon Pober. The Dental School enrollment expanded at this time and two additional full-time faculty (Frank J. Hohenleitner, Ph.D. and Jacob Zabara, Ph.D.) were appointed in 1967 along with a part-time instructor (Frank Kendall). The next personnel change occurred in 1969 when Dr. Mahmood Tabatabai rejoined the faculty for one year as a full-time member.

I could not help reminiscing upon the history of this Department during my early tenure. At that time the physical facilities of the Department consisted of one office, a storeroom, and a student laboratory equipped with kymographs, inductoria, and storage batteries. The turning point came in 1965 when Dr. Charles L. Howell was appointed Dean of Temple University School of Dentistry. One of his first observations was that the Department in general, and the student laboratory in particular, were hopelessly out of date. He was most interested in introducing modern physiology to the dental students even if this meant that he would have to forego something desirable but not absolutely necessary in the clinical areas. As a direct consequence of Dean Howell's own efforts we finally obtained modern research-grade equipment. At this same time the first publication from the Department appeared; it was a modest letter to "Nature" entitled "Influence of Sex Hormones on Frequency of Micturition."

The most remarkable indication of the Department's improvements was an immediate rise in the level of student performance on the National Board examinations. Secondly, we were able to attract modest extramural funding for research, and we were able to gain published acceptance of our work. We also were granted our first research award from the NIH pursuant to a proposal entitled "Serotonin Release in the Bowel."

Another noteworthy event of this period was that the Department entered into an agreement with the Department of Pharmaceutical Chemistry in the School of Pharmacy by which a graduate student (Roland P. Roth) in physiology began a program of study supported by an NIH predoctoral fellowship. Upon completion of the program, Mr. Roth was awarded the Ph.D. degree in Physiology in 1971. His initial position was a Staff Fellow in the Department of Pharmacology and Toxicology at the National Institutes of Environmental Health Sciences, Research Triangle Park, North Carolina.

In 1970, the Department assumed an additional teaching service commitment to the College of Allied Health Professions (Physical Therapy, Occupational Therapy, Medical Records, Medical Technology, and Nursing students) and acquired Dr. John Drees and Dr. David Innes as additional full-time faculty. In 1971, Frank Kendall, having completed his doctoral studies, joined the department as a full-time member. The expanding teaching and research activities of the Department still required augmentation by additional part-time instructors (Nicholas Grego and John S. Martin, 1969-70). Dr. John S. Martin joined the full-time faculty in 1972.

During this time, the members of the professional staff also were engaged in research projects in connection with various grants and contracts. These activities aroused in our young professional staff a keen interest in graduate eduction. This interest provided an impetus for the formulation of a proposal for a new graduate program in Physiology and Biophysics, a program oriented toward the physical and systems approach to Physiology.

Inasmuch as University policy had envolved a more stringent review process for program proposals, this proposal was subjected first to the formal review and approval of the Council of Graduate Schools in the United States before gaining acceptance by the graduate faculty and administration of the University. This proposal was reviewed and approved June 24-25, 1971, by Emmett N. Bergman, Professor of Physiology, Cornell University and John O. Hutchens, Professor of Pharmacology and Physiology, Universty of Chicago, representing the Council of Graduate Schools in the United States. Our efforts culminated when the proposed graduate programs in Physiology and Biophysics were approved for implementation on October 26, 1971 by the Graduate Board of Temple University.

During the next three years, the Department continued to pursue an active research program, attract extramural support, and acquire graduate students. Despite its advancements, the Department still depended on Drexel University to furnish some of the courses which constituted a basic biophysical requirement of the graduate programs in Physiology and Biophysics.

While the combination of Physiology with Biophysics in a single department does not represent a marriage between equals, it is stated to be an academically desirable combination of specialities in the contemporary world. The year 1975 was another turning point. Through the tireless design efforts of Dr. Frank Kendall and the continued fiscal support of Dean Howell, the Department of Physiology and Biophysics acquired its own laboratory which had direct, dedicated computer support.

In 1975, Dr. Claudio Nicolini joined the Department as a member of the full-time faculty. He joined with Dr. Kendall to form the Department's Biophysics Division. Creating the Biophysics Division concurred with a decision of the Department facutly to include a course in General Biophysics as part of the core curricular requirements of all our graduate degree programs. The Biophysics Division also served to correct one of the original criticisms of the proposed graduate programs which were reviewed by the Council of Graduate Schools in the United States: that the programs' curricula were almost totally dependent upon course offerings of Drexel University for biophysical support. The Biophysics Division added Departmental expertise and credibility in both teaching and research.

Listed among the resulting joint-appointments in the Department were: Dr. Alan Conger, Professor and Head, Department of Radiation Biology (1975-81), Dr. Martin Eisen (Associate Professor, Department of Mathematics (1975-78), Dr. John Schiller, Associate Professor, Department of Mathematics (1975-78), Dr. Nicholas Macri, Assistant Professor, Department of Mathematics (1977), and Dr. John E. Tarka, Associate Professor and Chairman, Department of Electrical and Biomedical Engineering (1975-78). Each of these individuals either presented a graduate-level course or participated significantly in at least one course. Current members of the Biophysics Division include: Dr. P. Donald Forbes, Associate Professor, Department of Dermatology (Radiobiology) and Dr. Stanley Zeitz, Assistant Professor, Department of Mathematics (Drexel University).

The Departmental graduate education accomplishments since 1971 can be summarized: seven Ph.D. and seven M.S. degrees have been awarded to graduate students who successfully completed their degree requirements; five postdoctoral students received training; and six visiting scientists were active in the laboratories for periods of at least one year.

Since 1968, the resident full-time faculty of this Department has received extramural support for 33 grants, grants-in-aid, and commercial contracts totalling well over one million dollars in direct costs. As the result of increased faculty research activity, this Deparment was primarily responsible for acquiring sufficient NIH funding (93% of the total direct and indirect costs) to qualify the School of Dentistry for a Biomedical Research Support Grant during 1977-78.

During the last 16 years the faculty has published over 150 full-length papers in refereed journals and has represented the University in making about the same number of presentations at national and international scientific meetings.

It is the opinion of this writer that active high quality research, both clinical and basic science, is crucial not only as a matter of providing career satisfaction for the professional staff, but also as an essential component of high quality graduate education. It improves the faculty competence and thereby stimulates the faculty providing new challenges and insights. The students benefit by being taught by more knowledgeable and more enthusiastic faculty.

Exposure to the thoughts and activities of others is the primary reason why this Department originated and continues to maintain a yearly series of Basic Science Seminars which are open to the faculty and student body of the School of Dentistry and the University. Seminars are held monthly during the academic year and feature guest speakers from Temple and other institutions. Since 1973, 65 guest lecturers have participated in the program.

In 1980, Dr. David Innes left the Department and Dr. Lyle W. Horn was recruited from the Department of Physiology, University of Maryland School of Medicine to bring the Department up to full strength and further enhance the biophysical expertise in the Department.

The writer would like to conclude this history by quoting a statement from Section VII, Basic Sciences of the Formal Report of the Commission on Dental Accreditation to the Administrations of Temple University and the School of Dentistry, on the Dental, Dental Hygiene and Advanced Educational Programs. The site evaluation was conducted October 28-31, 1980. "The visiting committee is particularly impressed with the quality level demonstrated by the Department of Physiology and Biophysics. This spirited, enthusiastic and well-coordinated department is expertly structured in all regards, i.e., teaching, research, service, seminars, grants, programs, equipment, future growth, etc., and can be regarded as a model basic science department."

The vitality and productivity of a Basic Science Department depends on both the spirit of its faculty and the support and encouragement which it receives from the School administration. In this respect, the Department of Physiology and Biophysics has been most fortunate to enjoy the continued encouragement of Dale F. Roeck, D.D.S., Dean of the School of Dentistry, by his support and commitment to the continued excellence of our academic and research programs.

Retrospective examination of the foregoing history shows that a fundamental change in the character of the Department of Physiology occurred during 1965-1975 and that progress since 1975 was due almost entirely to the events of that period. The support and encouragement of the growth of the Department of Physiology and Biophysics can be directly attributed to Charles L. Howell, D.D.S. (Dean, Temple University School of Dentistry, 1965-75). Dean Howell was always ready to listen to ideas and to back new ventures if they could be shown to have merit. Without this support the Department of Physiology and Biophysics would not have its present faculty, facilities, or equipment. Consequently, while the progress was strictly due to the efforts of the faculty, there would have been nothing unless someone with the power to make things happen had the spirit and foresight to create an environment in which they could happen. Therefore, it is fitting and proper to dedicate this history to Chuck Howell.

Martin F. Tansy

Animal Welfare Bill Hidden Costs Could Be $100,000 For Each Institution

The question as to the financial impact the "Humane Care and Substitutes for Animals in Research Act" would have on the nation's academic institutions has focused largely on the cost for accreditation. In the aggregate, this in itself is a staggering expense that has been estimated by the National Institutes of Health (NIH) to be at least $500,000,000 for those institutions that are not in compliance with the standards of the American Association for Accreditation of Laboratory Animal Care (AAALAC) and are now receiving NIH support funds.

However, the one major cost factor that has been ignored by the Congress and to a great extent by the research and educational institutions is the expense every institution will have to bear to administer this law should it be enacted in its present form. Current estimates are that the administration of this act could cost every research institution an average of $100,000 annually over each of the next 10 years, the proposed life of the bill.

Although the Congress originally authorized an appropriation of funds to assist in meeting some of the expense for institutions to attain accreditation status, this provision was deleted in later versions of the bill because of pressures from the Administration opposing any new expenditures of Federal funds. Also deleted from earlier versions of the bill were funds earmarked specifically for the development of alternative methods.

To offset these two proposed appropriations the Congress amended the current bill so that the development of alternative methods would have to compete head-to-head with other research grant requests (with no option for second-chance funding as proposed by the House Subcommittee on Science, Research, and Technology) and so that institutions would be given a 10-year period of time to attain compliance with standards for accreditation.

But the cost of administer the requirements stipulated in HR 6928 (formerly HR 6245) have been ignored by the House Committee on Science and Research, which reported the bill favorably with only three dissenting votes, and the House Committee on Energy and Commerce and its Subcommittee on Health and the Environment, which also considered the bill.

As a result, it is assumed that each institution will have to pay for these administrative expenses from the existing funds allocated for research.

Perhaps the largest single expense is the cost of administering the Institutional Animal Studies Committee. This cost includes the possibility of honoraria for a consulting veterinarian (if one is not on staff) and for an outside member to serve on the committee; the expense for at least two inspections annually of all facilities and animal study areas; the review of all animal research in progress for compliance with stated methodologies and practices; and the overhead and clerical costs for preparing reports, maintaining records, and conducting regularly scheduled meetings of the committee.

Although these costs will vary widely depending on the size of the institution, it has been estimated that the average annual expense to the institution could be approximately $50,000.

A second major expense to the institution is the requirement that educational courses and programs will be conducted for scientists, animal technicians, and other personnel involved in animal care, treatment, and use. Such continuing education programs are to be held at least annually and will include instruction and training in *1)* the humane practice of animal maintenance and experimentation and *2)* the concept, availability, and use of research and testing methods that minimize the use of animals or limit distress.

Again, these costs will vary widely depending on the size of the institution. However, it is estimated that the average annual expense for conducting such programs could be as much as $30,000.

The third area of expense to the institution is in the administration of providing Federal agencies with "assurances" prior to the review of any grant proposal *1)* that a consulting doctor of veterinarary medicine has been employed in the planning of the procedures involving the use of animals; *2)* that justification for anticipated animals distress in terms of the benefits of the research is assured; *3)* that proper use of tranquilizers, analgesics, anesthetics, and paralytics are provided; *4)* that appropriate pre- and postsurgical medical and nursing care is assured the animals; and *5)* that the withholding of tranquilizers, anesthesia, analgesia, or euthanasia is a scientific necessity and done for only the necessary period of time.

The preparation for such planning and the reports required in the preparation of grant applications could add as much as an additional $20,000 annually.

Using the conservation figure that 300 physiology departments could be affected by this bill, the total annual cost would be $30,000,000. For all the research institutions that would be affected the total annual cost has been estimated by NIH to be $65,000,000 and 1,300 additional staff would be needed just to meet the reporting requirements of the bill. NIH has also stated that an additional $250,000 would be required annually to fulfill its obligations regarding this legislation.

When the institutional administration costs are coupled with the costs of meeting the accreditation requirements the total expense to the nation's academic research centers over the 10-year life-span of the bill is projected to be $1,150,000,000.

Although the American Physiological Society is on record supporting the humane treatment of laboratory animals, the Society does not condone legislative regulations that unduly increase the burdens of the research as well as the burdens of costs that must be borne solely at institutional expense. Furthermore, it is unrealistic for the Congress to place these burdens on research and educational institutions at the time when the Administration itself is seeking deregulation and when

Federal funds for research are being reduced and institutional funds are already severely strained.

California Rejects Pound Bill in Last-Minute Action

In what amounted to an eleventh hour turnaround, the California State Assembly rejected a Senate bill that would have prohibited all animal pounds within the state the right to release unclaimed animals to approved research institutions. The bill, S. 1438, was patterned after the Los Angeles City ordinance approved in 1981 and was promoted strongly by both humane organizations and animal rights groups.

The bill had been held in the Senate Finance Committee for most of the year but was finally voted out favorably after having been turned down by the committee on three previous votes. After winning full Senate approval in the final three weeks of the session, the bill was sent to the Assembly's Committee on Health, where hearings were held after the deadline for all hearings had passed. The 14-member Committee rejected the bill on four "no" votes, three "aye" votes, four abstentions, and three not present. An effort to have the bill recommitted to the Committee for reconsideration also failed.

The bill's sponsors were then successful in getting their proposal to the Assembly's Ways and Means Committee for its consideration. Although the proposal did receive a favorable report from the Committee, the bill secured only 27 of the required 41 votes needed for passage in the Assembly. Following this rejection of the bill by the Health Committee, California animal rights groups initiate a media campaign portraying alleged animal misuse by California academic research centers. The animal rights activists have also threatened to initiate law suites against California universities for alleged misuse of laboratory animals.

The rejection of the bill by the Assembly Committee centered primarily on the increased cost to the state that would be incurred through the purchase of animals from dealers rather than from the pounds. The American Physiological Society, working in concert with the University of California system, provided the 14-member Committee with the data relating to such costs.

Though the bill was defeated this year, a new bill is expected to be introduced again next year.

Pound Laws Under Fire in Illinois and Florida

Two bills that would prohibit Chicago pounds from releasing unclaimed animals to research have been introduced in the Chicago City Council. The first bill was introduced last winter by a councilman and has been held in review by a council committee. However, Chicago Mayor Jane M. Byrne has now introduced her own bill to halt the practice of releasing pound animals for the purposes of research.

In Florida, three cities—Jacksonville, Pensacola, and Tampa—are considering ordinances that would prohibit the release of pound animals to research facilities and dealers.

William Samuels, CAE

A Letter to Dr. Orr E. Reynolds, Executive Vice President, APS

Thank you for your recent correspondence expressing your opposition to SB 1438, relating to the use of pound animals by research and medical facilities.

I appreciate your interest and concern over the fate of thousands of lost and abandoned pets. The State has a clear obligation to assure that animals never suffer unnecessarily and that lost pets are returned to their owners. The need to protect human health and encourage lifesaving medical research must be considered as well.

As you may know, the County of Los Angeles has prohibited the use of pound animals for research purposes. This is a very difficult issue, and I can assure you that your views will be given the utmost consideration.

Art Torres, Chairman
Assembly Health Committee

Announcements

Eleventh Annual New England Physiologist Meeting

The Eleventh Annual New England Physiologist Meeting will be held on Saturday, November 13, 1982, at the Harvard School of Public Health, Boston, MA. The theme of this year's meeting will be Comparative Physiology. A satellite symposium of the New England Respiratory Physiologists will be held Friday afternoon, November 12. The theme of the meeting will be Comparative Respiratory Physiology. *For information about attending, speaking, or presenting a poster contact:* Dr. Robert Banzett or Holly Morris, Dept. of Physiology, Harvard School of Public Health, 665 Huntington Ave., Boston, MA 02115. Telephone: (617)732-1193.

"Malice in Wonderland"

An amusingly written but analytical article on the operation of the peer review system in Canada with respect to research funding has been published in *Physiologist Canada* 12(3): 55-81, 1981, "Malice in Wonderland" by Daniel H. Osmond. US physiologists may find it interesting in light of discussions of the operation of peer review in the US that have appeared in scientific and lay press in recent months.

SOCIETY NEWS

APS Centennial Collection of Physiological Instruments and Equipment

In planning the celebration of the centennial of the American Physiological Society, much thought has been given to exhibitions of both historical and contemporary physiology.

Instruments, devices, and methods useful in the detection, measurement, and recording of physiological functions for research and teaching and for clinical treatments are of great importance. The collection of such instruments is valuable for appreciation of historical development, for teaching, and for stimulating new ideas.

As we pursued plans for an exhibition of "A Century of Physiological Progress" with the Smithsonian Institution, we became aware of the lack of adequate collections of material. In an effort to overcome the paucity, the Centennial Committee is establishing *The Centennial Collection of Physiological Instruments and Equipment*. Details regarding organization and handling of the collection are being developed.

To achieve some sense of membership participation in this venture, we are eager to hear from the members of the Society or any other readers of possible available contributions. Please send us a description of such equipment that you would be willing to send to the APS Centennial Collection, or if you have some items of historical value that you do not want to donate but would be willing to loan, please tell us. Do not send any equipment, just send us a letter.

M. C. Shelesnyak, Task Force Director
Centennial Celebration Committee.

APS Sections

Cell and General Physiology Section

We are pleased to announce that the Program Executive Committee has approved the three symposia topics suggested for the 1983 Spring FASEB Meeting by the Cell Section Steering Committee via R. B. Gunn, our Program Chairman. Each of these symposia will be held as a one-half day session: *1.* Cell-to-Cell Communication, organized by W. C. DeMello; *2.* Electrophysiology of Secretary Cells, organized by C. S. Pace; and *3.* Role of Calcium as a Second Messenger, organized by M. P. Blaustein. The last topic has been proposed as part of the Intersociety Calcium theme selected as one of the themes for the 1983 Spring Meeting.

N. Sperelakis, our present Chairperson, has solicited funds to support the activities of APS-Cell from pharmaceutical companies. We are sincerely grateful to the following companies for their generous support of our "fledgling" section: Smith Kline and French Laboratories, Philadelphia, PA; Ciba Geigy Corp., Summit, NJ; Boehringer- Ingelheim, Ltd., Ridgefield, CT; The Upjohn Co., Kalamazoo, MI.

The Steering Committee will present topics for symposia for the IUPS Congress to be held in Vancouver, British Columbia, in 1986. It is necessary to have the program topics by the summer of 1983. It is very important for the Cell Section to decide on topics representing our interests. The time to suggest and consider topics is now! We solicit suggestions from our members. These suggestions should be forwarded to R. B. Gunn, our Program Chairman.

C. S. Pace, Secretary/Treasurer

Renal Physiology Section

This is an informal midyear report of the activities of the Renal Section of the American Physiological Society.

The last meeting of this group was held in the Melrose Room of the Hilton Hotel in New Orleans, April 21, 1982. One hundred thirty-six persons enjoyed drinks, hors d' oeuvres, and dinner. The generous contributions from four pharmaceutical companies (Abbott, Hoechst-Roussel, Merck Sharp & Dohme, Smith Kline & French) kept the cost of this function within reach of all. After dinner, Dr. Jared Grantham delivered an entertaining and educational talk entitled "Barber's Pipette: Before Chambers and Richards."

The business meeting was chaired by Dr. Fred Wright. One of the first items on the agenda was the presentation of the Fourth Annual Awards for Excellence in Renal Research to three young investigators in recognition of the work they presented at the 1981 Fall Meeting of the American Physiological Society held in Cincinnati. Awards, consisting of a certificate prepared by the American Physiological Society and a check for $100, went to **Pamela Carmines**, Indiana Univ Sch. of Med., Indianapolis, IN (Abstract 565); **Patricia King**, Div. of Biology and Med., Brown Univ., Providence, RI (Abstract 603); and **Eric Pierce**, Univ. of Michigan Sch. of Med., Ann Arbor, MI (Abstract 34).

There was considerable discussion about awards based on presentations at the Fall Meetings. A consensus was reached that presentations at both the Fall Meetings (American Physiological Society) and the Spring Meeting (FASEB) be judged to compile the list of awardees and that the winners be announced the following year at the Spring Meeting during the annual meeting of the Renal Section. Thus the winners to be announced during the 1983 Spring Meetings (Chicago) will be selected from those presenting at the 1982 Fall Meetings (San Diego), but the winners to be announced during the 1984 Spring Meetings (St. Louis) will be selected from those presenting at the 1983 Spring Meetings (Chicago) and the 1983 Fall Meetings (Honolulu). To facilitate the task of judging presentations, Dr. Don Marsh suggested that, to be eligible, a student's advisor or a postdoctoral fellow's sponsor must nominate each person in writing to the Chairman of the Renal Section, submitting name and place, date, and time of the presentation. Please send your nominations to Dr. Marsh well in advance of the Fall and/or Spring Meetings.

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Please contact the program representatives with your ideas for symposia; contact any of the officers concerning the annual meeting programs, the annual dinner and other matters.

Paul C. Churchill, Secretary

Respiratory Physiology Section

The meeting chaired by R. E. Hyatt was held on April 20 1982. The report of the Steering Committee meeting held on October 12, 1981, in Cincinnati was given. At that meeting R. E. Hyatt was named Chairman of the Nominating Committee. It was pointed out that the bylaws were unclear as to whether the new Councillor would serve as Chairman of the Respiration Dinner but would not assume the official role of Councillor until July 1, following the Spring Meeting. There were also discussions related to the progress of establishing a permanent Study Section to deal with pulmonary problems. It was reported that a list of the membership who had expressed an interest in respiration could be obtained from either O. E. Reynolds or H. Brownstein.

Next the report of the Nominating Committee and the election results were given. The Committee consisted of R. E. Hyatt, B. Whipp, and M. P. Hlastala. The two candidates chosen were J. A. Nadel and John Butler. The membership was solicited by mail, 185 votes were cast, and Dr. Nadel was elected.

Membership of the Steering Committee of the Respiratory Section was then reviewed. R. E. Hyatt is in his last year and will serve as Chairman or 1982-1983. N. R. Anthonisen, whose term is from 1981 to 1984, will serve as Chairman the following year, and K. Wasserman, whose term is from 1982 to 1985, will serve as Chairman during the year 1984-1985. R. Fitzgerald is Secretary-Treasurer and serves from 1981 to 1984. The Program Advisory Committee Member is A. J. Berger, whose term is from 1982 to 1985.

Chairman of the Nominating Committee for the upcoming year will be Dr. Anthonisen. He will select two at-large members to serve with him and prior to the Spring Meeting will present two candidates for the new Councillor. This balloting will be conducted by mail.

G. M. Turino spoke with O. E. Reynolds regarding changes in the bylaws. It was Dr. Reynolds, suggestion that we wait two years before making such changes since other problems may arise and all changes can be handled at once. The Respiratory Physiology Section formally thanked Dr. Turino for the work he had performed on behalf of the Section, particularly in its early, somewhat confused, formative days.

There was a brief discussion regarding the permanent Study Section. Although an Executive Secretary has been appointed, the Study Section is still on an adhoc basis. It was felt that the Study Section should become permanent by midsummer of 1982.

A. P. Fishman, editor of the *Journal of Applied Physiology*, spoke briefly to the group asking for suggestions. The question was raised as to the possibility of changing the name of the journal from the *Journal of Applied Physiology: Respiratory, Environment, and Exercise Physiology* back to just *Journal of Applied Physiology* or to make Respiration another part of the *American Journal of Physiology*. Those favoring this suggestion felt that Respiration was certainly equal in status to Circulation, Cell, and so forth and that something was lost by having most respiratory work appearing under the Applied Physiology designation. Dr. Fishman pointed out that any such change would have to be in the form of a petition to the Publications Committee. No decision was reached, but a straw vote was taken showing that about one-third of those present favored the changing of the name and two-thirds were opposed to it, there being approximately 45 individuals in attendance. It was suggested that individuals may correspond with Dr. Fishman regarding this matter which should appear as a future agenda item for the Respiratory Physiology Section.

N. C. Staub discussed the current status of the symposia for the upcoming years and requested suggestions. There is to be a symposium on High Altitude at the San Diego meeting in the fall of 1982, but no other symposia are definitely scheduled.

It was pointed out that the Respiratory Physiology Section is the largest section with some 376 members specifying respiration as a primary interest in 1982; this is up from 311 in 1981.

There being no additional items of new business, the meeting was adjourned. There will be a meeting of the Steering Committee at the San Diego meeting in the fall of 1982.

R. E. Hyatt, Chairman

Future Meetings

1983	
FASEB Annual Meeting	Apr 10-15, Chicago
APS "Fall" Meeting	Aug 20-24, Honolulu
IUPS Congress	Aug 28-Sep 3, Sydney
1984	
FASEB Annual Meeting	Apr 1-6, St Louis
*APS "Fall" Meeting	Jul 29-Aug 7, Lexington
1985	
FASEB Annual Meeting	Apr 21-26, Anaheim
*APS "Fall" Meeting	Aug 4-9, Buffalo

*Campus meeting

Honorary Members

Honorary Members of the American Physiological Society are distinguished scientists outside of North America who have contributed to the advancement of physiology. The Society has elected forty scientists to Honorary Membership, and the date of their election is given.

E. D. Adrian†, Cambridge, UK (1946)
J. Barcroft†, Cambridge, UK (1946)
E. Braun-Menendez†, Buenos Aires, Argentina (1959)
F. Bremer†, Brussels, Belgium (1950)
A. Dastre†, Paris, France (1904)
P. Dejours, Strasbourg, France (1981)
Sir John C. Eccles, Canberra, Australia (1952)
T. W. Engelmann†, Berlin, Germany (1904)
B. Folkow, Goteborg, Sweden (1982)
R. Granit, Stockholm, Sweden (1963)
R. A. Gregory, Liverpool, UK (1981)
E. Gutman†, Prague, Czechoslovakia (1971)
O. Hammarsten†, Uppsala, Sweden (1907)
W. R. Hess†, Zurich, Switzerland (1950)
A. V. Hill†, London, UK (1946, 1950)
Sir Alan L. Hodgkin, Cambridge, UK (1952)
F. Hofmeister†, Strassburg, Germany (1904)
B. A. Houssay†, Buenos Aires, Argentina (1941)
A. Hurtado, Lima, Peru (1959)
A. Huxley, London, UK (1981)
H. E. Huxley, Cambridge, UK (1981)
G. Kato†, Tokyo, Japan (1965)
A. Krogh†, Copenhagen, Denmark (1946)
Y. Kuno†, Tokyo, Japan (1959)
J. N. Langley†, Cambridge, UK (1904)
L. Lapique†, Paris, France (1946)
G. Libjestrand†, Stockholm, Sweden (1950)
C. Monge†, Lima, Peru (1952)
G. Morruzzi, Pisa, Italy (1959)
L. A. Orbeli†, Leningrad, USSR (1946)
I. R. Pavlov†, Russia (1904)
E. Pflüger†, Bonn, Germany (1907)
W. T. Porter†, Dover, MA (1948)
F. J. W. Roughton†, Cambridge, UK (1957)
Sir Edward Sharpey-Schaefer†, UK (1912)
Sir Charles Sherrington†, Oxford, UK (1904)
H. H. Ussing, Copenhagen, Denmark (1950)
K. von Frisch, Munich, Germany (1952)
C. von Voit†, Munich, Germany (1970)
H. H. Weber†, Heidelberg, Germany (1959)

†Deceased

To F. J. Haddy:

I feel very honored by having been elected honorary member of the American Physiological Society. I will try to live up to this distinguished appointment, though I doubt I will be able to... I am of course very glad for this, and I hope you will convey my gratefulness to the members of the committee.

Björn Folkow
Fysiologiska Institutionen
Göteborgs Universitet
Göteborg, Sweden

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Contributions to the Society may be made to the General Operating Fund or other designated purpose. The donor may commemorate an event or memorialize an individual.

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KOCH, ALAN
KOEHLER, RAYMOND C
• KOEPF, GEORGE F
• KOHLSTAEDT, KENNETH G
• KOHN, HENRY I
KOLMEN, SAMUEL N
KONTOS, HERMES A
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KOPETZKY, MICHAEL T
KORCHAK, HELEN M
KORNEL, LUDWIG
KORY, ROSS C
KOSTOPOULOS, GEORGE
KOYAMA, SHOZO
KRATOCHVIL, CLYDE H
KRIEGER, DOROTHY T
KROC, ROBERT L
KRONFELD, DAVID S
KUNAU, ROBERT
KUNZ, ALBERT L
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LA FARGE, C GRANT
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LANDAU, BARBARA R
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• LANDIS, EUGENE M
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LEEMAN, SUSAN E
LEGAN, SANDRA J
LEHMKUHL, DON
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LEVINE, GARY M
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* LIPSCOMB, HARRY S
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SMITH, ARTHUR H
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SOKAL, JOSEPH E
SOLARO, R JOHN
SOMERO, GEORGE N
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* SWANK, ROY L
SZURSZEWSKI, JOSEPH H
TABORSKY, GERALD J
TAYLOR, REGINALD M
TEDESCHI, HENRY
TENNEY, STEPHEN M
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THURBER, ROBERT E
TIERNEY, DONALD F
TOBIN, RICHARD B
TONG, EDMUND Y
TORRES, JOSEPH C
TRAPANI, IGNATIUS L
TRAYSTMAN, RICHARD J
TSAGARIS, THEOFILOS J
TUCKER, ALAN
TURINO, GERARD M
ULRICH, FRANK
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* VAN HARREVELD, ANTHONIE
VAN LIEW, HUGH D
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* VON KAULLA, KURT N
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WAGNER, WILLIAM C
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* WEBSTER, MARION E
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* WINTER, CHARLES A
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YASHON, DAVID
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YOUNG, STEPHEN L
* YU, TSAI-FAN
ZADE-OPPEN, MARTIN A
ZAMBRASKI, EDWARD J
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ZELLER, JANICE M
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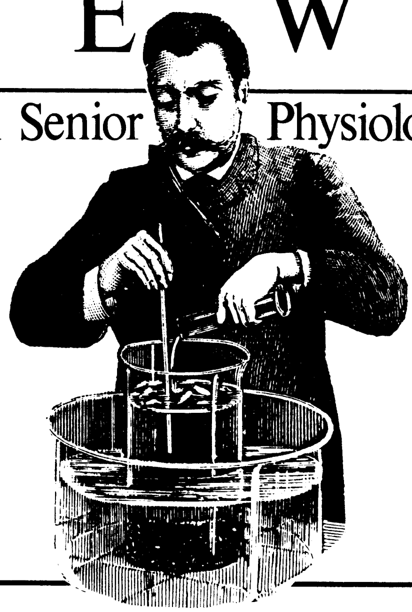
ZUCKER, MARJORIE B
ZWEIFACH, BENJAMIN W

NEWS from Senior Physiologists



Samuel L. Leonard to Edward Adolph:

Really not much different has happened to report since the last entry about my doings. I go to the lab each day when in Ithaca to read and talk over research with graduate students but do not work at the bench. Frontline research in my field today requires a great deal of financial support, which means that to do a conscientious job requires long days and loss of freedom to do things that you always thought about and couldn't do in earlier days. I am enjoying life, travel, and visiting my scattered children. A little trout fishing while camping out is in order for the summer in Montana. The wife and I travel in a small self-contained RV, which is quite economical in these days of inflation. She has her Ph.D. in Botany, and the flora out west is not like ours so she enjoys it too. We have been following this pattern since I retired 10 years ago. We are in good health and so go while we are able.

I am sending a copy of a seminar I gave here at Cornell at the urging of several colleagues. It was a "fun" thing—made short by time limitations. Dr. Ernst Knobil, one of my former graduate students, suggested it might be of some interest.

I have always enjoyed meeting you at meetings (Soc. Exp. Biol. Med., etc) and have been impressed with your research work. Your interest and trouble to write to us about our lives can be best repaid by a personal letter in appreciation of your effort.

Section of Genetics & Development
Cornell University
Ithaca, NY 14853

Louis A. Toth to Edward:

When I retired in Catherine and I spent the next two years living the life in New Orleans. We traveled some, visiting relatives we had not seen for some years. We decided to move to Clear Lake City to help our daughter Ann and take care of her two children. We have the children, ages 11 and 9, seven days a week, before and after school, while their mother is supervising the ambulatory clinic at a public health hospital here. To have the responsibility of rearing two youngsters after we had been without this for almost thirty years is quite a worry. I enjoy my daily contacts with my grandchildren and have helped coach their baseball teams for the past three years.

Father Time has not been too hard on me, but Catherine has had some troubles. As a result I have to do all the driving to take her shopping, take the grandchildren to and from school, to their ball games, etc. When we moved here we decided not to live in Ann's house. This means I have two houses and yards to keep up; so time is not heavy on my hands. I do get one afternoon by myself when I bowl with a senior citizens group.

I am happy to hear you still have your desk in room H 406. To have such surroundings for such a long time helps to keep a person warm and active. But I imagine many changes have taken place—so many I could not recognize the hall.

My advice to younger colleagues is "Do what you are happiest doing, even though it may mean a slower climb up the academic ladder." My first love was teaching, my contacts with students. Research was secondary, and for this reason my rank and salary were slow in climbing. Then when the athletic program died at LSU Medical Center prior to my coming, and I was certain the students should have such a program, I devoted my research time to reviving and running the program. I am not sorry I sacrificed my research for the athletic program because I still feel that the students benefited more from my efforts than the scientific world would have from more papers. But at times I feel you were disappointed in your first doctorate student. I have fond memories of our association, such as the Saturday we spent making picture frames. After completing the frames we remarked "We could have bought these frames for fifty cents each." But your remark was "But we had a lot of fun."

1639 Neptune Lane
Houston, TX 77062

David Rioch to Edward:

Thanks for your letter. I should have written in answer to kind inquiries from Hal Davies and others many years ago.

Several times a week I go to the Institute for Behavioral Research, where I am so-called "Senior Scientist." It is a handle for someone who sits around, talks, and does not do much. At the moment I am dictating some work on group cohesion and morale for Dr. David Marlowe, Chief, Dept. of Psychiatry at the Walter Reed Army Institute of Research. It is chiefly from my experience in Korea and Vietnam back in the fifties and sixties, embellished here and there with episodes from working with psychotic patients and with bits of neurophysiology. I still wonder how it is that the nervous system only rarely and then for very short times (one-half to five seconds, possibly) shows random activity, or at least what looks random. People talk a lot about panic and so forth, but even convulsions are well organized.

I have recently heard that "jet lag," resulting in "circadian desynchronosis," is thought to often be the cause of airplane accidents. It would be too bad if interest in jet lag distracted attention from where the troubles really lie. Some of us are applying for a government contract to review the published data on this critically.

My health is now fairly good except for some mild cardiopulmonary complaints. With best wishes and warm regards to you and several other old friends.

5525 Surrey St.
Chevy Chase, MD 20815

Hugh Dukes to Edward:

Thank you for your letter. I am glad to report that my health and that of my wife remain pretty good. I have written several letters on my postretirement activities and these, or parts of them, have been published in *The Physiologist.* The 10th edition of *Duke Physiology of Domestic Animals,* edtied by Dr. Melvin J. Swenson, is now in preparation. I understand that the publication will be in 1984. As editor Dr. Swenson has been in complete charge of the book for the 8th, 9th, and 10th editions. Various editions have been translated into Spanish (twice), Serbo-Croatian (twice), Hindi, and Chinese. A reprinting in English has been made in the Philippines. The semicentennial year of the book will be in 1983.

I am writing a history of the Department of Physiology, NYS College of Veterinary Medicine, Cornell, for the years I was there (1932-1960). Others will write the early and later history. The history is for the Centennial of APS.

I still attend occasional scientific and professional meetings in the Des Moines and Ames areas.

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

J. Newell Stannard to Edward:

It was pleasant to hear from you and to know that I am now counted as a senior physiologist. Despite specializing in other areas I view my interests as basically physiological.

California has been great for Grace, and she is fully adjusted. I still miss the University of Rochester and the host of people I am privileged to call friends. UCSD is a fine institution but belongs to a different, relatively impersonal, pattern.

17441Plaza Animado, #132
San Diego, CA 92128

Frederic T. Jung to Edward:

At age 83 I continue to live very contentedly in a fine home for retired men. One of its many advantages is its location within easy walking distance of post office, banks, police station, fire house, big stores, and especially small shops within this same block for all sorts of convenient items. I have no contact with laboratory research but try to keep up somewhat by reading the Journal of the American Medical Association, the Scientific American, and Science News.

Last December 1 I gave a paper at the Chicago Literary Club, "An Exciting Old Book: 1713." The book is an old family keepsake, a translation into 18th century German of a series of sermons delivered in Latin in 1519. It features five prefaces and auther's commentary on Paul's Epistle to the Galatians. It is a marvel of typesetter's art—type in Gothic, Greek, Latin, and italics. It is of physiological interest because this epistle is so much concerned with a surgical operation that it has been described as the "Evangelium Praeputii et Circumcisionis."

On December 18 I was awarded the first Honorary Life Membership by the Greater Chicago Area Chapter of the American Medical Writers Association at a dinner on the 95th floor of the magnificent John Hancock Building.

I am happy to be living near enough to Western Springs so that I can visit frequently with my son Paul and his thriving family.

James C. King Home
1555 Oak Ave.
Evanston, IL 60201

Robert Johnson to Ladd Prosser:

In response to your recent letter on behalf of senior physiologists, I am keeping active in research and writing. Indeed, I am now head of a company registered in Vermont to do research, development, and consulting in applied biology. I brought my colony of eastern box turtles with me when we moved from Illinois to Vermont permanently in 1981 summer. We are making plans to build a simple office, library, laboratory, and workshop near our residence. We live out in the Green Mountains, six miles from Montpelier, in an apartment attached to the old farmhouse occupied by my younger son Charles. Right now, I write in our bed-sitting room, the turtles live in the basement, and the books are awaiting a permanent library. For professional purposes, I use the Libraries of Vermont College, The Vermont Historical Society, and the University of Vermont. I do not plan to teach.

Margaret and I have completed (finally) the manuscript of a biograph of Frederick Schwatha, M.D. (1849-1892). 3

Horn of the Moon Enterprises
RFD #1
Montpelier, VT 05602

John F. Hall to Ladd:

I thank you for your letter of inquiry concerning my retirement activity and appreciate the opportunity to answer. Although active and in good health since my retirement in June 1972 from USAF (W-P AF Base; Aerospace Medical Research Lab.) I personally and my family also were devastated by the loss of my wife, Catherine, in March 1981 due to colon cancer.

Consequently my chief problem since has been one of mental and emotional adjustment, and I have attempted to obtain a voluntary type of research assistantship at any laboratory concerned with investigation into the cell physiology or pathology of malignant cells. My personal experience has emphasized to me that little or nothing is really known concerning the effective treatment, much less the cause, or process of metastasis in such type cancer. Since I have a modest independent income, I could serve to a very minimal pay level and in almost any minor research capacity, however humble.

Present activities aside from searching for such a voluntary research position have involved travel to visit friends and family; some photography, a hobby; and some outdoor lawn and garden efforts.

I feel deeply appreciative to have this opportunity to cooperate with the many fine people who are Society members both active and retired.

5989 Helenwood Dr.
Dayton, OH 45431

George W. Stavraky to Ladd:

Thank you for your inquiry about my recent activities. I retired from the University in 1970, and since then my wife and I have been doing all the things we were unable to do during our working years. We spend long summers on our island in Northern Ontario with our grandchildren, go to the Florida Keys for part of the winter, and have made several trips by cruise ship and freighter to the Orient, around the Pacific, around South America, to the Mediterranean, and with two groups to East Africa and India. Our lifestyle has not allowed me much time for writing or for laboratory activity, but it has given me an opportunity to see much of the world I have been interested in. Particularly enjoyable was retracing the voyage of the Beagle in its entirety and visiting the Darwin Station in the Galapagos Islands. We also went up the Amazon and its tributaries, making stops to see the rain forest and the indians and to visit the town and house where Bates, the great naturalist, studied the flora and fauna of the region a century ago.

I am afraid I have no significant correspondence or unpublished material to contribute, but you did ask what I was doing and this gives you an idea how my wife and I have spent the past ten years. We both are fortunate in having been blessed with good health and hope to stay active for some time to come.

250 Cheapside St.
London, Ontario N6A ZA1

Francis O. Schmitt to Ladd:

Some two years ago, after completion of the work I had been doing on the cerebral cortex, I became impressed with the great desirability of applying to neuroscience the concepts and techniques, particularly those of recombinant DNA technology, to neuroscience. Therefore, in the all of 1980, with the invaluable aid of a planning committee comprised of leaders in molecular genetics, a week-long conference was organized and from May 2 to 8, 1981; the conference was held at Woods Hole, MA. Tutorial lectures on the concepts and techniques of molecular genetics were followed by lectures on applications of these concepts that have already been made to endocrinology and to neuroscience.

Manuscripts representing the proceedings of this conference are in press, having been edited by Drs. F. E. Bloom, S. J. Bird, and myself. The book, entitled *Molecular Genetic Neuroscience* is expected to appear in the spring of 1982. Meanwhile, I have been considering which of the many exciting aspects of the subject might be appropriate for my further study.

Neurosciences Research Program
165 Allandale St.
Boston, MA 02130

Baird Hastings to Ladd:

Life goes on with me much as when you saw me last. I still come to my Physiological Research Laboratory office about 9:30 Mondays through Fridays, and I am picked up to return to the Chateau La Jolla at 4 P.M. While "at work," I write a little, read a lot, and talk some with the post doc and graduate students who seek me out.

Now that I'm about to become 86, I guess I am regarded as too aged to be asked to participate in a White House Conference on Aging. (Ten years ago I was on the President's Committee that planned the 1971 conference). At least the National Institution Aging is finally well under way.

On March 30-31, I attended a symposium held in Bethesda in honor of Chris Anfinsen's 65th birthday (it shocks me to think that my graduate students are retiring before I succeed in doing so). My title was "Historical Perspective of Biomedical Research" in 10 minutes!

To my younger colleagues I would only say, What are your plans for the future? Be it next year, next month, or tomorrow.

Scripps Institution of Oceanography
La Jolla, CA 92093

Ragnar Granit to Ladd:

Your letter made me recall a similar one from Hal Davis in 1978. I must have mentioned in my reply the publication of my book *The Purposive Brain* (The MIT Press 1977), now in paperback and in some translations. What I have done since, except devoting myself to the garden in my island home in the Baltic? I have written introductions to a number of Symposia, four in Stockholm and in Pisa, which was edited by Ottavio Pompeiano and myself. (Reflex Control of Posture and Movement. *Progr. Brain Res.* vol. 50, 1979); contributed to the planned publication *Foundations of Sensory Science* an invited historical paper entitled "My Personal Vision" (Editors, Professors Dawson and Enoch for Springer-Verlag); served since 1968 for the Italian National Research Council on the governing body of its Research Institute in Pisa, now headed by Lamberto Maffei. In October 1981 I gave a lecture at a Nobel Conference of the Gustavus Adolphus College, St. Peter, MN dealing with "The Place of Mind in Nature."

Now at 81 I intend to withdraw from activities of the kind mentioned and cherish some old interests in the humanities. This I have begun by editing a collection of essays celebrating the bicentenary of Linnaeus (his death) and also contributing to it (essay on Banks and Solander in 18th Century London).

Nobel Institute for Neurophysiology
Karolinska Institutet
S-104 01 Stockholm 60, Sweden

Eugene Robillard to Ladd:

I left the academic life in 1970 and began an administrative work with a educational connotation. Then I installed the division of medical education at the Professional Corporation of Physicians of Quebec. Two years ago, I joined the directional staff of the Corporation. My work, under the overstatement of research and development, consists of studying questions necessitating future decisions or special communications with universities or government representatives. I do not work on Fridays, and my working contract is annual. I feel as efficient as my younger colleagues, but I imagine I am not the best judge in that matter.

In my spare time, I read scientific literature for my information rather than for research purposes. I am wonderstruck by the current scientific progresses, although I deeply regret the oscillations of the financial support for research at each economical low or boom. Such oscillations can unbalance the permanent and constact function of research. They are apparently due to a difference in the time projection of the governments over a few years and of the research organization, which is for a much longer term.

Corporation Professionnelle des Médecins
du Québec
Montreal, Quebec H3G 1S5

S. Howard Bartley to Hallowell Davis:

I became Professor Emeritus at Michigan State University in 1971. Since that time I have been on the faculty of the Psychology Department at Memphis State University, first as Distinguished Visiting Professor and then as Distinguished Research Professor. During this time I have been interested in finding a way of extending or at least making broadly visible the pioneer work of my mentor, Raymond H. Wheeler, on the Relation of Climate to Human Affairs.

I have written an additional textbook, "Introduction to Perception." Even though this may sound like something out of the field of physiology, I have always seen psychology as based on physiology and the other biological sciences, so I have not strayed from the work that I was doing with George H. Bishop at Washington University. Another part of my time I have used to write essays on the nature of science and of psychology as a science.

Psychology Dept.
Memphis State University
Memphis, TN 38152

Bill Foster to Horace Davenport:

Thanks for your letter of inquiry on the activities of senior physiologists. When my teaching at the University of Pennsylvania came to a halt my emeritus status did not slow my laboratory activities. At the age of 77 I have continued my work at Jeanes Hospital as director of the clinical chemistry laboratory. Jeanes with the American Oncologic Hospital and the Institute for Cancer Research form the Fox Chase Medical Center. Our laboratory is responsible for all the lab work at the center. As a member of the Department of Medicine I consult on endocrine problems.

The years of teaching physiology have been invaluable to me in the clinical laboratory, especially when called upon to consult with our staff members, many of whom have been my former medical students.

Twenty years ago John Brobeck asked that I set up the Red Cell Volume experiment with use of radioactive chromium. Here at Jeanes we are now performing the same test for our hypo- or hypervolemic patients. A knowledge of the fundamentals of the blood gas interpretations taught in the physiology laboratory has been helpful. We have no animal facilities for research at Jeanes, but there is plenty of clinical material for investigative purposes. The late eminent pathologist, Dr. Fuller Albright, once said "Do measure something." I am making use of this clinical material.

As a result of a paper on urinary estriol in fetal distress presented at the New Orleans APS meeting, I received a letter from the Public Affairs Office of FASEB, suggesting that our paper might be useful in a Feature Service Story. It was pleasing to know that of the many papers presented at that meeting this was one of nine selected for the Feature Service Stories for Lay Language Reports of Research in the Life Sciences.

Dept. of Pathology
Jeanes Hospital
Philadelphia, PA 19111

On Lovic Herrington to Bob Alexander:

Following a very productive career in stress physiology and thermal adaptation, Dr. Herrington retired in 1962 from his position as Director of Research at the John B. Pierce Foundation and his affiliation with Yale's Public Health Department. After retirement he worked on the equational restatement of partitional calorimetric work. Since 1979 he has resided with his son's family.

113 Janet Dr.
Syracuse, NY 13224

S. A. Matthews to Bob:

It was very thoughtful of you to remember me on my 80th birthday. Can it be nearly half a century since you, Fred Ferguson, and the other eager students explored the rock pools of Nobska, the mud flats of North Falmouth, and all the other habitats with us? Some of the details of those years are more vivid in my memory than those of a few years ago. They were very pleasant summers—at least for me. I was reminded of them a few weeks ago when Bud Carpenter (an old Woods Holer, now retired from Tufts) came to see us with two reels of film he and Ben Coonfield had taken of scenes and personalities of Woods Hole in the 30's–Naushon pulling away from the dock, the Cayadetta loaded with Invertebrate field trippers, Morgan, Parker, Conklin, Chambers, and others in their labs. It certainly brought it all back.

P. O. Box 136
Williamstown, MA 01267

Thomas Noonan to Arthur Otis:

In April 1977, I retired from the Comparative Animal Research Laboratory. I have been really surprised to realize how sharp a break with scientific activity occurred then. I have done no writing and have kept in touch with research only through the pages of *Scientific American*. Except for some problems with vision my health has been good. I have made a few trips back to Rochester but otherwise travel very little. In reviewing the past five years I must admit that I should be bored, but for some reason I am not!

Advice to younger colleagues, Do not retire in a two-story house too much maintenance!

1030 West Outer Drive
Oak Ridge, TN 37830

Louis B. Jaques to Arthur:

Although retired by the University of Saskatchewan in 1979, I am continuing the research on the heparin which I began in 1934 at Toronto. In those early years the original workers in Toronto and Stockholm became aware that we were dealing with a drug which was quite different chemically and was clinically effective for reasons much more than the anticoagulant action that had called attention to it. It was evident that new procedures and approaches would be needed to solve these basic problems, and this we postponed so as not to delay use of the drug clinically. After 40 years of great clinical success of the drug, in the past 10 years methods have become available to investigate these basic problems, and my students and associates have produced the evidence to confirm the suspicions of the pioneer investigators. This is very gratifying to the survivor of that band of investigators, but there remains the problem of persuading the present generation to give up the preconceived ideas 40 years out of date. So I will be continuing my scientific writing for some time to come.

College of Dentistry
University of Saskatchewan
Saskatoon, Canada S7N 0W0

Ernest A. Spiegel to Roy O. Greep:

Thank you and the American Physiological Society very much for remembrering my 87th birthday and for your inquiry.

I have prepared a survey of the development of stereotaxy (stereoencephalotomy), the application of Horsley and Clarke's stereotactic method to the human brain, since I initiated it, together with my surgical associate, the late Henry T. Wycis, in 1947. This survey forms an introductory chapter in Schaltenbrand-Walker's "Stereotaxy of the Human Brain" that appeared this year. It may be noteworthy that this new branch of neurosurgery is practiced not only in the Americas and in nearly all European countries but also in Japan, India, and Thailand. In some universities, e.g., Freiburg, Goettingen, Wuerzburg, Germany, special departments devoted to this discipline have been established. Its scope has been enlarged by employing computerized tomography for localization and subcortical stimulation for relief of spasticity and of chronic pain.

I have been elected honorary fellow of the Mexican Academia Nacional de Medicina.

6807 Lawnton Ave.
Philadelphia, PA 19126

Howard Burchell to E. B. Brown:

My retirement from active practice and teaching is gradually becoming complete. For seven years, I have spent two to three months on the Stanford Campus (winters) as visiting professor in the Division of Cardiology, directed by Dr. Donald Harrison. I have become more ininvolved in the History of Medicine in recent years, two continuing projects being "Forensic Foxglove Lore" and "Models in Scientific Discoveries." I am fortunate in having only a few health problems until now.

260 Woodlawn Ave.
St. Paul, MN 55105

Russell H. Wilson to E. B.:

I used my Ph.D. from Minnesota with the training in Physiology to great advantage, becoming Professor and Chairman of Physiology and Pharmacology at the University of North Dakota between 1965 and 1973. I then came back to Dallas and obtained my appointment as Clinical Associate Professor of Internal Medicine at University of Texas Health Science Center at Dallas. I am at present at the Kaiser Foundation HMO as Internist and am also on the active staff at Parkland Memorial Hospital in Dallas. I am not doing research, but I see 20–30 patients daily and have some teaching responsibility.

6218 Walnut Hill Lane
Dallas, TX 75230

R. W. Dougherty to E. B.:

I am pleased to hear from you and also that there is still some interest in the activities of "us oldsters." My wife and I are living on a small acreage a few miles south of Ames. We had a small flock of Suffolk ewes. But lambing chores in midwinter became a little too much; so we sold most of the flock last summer. I am currently doing some woodworking, which I find to be interesting and challenging.

I have finished a book on "Experimental Surgery in Farm Animals," published by the Iowa State University Press, 1981. It is illustrated by the well-known medical illustrator, Marion Newson. I still give a few lectures on the digestive tract physiology of ruminants.

The letters from the senior physiologists are always interesting to me. My advice to younger colleagues is to keep doing something *useful* even after you retirement.

Route 2
Ames, IA 50010

Rapid Communications

In 1981 the *American Journal of Physiology: Cell Physiology* and the *American Journal of Physiology: Heart and Circulatory Physiology* began accepting Rapid Communications. At a recent meeting of the Publications Committee with the Journal Editors it was decided that the experiment of inviting a special category of manuscript, Rapid Communications, should be expanded to include all the journals of the *American Journal of Physiology*. Such manuscripts should contain results of unusual interest. Review of Rapid Communications will be accelerated. They will be accepted with no more than minor revisions or they will be rejected. Accepted manuscripts will appear in the next available issue. These communications must not exceed four journal pages in length, including figures, tables, and references. In general one printed page is equivalent to four double-spaced typewritten pages or to three figures or tables. Authors should indicate whether papers are submitted as regular or rapid communications.

Please get in touch with the Publications Office in Bethesda (301/530-7070) if you have any questions about this new experiment.

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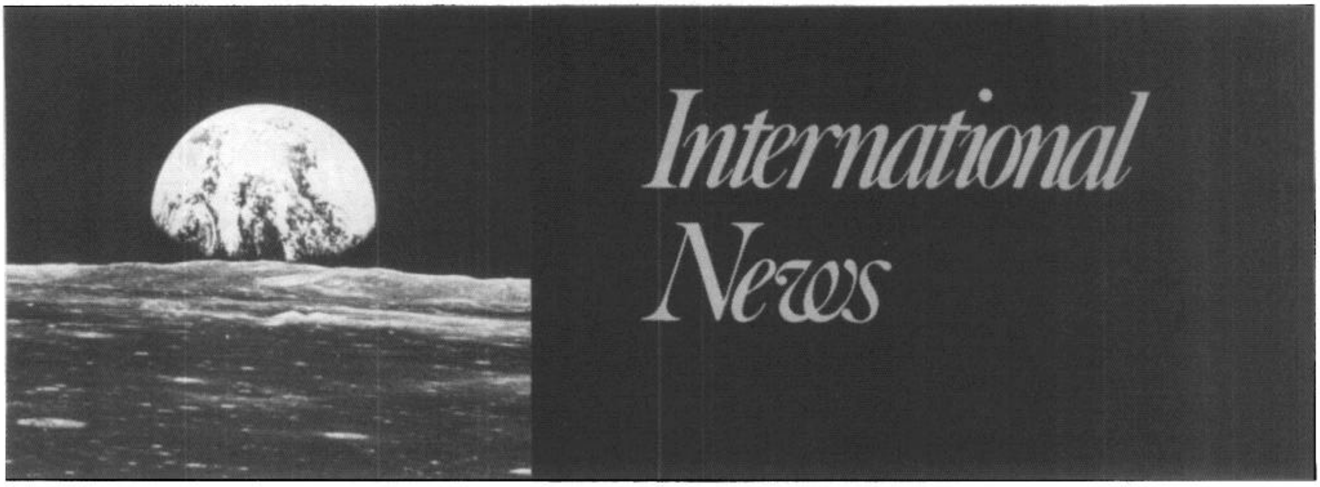
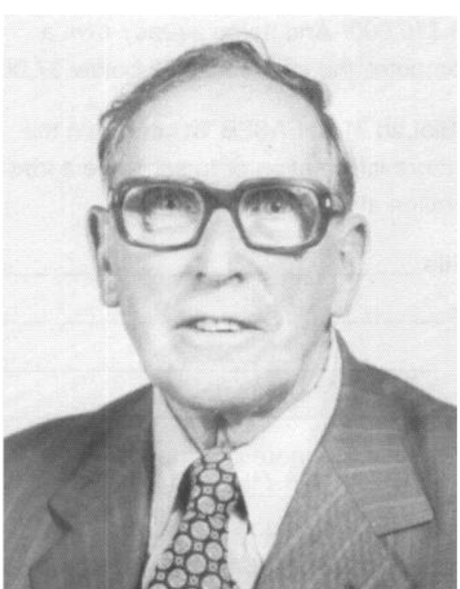


Yngve Zotterman
IUPS President 1971-1974

Professor Yngve Zotterman died suddenly at his home in Stockholm on 13 March 1982, 83 years old. In spite of his age, he was still enthusiastically active as the Secretary of the Wenner-Gren Foundation for International Scientific Cooperation and as Director of the Wenner-Gren symposium series.

Zotterman was known to physiologists around the world as the charming President of the International Union of Physiological Sciences from 1971 to 1974. He was an able leader in professional organizations and had innumerable friends and collaborators. In addition to his distinguished contributions to nerve and sensory physiology, he studied problems of diving for the Swedish Navy, the energy consumption of lumberjacks and food rationing during World War II, and many other problems where his expertise and broad experience were essential to wise Government decisions.

Zotterman seemed to know the leading physiologists everywhere, and many became his close friends. He was always full of joy and energy, and he had a marvelous sense of humor and a limitless supply of amusing anecdotes. He has described his unusual childhood and his later scientific work in a two-volume autobiography ("Touch, Tickle and Pain," Pergamon Press, 1969 and 1971). The honors that came to Zotterman were well deserved. He received many honorary degrees, including one from Cambridge, which he cherished because he had received much of his early scientific training with Adrian and A. V. Hill. His retirement from his position as Professor of Physiology in 1965 gave him time to increase his many activities in scientific organizations, in government commissions, as editor of *Acta Physiologica Scandinavica*, as a Trustee of the Nobel Foundation, and so on. In 1973, when he was 75 years old, he founded a research group for the study of problems of aging, and in this group he served as Chairman and editor for seven symposia and symposium volumes.



The many physiologists around the world who became Yngve Zotterman's friends will think of him with affection and gratitude; it was a privilege for us to know this extraordinarily active and enthusiastic physiologist.

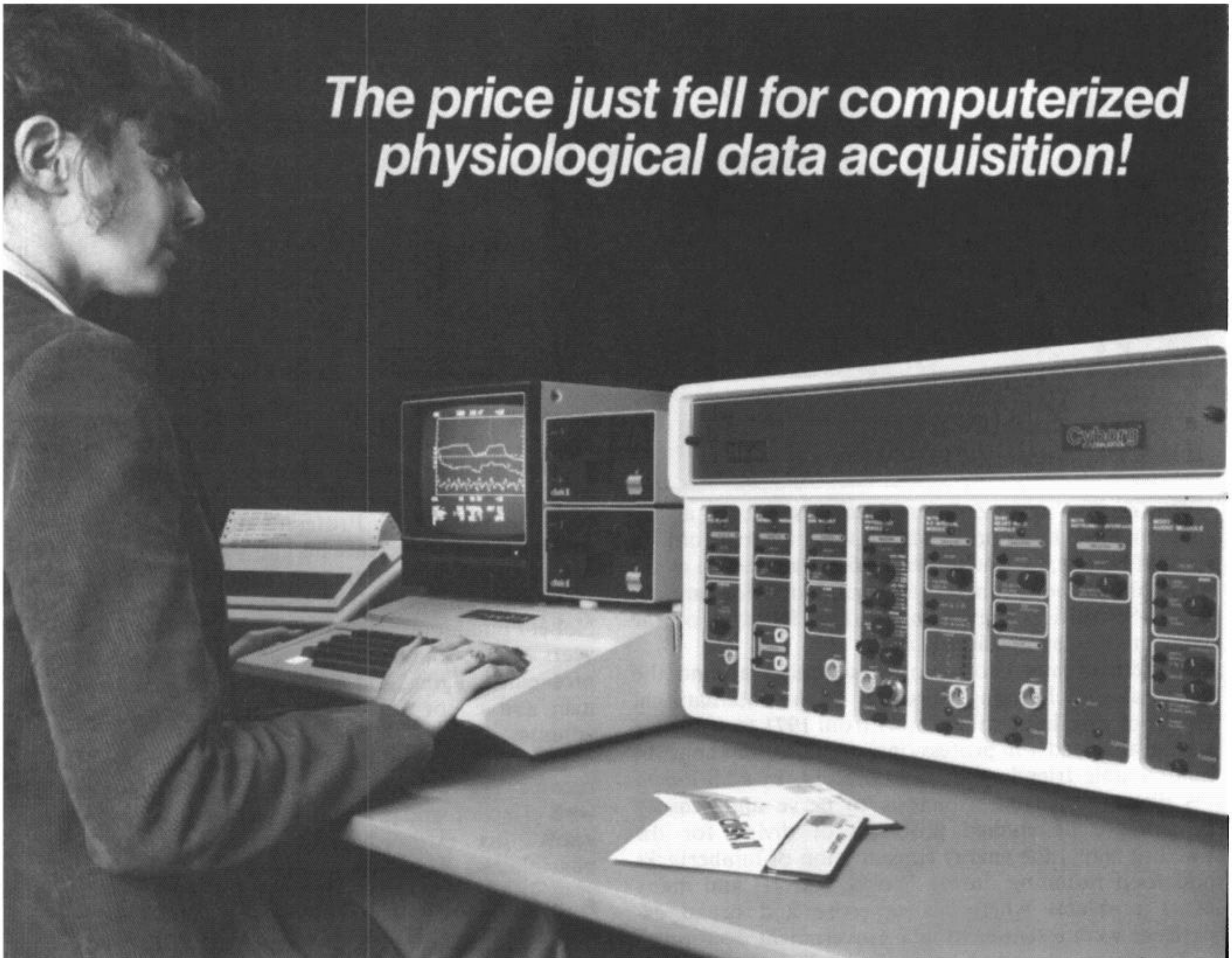
K. Schmidt-Nielsen

Heinz Karger Prize 1982 and 1983

The Heinz Karger Memorial Foundation invites the submission of papers on the following subjects. *1983*: An original research paper or a review summarizing an author's personal contributions to "Cellular Ageing." *1984*: An original research paper on "Invasion and Metastasis." (Concerning either basic or clinical investigations in order to shed light on the process of malignant cell dissemination.)

Conditions: Manuscripts shall not exceed 20 typewritten pages, including illustrations, tables, and bibliography. Manuscripts marked "Competition" must reach the publishers, S. Karger AG, Basel, Allschwilerstrasse 10, CH-4009 Basel, Switzerland, not later than February 28, 1983 and 1984. Manuscripts must be typewritten on one side only, double spaced, and submitted in quadruplicate and in accordance with the instructions contained in the "Rules for the Preparation of Manuscripts." This leaflet can be obtained free of charge from the publishers if the request is marked "Competition." *Language*: English, German, or French. *Publication*: The winning paper will be published in English in one of the Karger journals.

In 1983, the Foundation will commemorate its 20th anniversary by granting an award of SFr. 20,000. In 1984, the prize carries a cash award of SFr. 10,000. The Council of the Foundation will judge the papers and confer the prize.



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Cooling to Cardiac Arrest and Resuscitation in Anesthetized Rats

P. D. ROGERS AND G. P. WEBB
Department of Paramedical Sciences
North East London Polytechnic
London E15 4LZ, United Kingdom

ROGERS, P. D., and G. P. WEBB. Cooling to Cardiac Arrest and Resuscitation in Anesthetized Rats. *Physiologist* 25(5): 433-437, 1982. —A class demonstration is described in which anesthetized rats, cooled to cardiac arrest and maintained at temperatures approaching 0°C for 30 min, recover heartbeat and respiration on rewarming provided they are artifically ventilated during the hypothermic episode. Sample research results are presented that can supplement results obtained in less extensive class demonstrations. The paper introduces the historical background of clinically induced hypothermia and compares the results obtained from hypothermic hibernators and nonhibernators. Changes in pH of blood and water with temperature are presented; optimum pH at low body temperatures is discussed in relationship to results in hibernators and poikilotherms. The experimental procedure provides a simple way of producing heart block experimentally and thereby presents an opportunity for discussing the limitations of the electrocardiogram in providing information about mechanical events of the heart and cardiac output. The demonstration also provides an opportunity to discuss the characteristics and diagnosis of death.

A class demonstration of suspended animation.

Historical Background

There have been numerous reports of the therapeutic use of hypothermia to treat a wide range of conditions over the last 5000 years. In the Edwin Smith Papyrus (ca 3500 B.C.) cold applications were recommended for wounds of the head and local cold was used to treat ulcerated breasts. In the five millenia that followed, whole-body cooling was advocated to treat tetanus and fevers, to give narcosis, and to treat renal cholic. In the 1940's whole-body cooling to 24-30°C was tested, without success, as a treatment for terminal cancer.

In 1950 Bigelow et al. (3) showed conclusively that deep body cooling in dogs led to a fall in O_2 consumption despite maintenance of full O_2 saturation. Although this finding is taken for granted nowadays, it was contrary to the findings of many previous reports where shivering, an obvious response to the low ambient temperature, led to an increase in O_2 consumption. This clearly opened up the possibility of the safe interruption of circulation for several minutes, a possibility they confirmed in the dog. Cardiac surgeons quickly realized from these observations the potential for cardiac surgery in a bloodless field. Within a few years hypothermia down to 25°C became a relatively widespread practice in certain types of cardiac surgery for which it is still extensively used (2). One of the risks of this procedure was that of inducing ventricular fibrillation below 28°C although the heart often responded to defibrillatory techniques. Subsequently, clinical hypothermia at 28-30°C for some neurological procedures became widespread, and between 1955 and 1960 it was beneficially applied to a number of other surgical and therapeutic procedures.

Prior to 1951 the use of hypothermia was limited because as body temperatures fell, the heart slowed and eventually went into fibrillation and arrest. Attempts to resuscitate nonhibernating adult mammals from this condition were unsuccessful, and it was assumed that an animal cooled to cardiac arrest was dead. However, in 1951 Andjus and Smith (1), using the Giaja method, reported that adult rats could be cooled to 0°C and revived from cardiac arrest of up to 1 h duration. Similar findings had previously been demonstrated in hibernators and young mammals and were subsequently reported in dogs, monkeys, and humans. Cooling by means of an extracorporeal circulation using a heart-lung machine and heat exchanger resulted in a more controlled method of cooling in humans and larger mammals and allowed longer periods of arrest. This method is now used for many cases of clinically induced hypothermia. The cooling technique, used routinely by Andjus and Smith and others, may not be applicable for studies of accidential hypothermia. Hypothermia in experimental animals is induced by specilaized cooling techniques, i.e., the Giaja method. Rats were placed in a closed vessel in a refrigerator; the combination of cold, hypoxia, and hypercapnia induced a cold narcosis, and when the rats lost their righting reflex they were futher cooled by immersion in an ice bath. Other workers have used positive-pressure ventilation during cooling as described in this demonstration.

The Demonstration

Young rats of 150-200 g were anesthetized by intraperitoneal injection of 60 mg/kg body wt of pentobarbital sodium. Pin electrodes were inserted subcutaneously into the limbs and connected to an oscilloscope for the recording of an electrocardiogram (ECG). A thermometer was inserted approximately 3 cm into the rectum for continuous monitoring of rectal temperature. The animals were then completely immersed except for the limbs, tail, and head in crushed ice and water (see Fig. 1).

During the cooling process the animals were artificially ventilated with a small-animal respirator until cardiac arrest had occurred (respired rats). We have used an Ideal respirator, supplying 20 ml of air at a rate of approximately 30 times/min, connected to a piece of rubber tubing 1 cm in diameter held firmly over the nostrils; the mouth was not covered and therefore acted as a leak. The ventilation was continued until there was complete absence of ECG for 3 min. Heart rate, ECG parameters (such as P-R interval), and rectal temperature were noted at regular intervals during cooling. The animals remained in cardiac arrest for 30 min at rectal temperatures approaching 0°C. The rats were then immersed in a water bath at 40°C with only forelimbs and head not immersed. They were ventilated during rewarming, held in the water bath until an ECG returned and the heart rate had reached 60 beats/min. The animals were then removed and further warmed by a 100-W lamp placed just above the thorax until spontaneous respiration returned. Spontaneous respiration was sometimes seen to occur as chest contractions out of phase with the rhythm of the pump. Often the artificial ventilation had to be stopped for a few seconds to observe spontaneous respiration. If the rat did not breathe spontaneously, artificial respiration was administered and the process was repeated until spontaneous respiration was returned.[1]

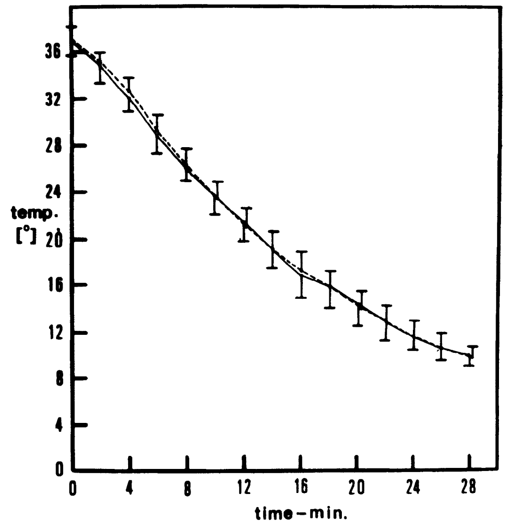

Figure 2
Cooling curves for respired and unrespired groups of rats (n = 20 each). *Dashed line* represents unrespired rats and *continuous line,* respired rats. Negative standard deviation of each measured point is shown for respired rats and positive for unrespired rats.

The effects of hypoxia during cooling have also been demonstrated by following the procedure outlined, omitting the artificial ventilation during cooling but not rewarming (unrespired rats).

Typical Results

The results described in this section are taken from Rogers (12), and some of the information has been published separately (4, 11, 13, 14). Rogers (12) found that about 90% of rats which had been artificially ventilated during cooling started breathing spontaneously when rewarmed and the heart restarted in all cases. Mean cooling curves and changes in heart rate and P-R interval with rectal temperature in respired and unrespired rats are shown in Figs. 2, 3, and 4, respectively. A typical set of ECG traces obtained during cooling in a respired rat is shown in Fig. 5.

The serious consequences of hypoxia even during hypothermia are clear from comparison of the results obtained with unrespired rats with those for respired rats. Rogers (12) found that less than 10% of animals cooled in this way started breathing spontaneously during rewarming. In respired rats carotid arterial blood pressure dropped simultaneously with cardiac arrest; in unrespired rats cardiac arrest occurred about 30 s after the collapse of blood pressure. Although the heart restarted, further beating was erratic and there was no blood circulation. This implied that hypoxia and hypothermia led to a massive vasodilation resulting

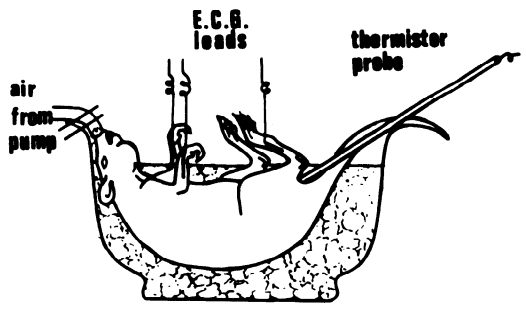

Figure 1
Technique used in cooling anesthetized rats.

[1] In the UK the use of living animals to demonstrate known facts to students is restricted to Home Office license holders with a C certificate and the demonostration must be done wholly under anesthetic. Successful resuscitation experiments for class demonostration have thus always been terminated as soon as regular spontaneous respiration occurred, but in research experiments animals have been revived to full consciousness and apparent normality.

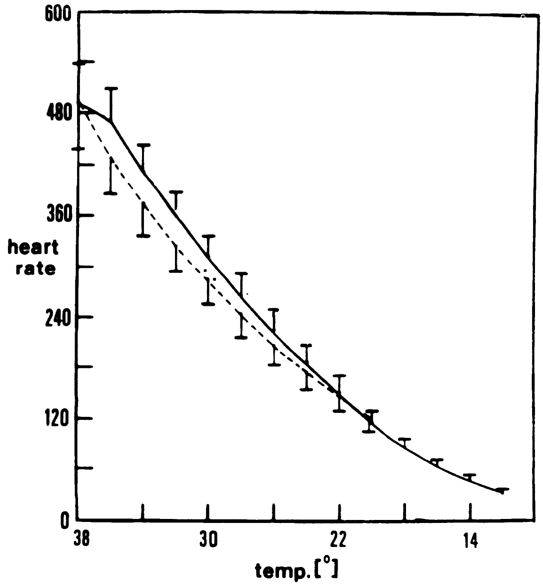

Figure 3
Heart rate-temperature relationship for unrespired (*broken line*) and respired (*continous line*) groups of rats (n = 20 each). Negative standard deviation of measured values is shown for unrespired rats and positive for respired.

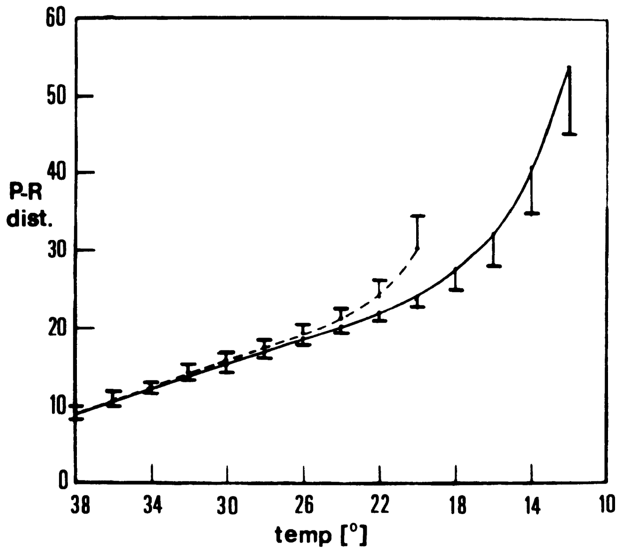

Figure 4
Relationship between P-R distance (arbitrary units) and temperature for unrespired (*broken line*) and respired (*continuous line*) groups of rats (n = 10 each). Positive and negative standard deviations are shown for unrespired and respired groups, respectively.

finally in cardiac arrest. On rewarming, the heart often did not restart; even if it did, it was unable to circulate the blood because of the vasodilation, and after a few beats there was no cardiac output even though QRS complexes were often recorded for up to 10 more min. Abdominal pumping during rewarming increased the proportion of animals in which spontaneous respiration occurred. Centripetal injections of Eagle's balanced salt solution followed by abdominal pumping allowed 70-90% of the cooled unrespired rats to recover (14). Figure 6 shows a typical series of ECG traces obtained during cooling in an unrespired rat. In general, during cooling the cardiac responses of unrespired rats were similar to those of respired rats down to about 20°C, when the hearts of the former stopped and resumed

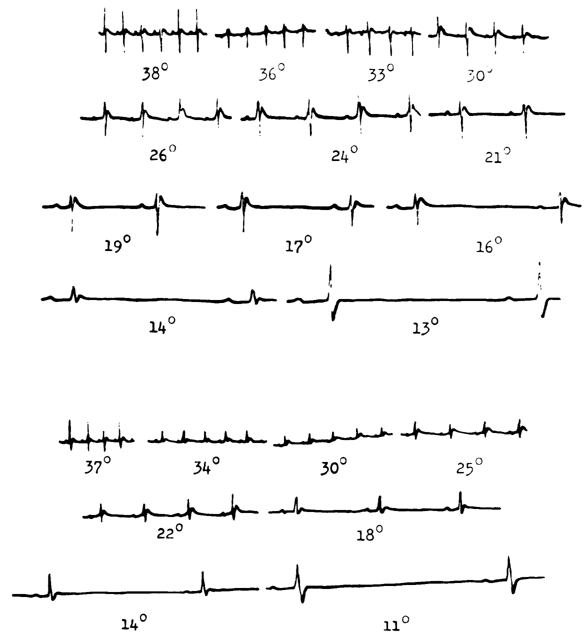

Figure 5
Typical electrocardiograms obtained during cooling in respired rats.

20-40 s later at an irregular rate. Following the temporary arrest in the unrespired rat, there was complete heart block and the atria were finally arrested before the ventricles.

Resuscitation of respired rats is uniformly successful using various available strains. Resuscitation of unrespired rats requires abdominal pumping and is only possible if the heart restarts.

Discussion[2]

One of the prime experimental principles that can be illustrated from this work is the need for properly controlled experiments in which all possible variables are considered. This is well illustrated in the historical review by the finding of Bigelow et al. (3) that deep body cooling in dogs reduces O_2 consumption. This observation may be undervalued when taken out of historical context, since the idea that reduced body temperature lowers metabolic requirements and thus minimizes the risk of hypoxic damage during interruption to the cerebral circulation is widely known and understood today even among nonbiologists. With the benefit of hindsight this and similar observations were clearly the basis for the therapeutic uses of hypothermia.

The demonstration allows several possible student preconceptions to be challenged. The most obvious is the characterization and determination of death. Most students consider the animals to be dead at the end of the cooling process, since respiration, heartbeat, and electroencephalogram activity have stopped (we have not measured the last in class demonstrations but have assumed its absence). The distinction between death and suspended animation even in nonhibernating mammals is apparent. The fact that the respired animals recover while the unrespired rats do not allows discussion of the possible differences between them. Hypoxia is assumed

[2]For suggested further reading, see Refs. 15-19.

to be the key factor in reducing the survival of the unrespired rats, but another possibility is that hypocapnia associated with changes in pH may be having a protective effect in the respired rats.

There is also an interesting paradox in that ventilation (prevention of hypoxia and hypercapnia) during cooling increases the chances of resuscitation, and yet in the first successful resuscitation of adult nonhibernating mammals from cardiac arrest reported by Andjus and Smith (1), a state of hypercapnia, hypoxia, and hypothermia was induced prior to immersion in an ice bath.

The relationship of these observations to accidental hypothermia in humans may also be significant. Clearly the finding that ventilation during cooling aids resuscitation is of limited practical value, but the fact that unrespired rats can be resuscitated (14) challenges our assumptions on the time at which death occurs. In addition, it offers the possibility of similar resuscitation after accidental cooling to cardiac arrest in people. This was strikingly illustrated in the case reported by Pickering et al. (9), where a 20-year-old girl was successfully resuscitated following accidental hypothermia down to 26.4°C and prolonged hypothermic cardiac arrest.

The ECG recording obtained from the unrespired rats during cooling (see Fig. 6) and from those in which the heart temporarily restarted on rewarming demonstrates heart block in an experimental situation. The observation that a QRS complex occurs in the absence of cardiac output illustrates the limitations of ECG measurements. The ECG is a record of electrical activity within the heart, and any conclusions about mechanical events are extrapolation, though usually with sound theoretical and empirical foundation. In fact, when the chest cavity is opened in unrespired animals with temporarily restarted hearts, it is possible to record QRS complexes in the absence of any apparent heartbeat, i.e., dissociation between excitation and contraction. In the rat, both respiration and then the heart stop at body temperatures above 15°C. Although body temperature will vary from species to species and even between individuals of the same species, a similar cardiac arrest at relatively high temperatures occurs in other nonhibernating homeotherms. This obviously limits the length of time that nonhibernators, including humans, can survive at body temperatures below the point of cardiac arrest. In hibernating mammals, however, body temperature falls to 4-7°C during the hibernation period; body temperature is maintained at this level for long periods of time, and yet respiration and heartbeat are maintained (even though at very slow rates). When the hearts of hibernators and nonhiberators were studied in vitro, it was found that hibernators' hearts continued to beat at lower temperatures than those of nonhibernators (7). An understanding of how respiratory and cardiac function are maintained in hibernators at low temperatures may enable a state of prolonged suspended animation of artificial hibernation to be produced safely in nonhibernators and perhaps even humans.

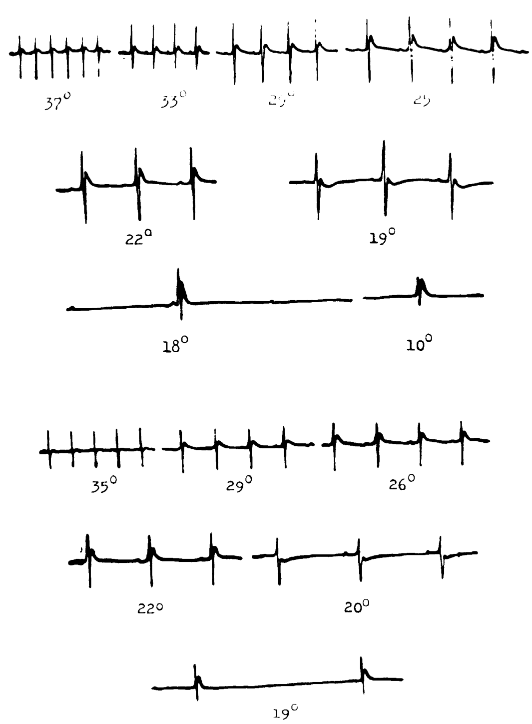

Figure 6
Typical electrocardiograms obtained during cooling in unrespired rats.

Another interesting topic for discussion that arises from this work concerns the optimal pH in the hypothermic animal. The generally accepted normal range for normothermic arterial blood pH is 7.35–7.45, and homeostatic mechanisms operate to maintain this range. This means that arterial blood is slightly on the alkaline side of neutrality, which for normothermia is pH 6.8 (pH 7, which one usually thinks of as being neutral is the neutral value at a temperature of 25°C). Since the pH of a solution is temperature dependent, two questions immediately arise with hypothermic blood. First, at what temperature should the pH be measured? By convention blood pH is normally measured at 38°C, and therefore the value must be corrected to the temperature at withdrawal. The mean change of pH with temperature of water over the range 25-40°C is 0.0155/°C, similar to the in vitro value obtained for blood; these changes appear small, but it must be remembered that the pH scale is logarithmic. Given that the pH of blood will change if cooled in vitro, the second question is, should it change in vivo to parallel the changes in water and thus remain as alkaline at low temperatures as it is at 38°C, or alternatively, should it still be homeostatically maintained at pH 7.4 as it is at normothermia? The evidence is contradicatory. In cold-blooded vertebrates it seems that pH is regulated at varying body temperatures to parallel pH changes of water temperature (5, 10). Hibernating mammals, however, seem to maintain constant pH regardless of temperature (6). In both of these cases the control of pH is linked to regulation of respiration, but in the hypothermic nonhibernator respiration ceases below 20°C; perhaps, therefore, in these animals the optinum pH is the one that allows longest survival. Although the pH that allows longest survival in profoundly hypothermic nonhibernating mammals is unknown, it may be relevant to consider the changes in the O_2-hemoglobin dissociation curve that occur with cooling. At low body temperatures, the affinity of hemoglobin for O_2 increases, and this would tend to reduce O_2 availablity to the tissues; a similar tendency occurs with increasing alkalinity.

Possible Extension of the Demonstration

The demonstration as described has been designed to best serve the needs of students as well as considering the limitations of time and facilities. There are a number of ways in which the demonstration could be extended for different circumstances; it would be possible to cannulate the carotid artery of the rats and thus to monitor blood pressure, to remove blood samples for pH and gas analysis during the experiment, and even perhaps to monitor an electroencephalogram. Also, pH can be measured at ambient temperatures that are comparable to body temperatures, thus eliminating correction factors (8).

It would also be possible to further assess whether the collapse of blood pressure during cooling in unrespired rats can be prevented with vasoactive substances and if so, whether this improves the chances of resuscitation.

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A Pen-Vibrator Adapter to Increase the Sensitivity of an Ink-Writing Kymograph

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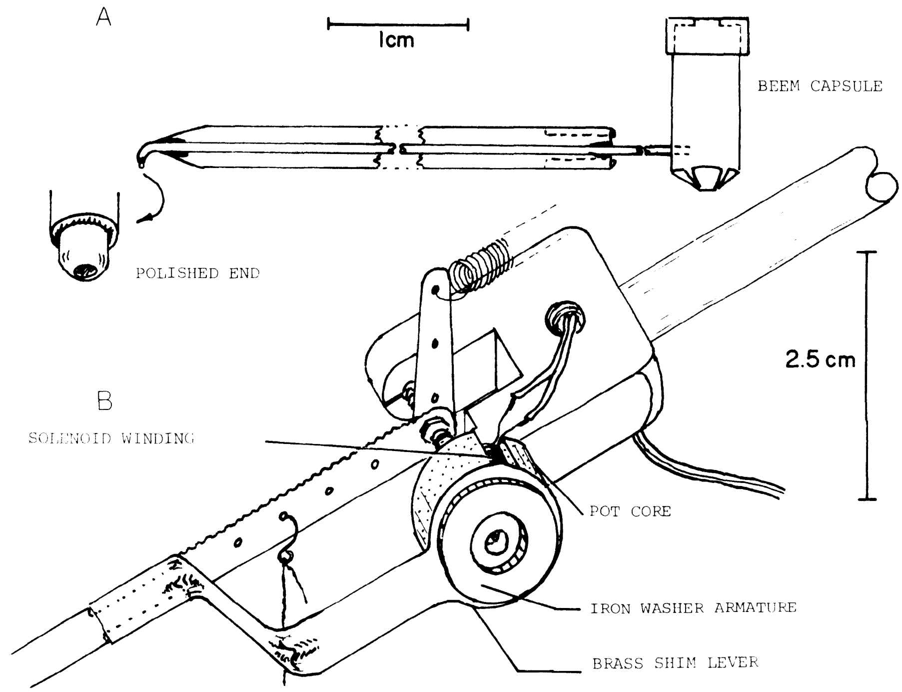
Recent years have seen a gradual displacement of the direct-writing kymograph and lever system in favor of electronic polygraphs and their associated transducers. This is partly because they are "more modern," and hence indicate progressive teaching methods, and partly because of well-justified frustration with smoked drums and messy and inefficient kymograph inking systems. Nevertheless, for freshman courses, the kymograph offers unparalleled simplicity of operation. Its use prevents the considerable complexities of electronic transducers and their associated amplifiers and controls, distracting the student from the object of the laboratory exercise. Needless to say, this does not only apply to freshman courses.

When it was acceptable to use smoked paper and styli, the sensitivity of the kymograph for smooth muscle work often rivaled that of present electronic systems, and in addition the equipment was almost immune from the effects of extraneous vibration. However, ink-writing systems are far more aesthetically acceptable; attempts to use ink with kymographs, while resulting in clearer and more readily copied traces, have led to a further decline in their use. This is because a new problem was introduced: the capillary attraction between the pen and the paper, amplified by the lever, drastically reduced the sensitivity of the system. Attempts have been made to overcome this problem, such as the use of gimbaled levers, electrosensitive paper, and so on, but these do not appear to have been particularly successful.

The approach outlined here, using a coaxial vibrator built into the lever system, has completely overcome these limitations, resulting in traces of equal sensitivity to those produced using a smoked drum and at the same time retaining the marvellous simplicity of operation of the direct-writing kymograph. Essentially, the device consists of a low-voltage AC-energized solenoid mounted coaxially with the axis of the pen-lever pivot. An iron washer, which acts as an armature, is connected to the pen-lever by a rigid arm constructed out of shim brass; movement of the armature toward the solenoid results in the pen tip flexing off the paper, thereby breaking the capillary adhesion between pen tip and paper. No rotational force is developed, so that the vibration is not transmitted to the preparation.

Figure 1



A: Pen and ink reservoir. In the illustration, the pen tip is shown twisted down by 90°, whereas in fact it lies perpendicular to the pen web. *B*: Vibrator adapter mounted on the pivot assemble of a standard isotonic lever (in this case Palmer Instr.). The iron washer armature is soldered onto the key-shaped brass shim bracket. The corners of the bracket are folded slightly, and a small fillet of solder is applied to the corners to increase rigidity. The solenoid assembly is cemented onto the lever yoke in such a way that the central hole in the half-pot core surrounds the pivot screw. The leads to the transform should be anchored as that they cannot be accidentally removed. (Scale 2.5 cm.)

Constructional details are given in Fig. 1. The actual magnetic material from which the pot core is made is not critical for this purpose. [A 14-mm-diameter 3B7 pot core (Philips-Norelco) was used in our version.] The solenoid coil must be wound as a "pancake" on a form consisting of a suitably sized rod (e.g., of nylon) fitted with removable facing washers between which the insulated coil wire (approx 40 gauge) is wound. Before removal, the coil is coated with diluted polyvinyl acetate (white) glue and baked dry. The coil must fit snugly into the cavity of the pot core and must not protrude beyond the face. The coil must be cemented in place inside the pot core, otherwise it will tend to move as well. The gap between the steel washer and the face of the solenoid pot core should be about 0.25 mm for optimum operation.

The pen used consists of a 14-cm length of 22-gauge thin-walled hypodermic tubing connected to an ink reservoir situated near the rotational axis to allow ready filling of the pen while the kymograph is in use. The ink reservoir is constructed from a BEEM electron-microscopy embedding capsule that has a hole punched in the cap to allow refilling. A short length of 27-gauge hypodermic tubing is used as the pen tip. It is soldered in place, and the writing tip is rounded and polished with an Arkansas stone.

The transformer powering the solenoid can be mounted within the kymograph body (and in the case of kymographs that have intergral stimulators, it can be omitted and the solenoid energized from the low-voltage AC output of the power transformer through a suitable current-limiting resistance). The low-voltage side of the transformer can be connected to two banana jacks mounted on the kymograph body to allow ready connection of the pen unit. For a coil resistance of 8-10 Ω an excitation voltage of 4 V AC was found to be adequate.

In operation the pen pressure and the distance between the iron washer and the pot core should be adjusted so that the pen can be seen to be just tapping, at mains frequency, on the surface of the paper (see Fig. 2). This vibration achieves two effects. First it continually breaks the surface tension between the pen and paper, thereby allowing the preparation to move the pen to the new position. In addition, the vibrator "loosens" the bearings of the lever system, thus further increasing the sensitivity of the lever arm.

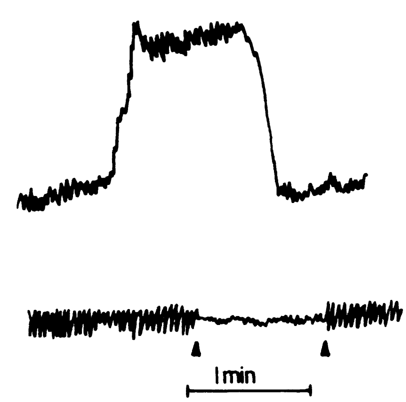


Figure 2

Two traces made using the vibrator and an isotonic writing-lever system. *Upper trace* is the response of rat intestine to an addition of 10^{-6} M norepinephrine to the organ bath. *Lower trace* illustrates the effect of tip adhesion to the paper. Between the two arrows the vibration was turned off (with the pen tip just touching the paper). As is evident, there is an approximately 10-fold decrease in the size of the trace due to tip capillary adhesion. (Paper speed 2.5 cm/min.)

Physiology of the Mesenteric Circulation

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The purpose of this educational exercise is to describe some of the salient features of the physiology of the mesenteric circulation, focusing particularly on the regulation of its blood flow. The reader is referred to several recent reviews of the subject that are more extensively referenced with original sources (5, 6, 10, 11). Although the terms "mesenteric circulation" and "splanchnic circulation" are sometimes used synonymously, they are distinct: the mesenteric circulation refers specifically to the vasculature of the intestines, whereas the splanchnic circulation provides blood flow to the entire abdominal portion of the digestive system. In a 70-kg resting adult human male in good health, the major inflow vessel of the mesenteric circulation, the superior mesenteric artery, delivers about 12% of the cardiac output and is therefore unsurpassed in size among all branches of the entire aorta. This vessel supplies the entire small intestine, the proximal half of the colon, and part of the pancreas.

After blood has been distributed by the superior mesenteric artery to the small intestine, it accumulates in the mesenteric veins en route to the great portal vein, which transports the blood to the liver. Since the arterial supply of the liver is provided by the hepatic artery, a branch of another splanchnic vessel (celiac artery), the mesenteric circulation is in parallel with the hepatic artery and in series with the portal vein (Fig. 1). Within the walls of the small intestine the mesenteric circulation is also organized in a manner featuring both in-series and in-parallel relationships. Thus the circulation of the mucosa is in an in-series relationship with the submucosal circulation from which the mucosal vessels arise and is also in an in-parallel relationship with the microcirculation of the muscular layer of the wall. These kinds of relationships permit internal redistribution of blood flow within the organ without altering total blood flow.

The mesenteric microcirculation has three major functional vascular elements (Fig. 2) (1,3). The first category of vessels consists of the microscopic arteries and the arterioles. These vessels have relatively thick walls composed mostly of vascular smooth muscle and are reactive to various stimuli, especially the catecholamines (13). The largest portion of the resistance to blood flow in the entire mesenteric circulation from its origin at the aorta to the portal vein occurs as the blood flows through the microscopic arteries and arterioles; hence they are termed the "resistance vessels" (3). For a drug to increase or decrease blood flow markedly in the mesenteric circulation, the agent must act on the walls of the resistance vessels.

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From the arteriole the blood flows into the capillaries located adjacent to the parenchymal cells. Nearly all transport of materials between the blood and the cells takes place at the level of the capillary component of the circulation. Thus O_2, nutrients, and fluids move from the blood into the cells, whereas CO_2, heat, metabolites, and fluids move in the opposite direction. Hence the capillary units have been termed the "exchange vessels" (3). The degree of exchange will depend on the population density of perfused capillaries because only a frac-

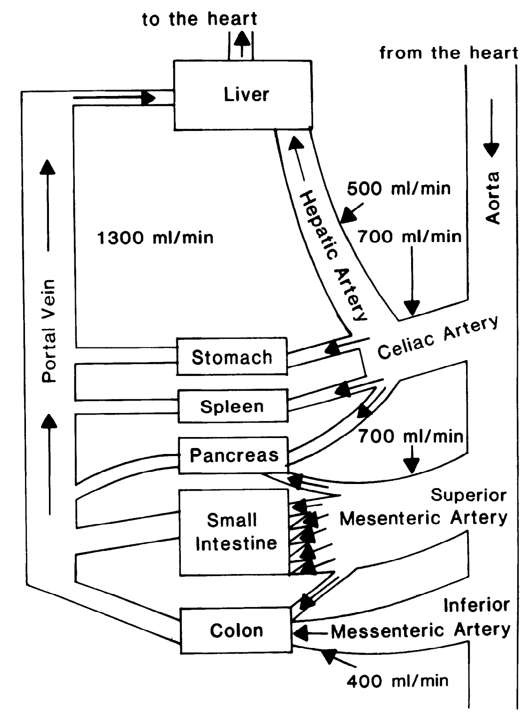


Figure 1
Diagram of splanchnic organs and their blood supply.

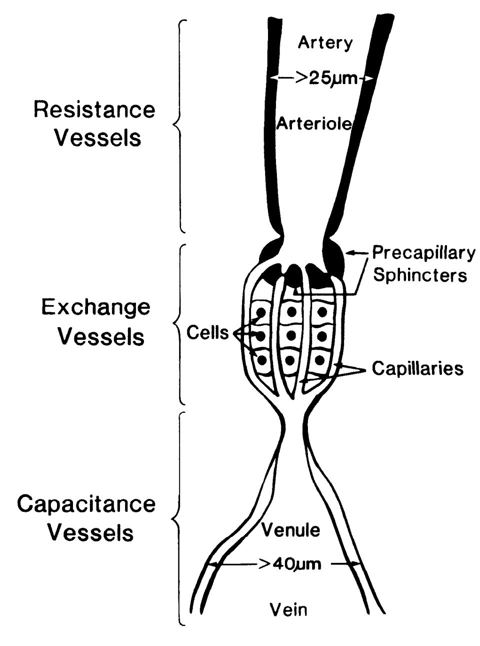


Figure 2
Mesenteric microcirculation. Dimensions represent vessel width below which vessel is termed an arteriole (25µm), as opposed to a microscopic artery, or venule (40µm), as opposed to a microscopic vein.

tion of all capillaries is open to the flow of blood at any moment in time (4). The structure regulating blood flow through the individual capillary is a smooth muscle thickening around the origin of the microvessel. This thickening has been termed the "precapillary sphincter." When this sphincter contracts it closes off the capillary to the flow of blood and thereby reduces exchange between blood in that capillary and adjacent cells. When the sphincter relaxes from the contracted state, the capillary is again perfused with blood, thereby accelerating the exchange. The open capillaries at any moment in time are also referred to as the "nutrient circulation."

The third functionally important component of the mesenteric microcirculation is the microscopic veins that drain the blood from the capillaries. The thin walls of these low-pressure vessels also contain smooth muscle and are responsive to extrinsic stimuli. When their walls contract, blood is expressed centrally from the veins. Since 80% of the total blood in the mesenteric circulation is stored in these microscopic veins, contraction of their walls propels previously stored blood back to the heart, as occurs at the outset of exercise. Because of this storage function the venules have been referred to as "capacitance vessels" (3).

The major categories of regulators of mesenteric blood flow include central cardiovascular control, autonomic neuroregulators, neurohumoral substances, local metabolic factors, and intrinsic vascular properties (Fig. 3). The central cardiovascular regulators are those forces and their relationships that we understand under the rubrics of cardiac output, systemic arterial blood pressure, venous return, and blood volume. Any marked change in these central functions will be reflected by a change in mesenteric blood flow. Thus, for example, if an individual sustains a severe hemorrhage, with decreases in blood volume, venous return to the heart, cardiac output, and arterial pressure, it is hardly surprising that there will also be a decrease in mesenteric blood flow.

The autonomic neuroregulators consist of the sympathetic and parasympathetic nervous systems. The

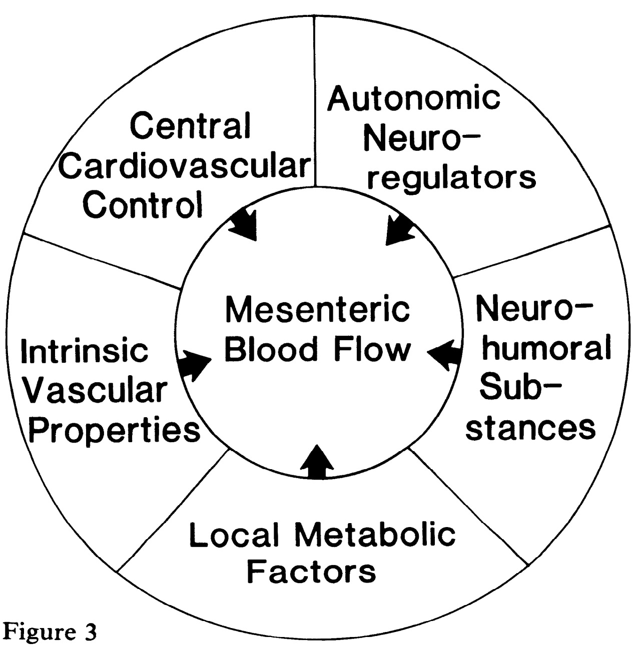


Figure 3
Regulators of mesenteric blood flow.

sympathet postganglionic vasomotor fibers are distributed along with the branches of the superior mesenteric artery, and the nerves terminate on the vascular smooth muscle of the microscopic arteries, arterioles, venules, and microscopic veins, where they release predominantly norepinephrine.

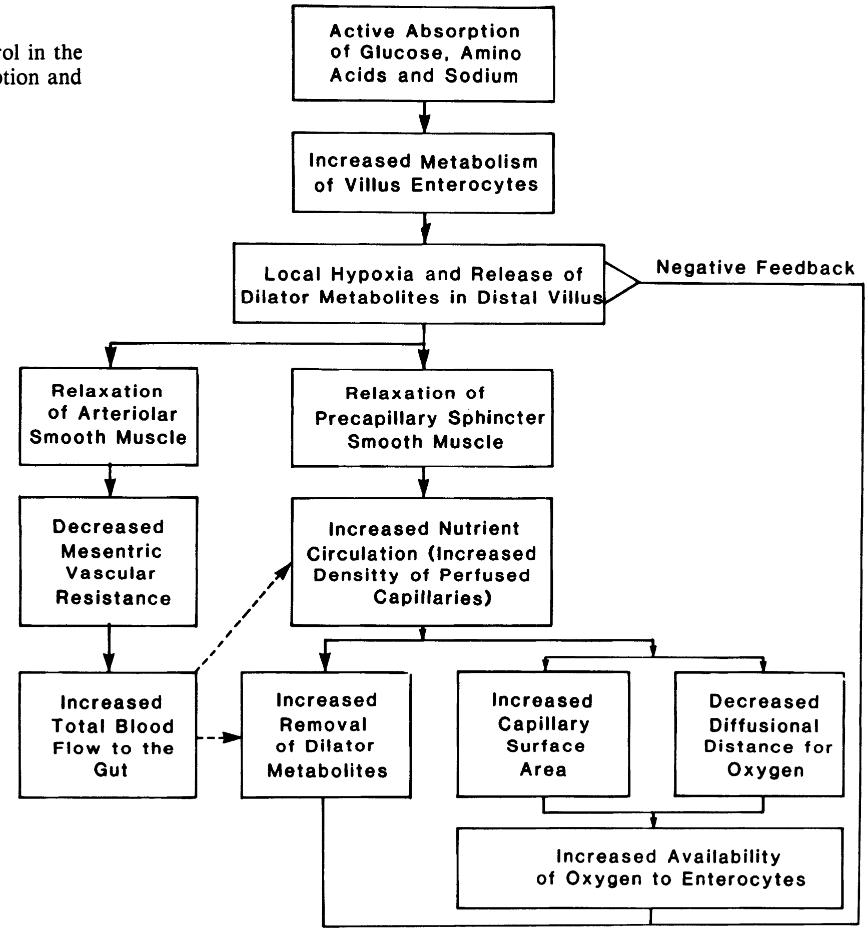
The results of sympathetic stimulation are a transient decline in blood flow through the mesenteric circulation and a mobilization of blood from the capacitance vessels. The parasympathetic nervous system distributes its postganglionic fibers to this region, but these nerves are not directly vasomotor in character; rather they release acetylcholine near parenchymal cells, resulting in the activation of visceral muscle and secretory units. The result is an increase in motility and secretion that may contribute modestly to an increase in blood flow. Acetylcholine is a vasodilator agent when infused directly into the mesenteric circulation, although it is unlikely that this neurotransmitter actually reaches the vascular smooth muscle of the gut as a result of nerve stimulation.

There are two groups of neurohumoral substances that may have effects on mesenteric blood flow depending on the conditions which have increased the concentrations of these blood-borne substances within the mesenteric circulation. The first group includes the classical vasoconstrictor agents of the body. With stresses such as severe exercise, the plasma concentrations of catecholamines will rise and evoke an increase in vascular resistance. In disease states, such as circulatory shock or congestive cardiac failure, the circulating levels of angiotensin II and vasopressin will increase, again provoking vasoconstriction with a reduction in mesenteric blood flow. The second group of blood-borne materials is the gastrointestinal hormones that are released under more physiological conditions. These peptides have no effect on the smooth muscle of resistance vessels in their usual concentrations, such as those found following the ingestion of a meal. However, these humoral agents do stimulate an increase in motility and exocrine secretion, thereby increasing metabolic need for blood flow to the gut.

Another category of regulators consists of local metabolic factors that are part of the changing metabolic environment near vascular smooth muscle which occurs when the oxidative metabolism of parenchymal cells undergoes an increase. The changes include a decrease in the P_{O_2} as the cells consume more O_2, an increase in the production of metabolites such as CO_2, and increased production of paracrine substances such as prostaglandins, adenosine, histamine, and bradykinin. These changes in the metabolic environment cause relaxation of vascular smooth muscle with a reduction in vascular resistance and an increase in mesenteric blood flow. Generally the effect is more marked on exchange parameters that are governed by relaxation of precapillary sphincters than on parameters that reflect relaxation of the smooth muscle of the resistance vessels; thus the increases in O_2 consumption and extraction proportionately exceed the increase in blood flow, and the decrease in mesenteric vascular resistance is usually small (7).

The sequence of events that take place during the stimulation of metabolism in the gut is represented in Fig. 4. When the intestinal lumen contains a solution containing sodium and glucose or sodium and amino

Figure 4
Metabolic feedback control in the gut: a coupling of absorption and blood flow.



acids, active cotransport of these solutes from the lumen is initiated. This functional activation is paralleled by increased metabolism of the mature enterocytes in the distal villus. The result is an increase in the consumption of O_2 and the release of dilator metabolites from the activated cells. These changes in the metabolic environment relax the precapillary sphincters, thereby causing an increase in the density of perfused capillaries. At the same time there is some relaxation of arteriolar smooth muscle that decreases vascular resistance and leads to an increase in total blood flow through the gut. With recruitment of more capillaries receiving more blood flow, there is an increased removal of a the accumulated metabolites. Because of the increased surface area available for diffusion of O_2 and the shorter diffusional distance, more O_2 becomes available for the enterocytes. As a result a negative feedback come into play, which restores the tone of the sphincteric muscle and decreases the perfusion of capillaries. This cycle of ebb and flow through the nutrient circulation is reenacted repeatedly so long as the enterocytes are actively absorbing solutes and placing an increased metabolic demand on the circulation for continued support.

The final category of regulators of the mesenteric circulation the intrinsic vascular properties of this circulation, some of which are fairly unique. One of these characteristics is called "escape" and can be seen during continuous sympathetic stimulation, infusion of catecholamines, or angiotensin II (3, 9). When continuous constrictor stimulation is started, there is a sharp initial decrease in blood flow, but this decrease is transient and the flow returns considerably toward the control value despite continuous constrictor input. Increasing the degree of continuous constrictor influence again causes a transient but smaller decrease in flow, which again subsides despite the continuous presence of the constrictor influence. The mechanism underlying escape is uncertain, although there is evidence for the release of a dilator intermediary, such as histamine, in response to the decrease in blood flow.

The mesenteric circulation exhibits autoregulation of blood flow in the face of changes in arterial pressure. Autoregulation in the gut is less pronounced than in either the kidney or brain. Within the wall of the small intestine there are both autoregulatory vessels and vessels that display a passive response to changes in intravascular pressure. In the muscularis, vessels that exhibit the passive response are those in which some of the kinetic energy represented by the increase in pressure is expended in overcoming the compliance of the walls of the vessel. As a result there is stretch of the vascular wall with an increase in the internal cross-sectional area of the vessel and a decrease in vascular resistance as the pressure rises. The result is that the increased driving head of pressure meets with a lower resistance and the increase in blood flow is proportionately greater than the increase in blood pressure. By contrast, *in the* autoregulating blood vessels of the mucosa the increase om blood pressure is met with by active contraction of vascular smooth muscle and a reduction in cross-sectional area. This causes an increase in vascular resistance. Thus the increase in the driving head of pressure results in an increase in blood flow that is proportionately less than the increase in pressure. Autoregulation guarantees better control of blood flow, which is conductive to the maintenance of a steady tissue O_2 uptake. Interestingly, autoregulation of intestinal blood flow is enhanced by feeding.

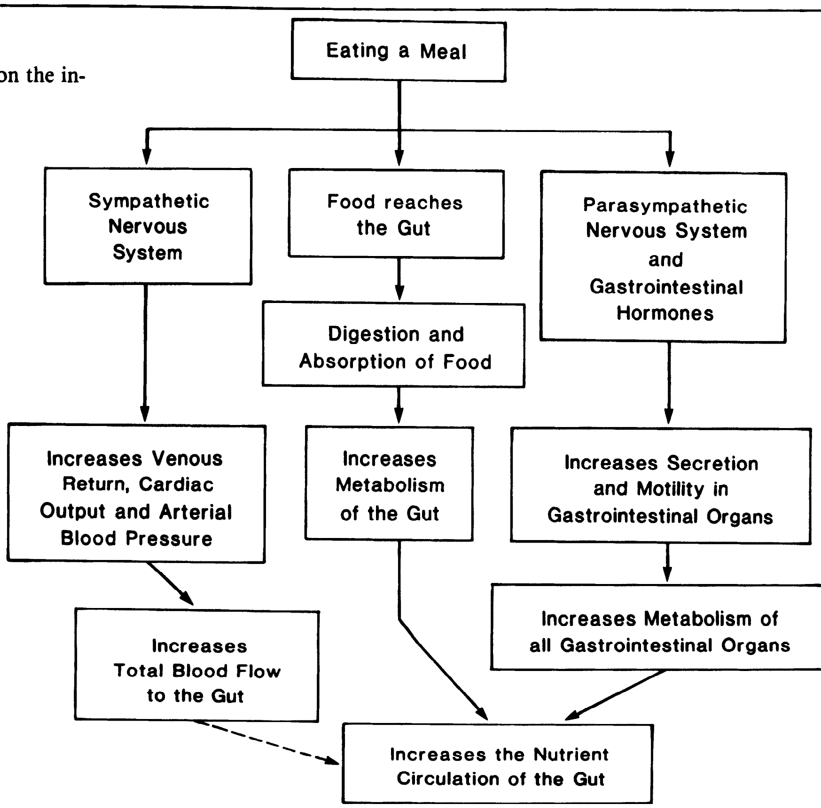
Two major theories have been summoned to explain autoregulatory phenomena in the circulation. One, termed the "myogenic theory," assumes that the increase in transmural pressure across the wall of the artery (which occurs when the blood pressure is transiently raised) evokes an active contractile response from vascular smooth muscle of autoregulating circulations. The second, "metabolic theory" assumes that decreased tissue perfusion which occurs when there is a transient fall in blood flow evokes a feedback signal to relax precapillary vascular smooth muscle, thereby overcoming the vascular insufficiency. Both proposed mechanisms appear to operate. The identity of the chemical mediators that contract or relax vascular smooth muscle in autoregulation is unknown, although some evidence points to histamine.

The villi are metabolically the most active portion of the entire intestinal wall. These fingerlike structures project into the lumen of the gut and are responsible for the active cotransport of sodium and nutrients. The configuration of the villus and its microcirculation is conducive to countercurrent exchange (3, 11). Depending on the species of animal, the organization of the villus circulation consists of one or more inflow arterioles, which give off capillaries, usually in a fountainlike distribution at the tip of the villus. The capillaries direct blood flow away from the tip toward the base of the villus and empty into one or more venules, which drain the blood away. The arteriole is situated within 20 μm of capillaries, and the venules and the directions of blood flow in these vessels are countercurrent. Therefore, it is possible for a dissolved substance that is lipid soluble and is present in a higher concentration in the arteriole than in the capillaries or venule to be shunted from the areteriole to the other vessels. O_2 is one such substance. Some of the physically dissolved O_2 in the plasma can diffuse from the arteriole to the venule at the base of the villus. As a result of the Po_2 is about 25 mmHg greater at the base than at the tip of the villus (2). This O_2 gradient may contribute to the rapid turnover of epithelial cells in the mucosa. These cells arise in the crypts at the base and migrate over the surface of the villus to the tip, where they die and are sloughed into the lumen. This process of birth to demise of epithelial cells has a half-life of 24 h. When the flow of blood through the villi is slowed by a pathological condition, such as nonocclusive intestinal ischemia, there is amplification of the countercurrent exchanger for O_2 and the first area to suffer necrosis during persistent ischemia is the tip of the villus.

Let us consider several integrating experiences that may confront the mesenteric circulation. The first of these is a frequent occurrence and is physiological, namely the eating of a meal (Fig. 5). The events surrounding eating are stimulating to various areas of the brain and initiate sympathetic nervous responses that constrict the capacitance vessels of the gut and enhance venous return, cardiac output, and arterial pressure. These result in an increase in total blood flow to the gut. Simultaneously, parasympathetic nervous stimulation and the release of gastrointestinal hormones increase exocrine secretion and motility in the gut. This enhanced functional activity leads to increased metabolism of the intestinal parenchyma, which requires an increase in the nutrient circulation for its support. Following ingestion, the food reaches the gut, where the processes of digestion and absorption occur. Again these increases in intestinal function increase metabolism of the enterocytes and also result in augmentation of the nutrient circulation.

Another integrating event, although pathological, is the effect of acute hemorrhage on the mesenteric circulation. If the degree of hemorrhage is not overwhelm-

Figure 5
Effects of eating a meal on the intestinal circulation.



ing, there will be compensations involving abdominal viscera, among other organs, which permit restoration of hemodynamic parameters to normal despite the oligemic insult. With acute blood loss there is a decrease in the circulating blood volume and a decline in the venous return to the heart. The result is a fall in both cardiac output and arterial blood pressure. This signals the activation of a variety of short-term and long-term compensatory mechanisms. Among the long-term processes are shifts of fluid between bodily compartments with fluid moving from intracellular to extracellular spaces and fluid moving from the interstitium into the vascular compartment. The kidney will reabsorb sodium more avidly to increase the return of fluid to the circulation. The shorterterm events include sympathetic nervous stimulation and release of constrictor agents into the circulation, resulting in venoconstriction with mobilization of stored blood from capacitance vessels in the intestine, liver, spleen, and gut and a subsequent increase in the venous return to the heart. As the heart rate and force of contraction are stimulated by the sympathetic nervous system and as the flow of blood from the veins grows, there is an increase in the cardiac output. Sympathetic constriction also acts on the resistance vessels of the splanchnic organs and elsewhere to restore systemic arterial pressure. If the degree of hemorrhage has not been great, these compensatory mechanisms operate within a matter of minutes to restore the arterial pressure and cardiac output to the prehemorrhage levels.

The third example of an integrating experience in the regulation of mesenteric blood flow involves the response to pharmacological agents that either increase or decrease mesenteric blood flow. There are a numerous dilator and constrictor chemicals that have been synthesized and utilized in this circulation, either experimentally or therapeutically, to manipulate blood flow.

In addition, there are numerous naturally occurring substances that influence blood flow to the gut (Table 1). One of the more thoroughly studied intestinal dilator agents is histamine (8). This amine has two types of vascular receptors, namely the H_1 and the H_2, each of which will bind histamine. For each of these receptors chemists have synthesized selective agonists and antagonists. These receptors mediate separate intestinal dilator responses to histamine, with the H_1 prompting a transient increase in mesenteric blood flow and the H_2 mediating a less intense but longer lasting hyperemia.

Prostaglandins of the A, D, E, and I types are potent vasodilators in the gut (11). In particular, prostacyclin has a potency such that a dose of 10 nanagrams per kilogram-minute directly infused into the mesenteric circulation of a dog will increase blood flow significantly (7). Among synthetic vasodilator agents the calcium antagonist drugs are effective in the mesenteric circulation and have been found to interfere with both the slow inward diffusion of calcium into the smooth muscle cell and the intracellular release of calcium (12).

Constrictor agents that have been employed therapeutically to control gastrointestinal hemorrhage include vasopression, norepinephrine, and angiotensin II.

The existence of a multiplicity of regulatory mechanisms in the mesenteric circulation provides overlapping controls and restricts radical changes in tissue perfusion. This permits moment-to-moment stability in the circulation that favors a steady tissue economy. On the other hand, it is possible with appropriate physiological stimuli, such as eating or exercise, stress states, and drugs, to modify the flow of blood into the gut. We are likely to see the development of more powerful chemical and other approaches to the external manipulation of this blood flow for the benefit of patients suffering from ischemic diseases or hemorrhage.

Table 1
Drugs Affecting Mesenteric Blood Flow

Dilator Drugs	
Amines	Histamine, H_1-receptor agonists (2-methylhistamine), H_2-receptor agonists (dimaprit, impromidine)
Peptides	Glucagon, bradykinin
Prostaglandins	A, D, E, and I types
Nucleotides	Adenosine, cAMP, ATP
Cholinergics	Acetylcholine
β-Adrenergics	Isoproterenol
Calcium antagonists	Diltiazem, verapamil, nifedipine
Endorphins	Met-enkephalin
Constrictor Drugs	
Amines	5-Hydroxytryptamine (serotonin)
Peptides	Angiotensin II, vasopressin
Prostaglandins	$F_{2\alpha}$, tromboxanes
Prostaglandin synthesis inhibitors	Indomethacin
α-Adrenergics	Norepinephrine

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Historical Issues Concerning Animal Experimentation in the United States

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The use of animals for research and teaching has now become an issue of great concern in the United States. In contrast to the legislative systems in Britain, Scandinavia and many European countries, American scientists can pursue research projects with relative freedom. Recent activities in the United States may effect this practice and future animal experimentation may be subjected to restriction and control by legislation. Events leading to this possibility are similar in many ways to those in 19th century Britain prior to the passage of the Cruelty to Animals Act in 1876 (which licenses scientists, regulates experimentation and carries out inspections). Historically, it seemed that the immediate effect of the 1876 act was to decrease the number of scientists who could conduct experiments on live vertebrate animals in Great Britain and hence the number of experiments and animals. Yet, antivivisection activity in Britain did not decrease but continued toward its goal of abolishing all research with animals. By 1882, the medical scientific community established the Association for the Advancement of Medicine by Research which began to advise the Home Secretary on licensing scientists. This was a turning point for British science since large numbers of qualified investigators were licensed, the number of animal experiments increased, and experimental medicine and science in the United States soon became dominant. Thus, although the antivivisection movement in Britain did not ultimately halt animal research, it did raise the consciousness of scientists, the government, and the general public about the need for humane treatment of research animals and the limits to which those animals should be used.

Although the first Humane Society in the United States was established in 1866, it was not until the end of the 19th century when scientific disciplines were necessary for the education of physicians that protests against the use of animals for experimentation became organized. Activities by American animal protection groups have increased since that time and have now culminated in proposed legislation which if passed would not only restrict the use of animals for research but would also interfere with the kinds of research that could be conducted.

Legislation in Britain, Scandinavia and in many European Countries appears to be efficient and effective because of the relatively small number of research institutions and scientists in those countries. Is legislation in the United States feasible considering the extremely large number of scientists and research institutions? American scientists are facing three possibilities: mandatory regulation (legislation), self-regulation, or some combination of both. Self-regulation of animal experimentation appears to be the optimal choice. It would reflect the success of animal protection groups in raising the consciousness and concerns of scientists about the humane treatment of experimental animals: (1) reducing the numbers of animals used for experimentation, (2) unnecessary duplication of experiments, and (3) minimizing pain and distress. Although scientists are proceeding toward a program(s) of self-regulation, this approach will be based on the scientific method and will not satisfy completely the differences between scientific and animal protection groups. Scientists have become concerned with "the moral and ethical responsibility for the humane treatment of animals in experimentation" whereas animal protection groups are concerned with "the moral rights of animals not to be used as subjects for experiments." Nevertheless, we hope that the development of a program of self-regulation by scientists will achieve a balance between scientists and animal protectionists and that it will result in important and constructive interaction between the two groups.

Abstract reprinted from *Soc. Sci. Med.* 15F:13-17, 1981.

Legislation and Training for Licenses— A Discussion Meeting

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A meeting was held under the auspices of the Education and Information Sub-Committee of the Physiological Society, in Cambridge on 15th July, devoted to the subject of training those who have recently received a license to experiment on living animals. Ten years ago any student obtaining a B.Sc. degree in Physiology would probably expect to have received extensive training in experimental mammalian physiology. For a variety of reasons, this is no longer the case. However, in the course of their subsequent careers they may well be expected to participate in experiments on animals, and at such stage a formal course of training may not be available. It was therefore decided to hold a meeting to discuss ways in which training could be accomplished. It is possible that provision of such training courses could be the subject of legislation in the future, and time was devoted to animal experiments and the law.

The session was opened by the Chairman, Lord Adrian, who pointed out that despite five years of activity on the subject of legislation little had been achieved. Two private members' bills on the subject of animal experimentation had been presented to Parliament, the Fry Bill in the House of Commons and the Halsbury Bill in the House of Lords. The Government had reconstituted its advisory committee, and the Council of Europe was working on a Convention to protect experimental animals. A major theme in all these considerations was the problem of pain, definition of the limits of possible pain, and whether such limits should be introducted into legislation. Recognition of the need for defined training of licenses had also emerged from the debates.

The first speaker was Mr. J. L. Pascoe of University College, London, who gave "An introduction of experimentation on living animals in universities: physiology, ethics and the law." He felt that all new licensees should be prepared to answer a number of fundamental questions, the first being "Why do people in universities experiment on animals?" The answer should be first, in order to shed light on living processes and second, to solve practical problems, and while only the second appears immediately fruitful, the first is just as important and may bear fruit in the future in unpredictable ways. The second question is what are the ethical problems posed by animal experiments? Man had empathy with the other animals and so should try to avoid inflicting on them the 5Ds: discomfort, deprivation, damage, danger, and death. Unnecessary infliction of these is cruel. Cruelty is difficult to define and is often mixed up in our minds with guilt feelings, but it must be admitted that cruelty is an evil and makes the world a more dangerous place to live in. However, it is not necessarily more "ethical" to use tissue isolates than a whole animal. How many animals should be used in experiments? The number required to give results that will convince your scientific colleagues. How far should you be prepared to go in your experiment if pain is likely to be inflicted? A university education should remove constraints from the mind; so in considering this question gut reactions and preconceived ideas should be examined critically. Available knowledge and human experience should be used to predict the effect of the experiment on the animal and to devise ways to avoid pain. The project should be discussed with colleagues as well as with the Home Office Inspector. If they turn it down, the plan must be considered again to assess its scientific value and possible alternative methods. Breaking the law can have unpleasant consequences and should be avoided, but the law is ephemeral and only a longstop. The experimenter should be aiming to achieve both scientific excellence and high ethical standards based on reason.

We were left with one final question "How effectively should we defend ourselves?"

Mr. G. Morrissey then described how one major pharmaceutical company, ICI Pharmaceuticals, approached the question of initial training of licensees in industry. There were about 500 licensees throughout the company, varying from those working on advanced surgery to junior technicians, although at any one time not all would be actively involved in animal experimentation. The training program was devised after consultation at various levels within the company and with the Home Office and is attended by all graduates and technicians working in the pharmaceutical section. The program consists of courses at three levels, each course being run two or three times a year with an average of 10 people attending each course.

Course 1 (Appreciation) lasts one day and is intended for all people, including postgraduates and overseas workers, moving into the UK animal experimentation environment for the first time. It covers the following topics: the role of animals in the discovery and development of a drug including discussion of ethics and alternatives; regulatory influences, such as the Health and Safety at Work Act, 1972, and the Cruelty to Animals Act 1876; safety in biological laboratories; animal husbandry; and painless destruction of animals.

Course 2 lasts one day and is intended for those applying for or having recently received a license and certificate A and is comprised of the following topics: introduction to the 1876 Act; a written exercise on points of the Act; the inspectorial process; effects of drug administration; choice of species and routes of drug administration followed by a practical session on the handling of animals; and license alone work, including good surgical practices and an introduction to videotapes on the subject. It was not the aim of this course to teach techniques but to show basic skills in a consistent fashion.

Course 3 lasts two days and is intended for staff applying for or having recently received their first certificate B. The content is basic principles of anesthesia and choice of anesthetics; a practical demonstration of anesthetic procedures; general surgical techniques; and postoperative care and complications.

In addition to these courses, there was training in the individual laboratories, a program of specially prepared videotapes, and many attended day-release courses. In discussion of this paper, a Home Office Inspector said he considered *course 3* too short. Moreover, it was advisable that students attend all three courses before they apply for certificates.

After a break during which one of the video training films was run, Mr. D. R. Dewick of the Home Office spoke on the subject of "legislation in Britain and Europe." The present act governing animal experimentation, passed in 1876, was the result of a Royal Commission. Animal studies at that time were mainly for surgery. However, the public were alarmed by reports from abroad, especially France, where Magendie was said to substitute experiment for thought. A second Royal Commission sat from 1906 to 1912. The law was not changed, but a number of recommendations were made and subsequently implemented. In 1965 the Littlewood Committee acknowledged that the act had been generally successful, but that the provisions had not kept pace with scientific advances. Then followed the Fry and the Halsbury Bills. It is now generally accepted that there are deficiencies in the 1876 Act and that new legislation is necessary. The possibility of new legislation is made all the more certain because of the fact that as a result of pressures in the 1970's from the animal welfare lobby, animals entered politics and promises of reform were included in the party manifestos.

There will be no further attempts at legislation until the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes is ratified. Among the objectives of the Draft Convention are provisions of basic standards of husbandry, the need to consider alternatives, the need for anesthetics, consideration of the fate of the animal at the end of the experiment, provision of facilities for registration, and the provision of statistics. If the convention can be final in November, it will be remitted to the Committee of Ministers of the Council of Europe in early 1983. At present the nature of future legislation in the United Kingdom is a matter of speculation, but Home Office opinion is that the principles of the Cruelty to Animals Act are sound and should not be radically altered.

Finally Mr. James Noble gave a short discourse on the work of the Research Defense Society (RDS), a Society of which the aims are implicit in its title. It now has two types of membership, group membership through learned societies etc. and ordinary membership. The society is concentrating on two main aspects at present. The first is security of buildings housing animals and in which animal experiments are carried out. If such buildings are broken into by animals' rights groups, then the RDS would support legal action against such groups. The second important aspect is publicity. There is increasing publicity against the use of animals, and the RDS is attempting to present the other side of the case.

A brief but lively discussion followed each of the papers. Unfortunately the final discussion of the day centered on hypothetical problems arising from possible future legislation, leaving no time to discuss the need for training of new licensees, or of how this training would be best accomplished. However, since the meeting generated considerable interest, it is hoped it will stimulate further such gatherings where these problems may be discussed.

The Elegant Record

Dedicated to Hebbel E. Hoff

Étienne Jules Marey said that the graphic record constitutes a universal means of communication among physiologists and is free from the barriers of language. In this role it has served the needs of physiologists and others in science admirably for more than a century, documenting phenomena and usually providing explanations for them. The graphic record is also an excellent teaching tool, which can be used to instruct students in learning how to think and to solve problems. Hebbel Hoff, retired Benjamin Hambelton Professor of Physiology at Baylor Medical College, introduced the term "the elegant record" and used this tool effectively in teaching for the 22 years the author had the honor of being his student, then colleague.

What is an "elegant record" and why is it useful in teaching? This short report aims to provide answers to these questions with a view of encouraging teachers of physiology to use it as a teaching tool.

Like a work of art, the elegant record provides a message, being both subtle yet commanding. It is usually well framed by the total picture. To illustrate the point, examine Fig. 1, which is a simple record of the electrocardiogram (ECG) and blood pressure of the dog. A short period of vagal stimulation provided slowing of the heart rate. On the first glance, there is nothing remarkable in the record; look again. The ECG is clearly labeled and a calibration has been provided, as is the case for the blood pressure tracing. Time marks calibrate the *x*-axis of the record. In all elegant records there are calibrations for the *y*-axes of each tracing.

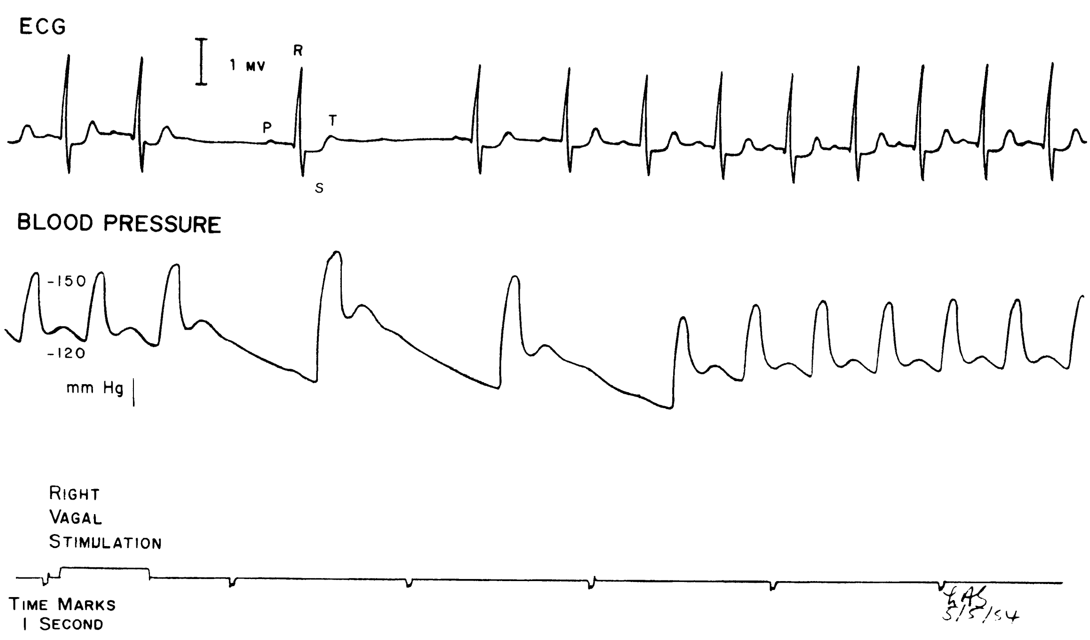
The first step in using the elegant record as a teaching tool is to have a student rise and simply discribe it to his/her classmates. This trivial task is almost impossible for students, who misinterpret the instruction "describe." Usually they hasten to offer complex explanations for what is portrayed by the recording. An approximate description for Fig. 1 is simply, "This is a two-channel record of the electrocardiogram and blood pressure with a time-and-event channel appearing at the bottom. There are calibrations for the ECG and blood pressure tracings. Near the center of the record the heart rate was reduced by vagal stimulation." As yet, no explanation has been given for what is in the record, and absolutely no knowledge of physiology was needed. There is much to be gained by careful description as we will soon see.

The second step in using the elegant record involves stating the obvious, which merely requires a simple physiological description of the portrayed events. For example, "In the ECG there are P waves preceding the QRS-T complexes, indicating normal sinus rhythm. There is a small S-T segment depression, indicating myocardial ischemia. The T waves are upright, which is expected in lead II. There is a QRS complex preceding the blood pressure pulses. During cardiac slowing there appears to be a P wave preceding the QRS complex, indicating that the slowing was not due to atrioventricular block. The diastolic runoff is revealed, and the diastolic pressure is lowered. However, the pulse pressure is higher, probably due to increased diastolic filling. The delay between the onset of vagal stimulation and cardiac slowing is probably due to the time taken for acetylcholine to be released and act on the pacemaker.

So far so good—but the first describer of the record and the second stater of the obvious had taken time to observe carefully during the presentations, it would have been absolutely obvious that there is a single QRS-T complex, identical to the others, but without an ensuing blood pressure pulse. This is the elegance in the elegant record, and the obvious teaching message is that the ECG cannot report on dynamic events.

The next step in using the elegant record as a teaching tool involves speculation on the cause of the event that makes the record noteworthy and elegant. In the present case, it is likely that there was ventricular overemptying by the preceding beat and inadequate filling and inadequate myocardial stretch to result in a pressure high

Figure 1



enough to open the aortic valve. One would then ask how this could be proved and await suggestions for a decisive experiment, which would, of course, have been to measure left ventricular pressure.

The four steps in using an elegant record as a teaching tool are pure description, stating the obvious, finding the unusual or unexpected event, and discussing experiments that could be performed to support (or destroy) the explanation offered.

Physiology teaching, especially in the laboratory, abounds with opportunities to collect elegant records and use them as focal points for teaching, which, in addition to purveying facts, cannot be considered successful unless thinking and reasoning are included as essential components.

Finally, like all works of art, the elegant record should be signed by its author and dated for posterity, for who knows—the record may be publishable.

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Practice of Liquid Scintillation Counting

The Nuclear Engineering Department of North Carolina State University and the Division of Continuing Education announce a three-day course entitled "The Practice of Liquid Scintillation Counting." The course will be offered August 23-25, 1982, at Burlington Engineering Laboratories and Gardner Hall on the North Carolina State University campus. Through lectures and laboratories, participants will learn to understand and to properly use liquid scintillation counters. *For additional information and an application contact:* Rosemary Jones, Division of Continuing Education, North Carolina State University, P.O. Box 5125, Raleigh, NC 27650. Telephone: (919) 737-2261.

Correction

Physiologist 25(2): 104-110, 1982. L. I. Kleinman. "Developmental Renal Physiology."

Page 106: Figure 3 shows the GFR in a neonate dog; Figure 4 shows the GFR in a fetal lamb.

Page 106: column 2, line 2 should read: In the presence of filtration equilibrium, changes in K_F have little effect, and GPF is a very important determinant of GFR.

Physiologist 25(2): 111-117, 1982. D. A. Miller and W. M. Granger. "A Block Diagram, Graphical and Microcomputer Analysis of the O_2 Transport System."

Page 111: line 3 of the Abstract should read: *Physiologist* 25(2): 111-117, 1982.

Page 113: column 1, the last two sentences before "Graphical Analysis" should read: However, $\dot{V}O_2$ also appears in block 1 of the diagram and has a major influence on PA_{O_2} and CA_{O_2} and hence on PA_{O_2} under these conditions. In contrast $\dot{Q}T$ affects Ca_{O_2} only in block 4 and therefore has a minimal influence when Fs is small.

Page 114: the legends for Figures 4 and 5 should be exchanged.

Book Reviews

Excitable Cells in Tissue Culture.
P. G. Nelson and M. Lieberman (Editors)
New York, Plenum, 1981, 422 pp., illus., index, $42.50

This multiauthored book presents a much needed collection of materials on an important and fast-moving research area. As such, it seems to be written for those active in excitable cell research, but the book is very readable and could serve as a text for an advanced graduate course. The stated aim of the book is not that of an exhaustive review; rather, it emphasizes systems most pertinent to the study of the unique properties of membranes in excitable cells: their passive electrical properties, ionic channels, neuropharmacology, and to a lesser extent, the formation of specialized cell-to-cell connections. The chapters have been written by a series of contributors expert in different areas. This imparts a highly specialized and authoritative flavor to each article. Chapters are well referenced up to about 1979, with scattered and somewhat limited citations to articles after that time.

There are many other points in the book's favor. Both the illustrations and text are clearly and accurately labeled, thereby by enhancing visual understanding and facilitating learning. After each of the major headings in dark or red bold type the various figures and tables are noted as referring to the underlying text. Also, there are numerous illustrations (525), tables, anatomic diagrams, schematic representations, and charts throughout the text that summarize and organize previously mentioned anatomic relationships. For example, in the unit on muscles, various groups of muscles are arranged in columnar form that includes names, origins, insertions, functions, and nerve innervations. Another tremendous aid to the reader consists of many color-coded figures depicting arteries, veins, nerves, and muscles. Additionally, the appendix includes several useful sections: prefixes, suffixes, combining forms, metric units and US equivalents, suggested additional reading, and a glossary of terms.

There is one shortcoming. In general the laboratory manual lacks the textbook's depth and detail. In my opinion, many experiments, although supplemental to the textbook, are too superficial and do not reflect the caliber of the textbook. I found both the textbook and laboratory manual to be generally well written. However, the format, terminology, and depth make it more suitable for an elementary course in anatomy and physiology. I would suggest that these books be used together for the beginning student preparing for a health-related career.

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Smooth Muscle: An Assessment of Current Knowledge. E. Bülbring, A. F. Brading, A. W. Jones, and T. Tomita (Editors)
Austin, TX: Univ. of Texas Press, 1981. 563 pp., illus., index, $95.00

Most physiologists realize that interesting and significant things happen in smooth muscle. Reading Edith Bülbrings's second classical compendium on the subject convinces us how exciting these events really are and makes us appreciate the dynamism of its researchers and of the research that is currently probing the inner workings of smooth muscle. For three decades, Elizabeth Bülbring has kept a stable of world-class investigators generating new insights into the operations of this machine. In 1970, the winning performers from this stable got together and generated a volume that gave an account of their research and of the world knowledge of the subject at that time. The former was a major contribution to the latter. Now, over a decade later, they have reassembled and created this second volume primarily to give an account of what has evolved in the interim. This past decade has contributed about as much as had all of the preceding time.

Although the book would be attractive to anyone interested in biomedical research, it should be of particular value as an information source book for those doing research and teaching in biology or basic medical sciences. It is indispensable for those doing research on organs depending on smooth muscle function.

Its twenty chapters, each written by a world-recognized authority in the specific area, may be categorized as follows. Eleven chapters deal with the general structure, physiology, biochemistry, and pharmacology of smooth muscle. Greatest emphasis is placed on the electrophysiology and the electrolyte fluxes and content of smooth muscle. One chapter is dedicated to the voltage clamp technique as it is used in the analysis of ionic conductances in smooth muscle. In the chapters dealing with the general function of smooth muscle, excitation-contraction coupling and its characterization in different types of smooth muscle are described in detail. Relatively little attention is given to the contractile proteins or energy metabolism of smooth muscle. Two addtional chapters deal with the innervation of smooth muscle, and individual chapters deal with the uterus, male reproductive tract, ureter, tracheobronchial, and vascular smooth muscles. Alterations in vascular smooth muscle in hypertension are also well covered. A final chapter deals with the development of smooth muscle and its innervation.

Each chapter starts with a basic orientation, so that it is comfortable reading for the nonexpert in the field. There is surprisingly uniform high quality of writing for a compendium such as this written by twenty different authors. Further evidence of valuable editorial work is seen in the extensive cross-referencing and in the list of references that is comprised of a ninety-one page bibliography. The book is very well indexed.

It makes one proud to be in the smooth muscle field.

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Structure and Function in Man.
S. W. Jacob, C. A. Francone, and W. L. Lossow

Philadelphia, PA: Saunders, 1982, 697 pp. (book), 276 pp. (lab. manual)., illus., index, $26.95 (book), $11.95 (lab. manual)

Jacob, Francone, and Lossow successfully present a textbook and laboratory manual that integrate anatomy and physiology. Both books are coordinated in a logical and organized sequence as shown by their coverage of four units emphasizing physiology: 1) a general introduction on the body as a whole, the cell, and tissues; 2) the framework of the body including the skin, skeletal, articular, and muscular systems; 3) integration and metabolism with sections on fluids and electrolytes, special senses, nervous, circulatory, lymphatic, respiratory, digestive, urinary, and endocrine systems; and 4) the reproductive system. The authors state in the preface that many of the chapters have been either partially or completely revised since the last edition. Each textbook chapter begins with a list of behavioral objectives followed by the organ anatomy in which important terms are in boldface print. Thereafter an extensive description of the physiological system or organ ensues. Of particular importance are the clinical pathologies that are discussed for most of the physiological systems. The reader will also appreciate the detailed summary outline and the review questions at the end of each chapter, which afford the student the opportunity of testing his comprehension of the subject matter.

The book divides naturally into four major sections. The first section discusses peripheral and central neuronal systems, the second reviews biophysical techniques used in tissue culture systems, the third deals with research in clonal systems, and the final section deals with the various forms of muscle cells.

In the first chapter, Burton and Bunge review work on autonomic neurons as representative of the peripheral nervous system. The history of autonomic neuron cultures, and particularly their utilization and response to neurotransmitters, is well reviewed. The bulk of the material centers around reports on the behavior of rat superior cervical ganglion cells in culture. Nelson and colleagues review dissociated cell cultures of central nervous system tissues with an emphasis on use of such cultures in defining central synaptic transmission. While an appendix gives "how-to" descriptions on the preparation of tissue cultures from rat cerebellum, mouse spinal cord, and rat celebral cortex, the discussion within the chapter itself is confined almost exclusively to chick and rodent spinal cord and dorsal root ganglion cultures. Macdonald and Barker discuss in detailed fashion the pharmacology of central synaptic transmission, again considering only spinal cord neuronal preparations. γ-Aminobutyric acid (GABA), glycine, β-alanine, and glutamate are the transmitters emphasized. A possible drawback of this first section is that spinal cord neuronal preparations, taken as models of central neurons, still are tissues that may be too "peripheral" for the dedicated "centralists" among us.

The next two chapters on electrophysiological techniques are good for both the novice and the experienced worker. Smith and colleagues present a good overview on the use of voltage clamp methodology in elucidating the time and voltage dependence of ionic currents across the cell membrane. Cultured muscle cells and spinal cord neurons are compared, illustrating that different electrode and current driver systems are needed for different cell types. While carefully presenting the limitations, the authors demonstrate very nicely where voltage-clamp techniques can be used to a great advantage. Lecar and Sachs describe membrane noise analysis; although a little more difficult for the novice to read, the article presents a good overview on how channel noise can be measured and interpreted. Current fluctuations due to opening and closing of single channels and currents summed from simultaneous fluctuations of many channels and the distinction between channel noise and other sources of electrical noise in the system are presented clearly. This leads nicely into understanding the new and powerful "patch-clamp" techniques, which can be used to observe fluctuations in a single channel while controlling membrane potential.

The section on clonal cell systems is also very worthwhile. These cells differ from others discussed in the book in that they are permanent cell lines dividing continuously in tissue culture and, as such, have had to arise from tumor or embryonic explnts. These chapters detail the advantages of such tissue culture systems for excitable cell studies and point out extensive possiblities for their use. A nice example is the use of artificial fusion techniques to produce large cells highly suitable for microelectrode manipulations in electrophysiological studies. The advantages (and caveats) implicit in using tissue culture systems to provide parallels to differentiating excitable cells are discussed. Kimhi reviews extensively the biology of neuroblastoma cultured cells and, to a lesser extent, pheochromocytoma cultured cells. Spector covers electrophysiological studies in clonal nerve cell lines. Catterall describes data in neuroblastoma cells, pointing to a two-state allosteric model of sodium channels in which alkaloid neurotoxins activate the channel and increase sodium flux by binding preferentially to the activated state; scorpion toxin binding at a second site reduces the energy required for activation, as for heterotropic cooperativity in allosteric enzymes. Channel inhibitors like tetrodotoxin bind at a third site. Sodium channels in skeletal and cardiac muscle have similar behavior but differ quantitatively.

The last section concerns muscle cells. Kidokoro traces the development of tetrodotoxin-sensitive sodium channels and action potentials in myoblasts, multinucleate myotubes, and adult skeletal muscle cells. Myoblasts and myotubes exhibit calcium currents that give their action potentials a similarity to those in cardiac muscles but later disappear. Purves enumerates the technical problems in making electrophysiological observations in cultures of smooth muscle cells and the variability among cell types. Calcium exchange in myocardial cell cultures is reviewed by Langer, with an emphasis on the role of the components of the cell surface coat. Lieberman and colleagues review their timely and original efforts on the uses of chick heart cell cultures grown into linear strands or spherical clusters for electrophysiological and tracer studies. These have given improve precision, for example, in characterizing sodium currents, a technical feat.

In summary, the book is highly readable. It well merits purchasing by libraries and by investigators in the field. It suggests broadened approaches for those in tissue culture research and new substrat for those in electrophysiological research.

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William Beaumont. A Pioneer American Physiologist.

St. Louis, MO: Mosby, 1981, 405 pp., 30 illus., $25 (to APS members)

Every student of physiology and medicine has heard the story of William Beaumont and the experiments that he conducted on Alexis St. Martin, who was left with a gastric fistula following an accidental gunshot wound to the left side of the body. But few have an understanding of Beaumont as an individual, of the state of medicine and physiology during his lifetime (1785-1853), or of the conditions under which he conducted his research. These topics are of interest not only to the medical historian but to all who are concerned with the scientific enterprise and the growth of ideas.

William Beaumont, who was often referred to as the "Father of American Physiology," was a clinical investigator working in a setting that was unsympathetic to research. He was a frontier physician in a newly founded medical corps whose most pressing concerns were the management of fevers, the consequences of trauma, and the disorders of improper sanitation and personal hygiene, at a time when virtually nothing was known about their etiology or pathogenesis and treatment was symptomatic. His diaries, notebooks, and correspondence indicate that by close observation, extraordinary zeal, and relentless pursuit through reading of current medical knowledge, he developed the skills and experience of an outstanding physician. His talents along this line were greatly appreciated by his patients, colleagues, and superiors in the military. But much less appreciated was his devotion to inquiry. The Federal Government had no interest in underwriting scientific research or publication. Therefore, Beaumont's physiological experiments were usually done at personal expense and under the most trying conditions.

The centerpiece of this book is Beaumont's own treatise, "Experiments and Observations on the Gastric Juice and the Physiology of Digestion," which was published in 1833. A preface by Dr. Robert E. Shank provides a modern perspective on this work wi?P respect to gastric physiology. Included under the same cover is a new (third) edition of the "Life and Letters of Dr. William Beaumont," a biography by Dr. Jesse S. Myer, originally published in 1912. As additional prefaces to the biography, the publishers have included Osler's Introduction to the original edition and Andrew C. Ivy's Appreciation in the Second Edition (1939). These diverse elements provide the reader with a remarkably full and attractive view of Beaumont, his work, and its reception during the past 150 years. To top it all off, the book was created as an example of the publisher's art, to reflect the great respect of the publisher for the subject. It is truly a library edition, attractive in binding and in format, and easy to read. The frontispiece, a portrait of William Beaumont by Chester Harding, in color, is well done. Unfortunately, the other illustrations, in black and white, do not fare quite as well in reproduction. But, all in all, this is the kind of book that is an adornment to a personal library.

This book is a St. Louis production. The publisher, the C. V. Mosby Company, opted to reprint this material in celebration of its 75th birthday. Mosby, a St. Louis-based firm, was influenced in its choice of Beaumont as the distinguished scientist to honor by the fact that he spent the last twenty years of his life in St. Louis. In addition, the contemporary contributors to this volume are also from Missouri. However, despite these seemingly parochial aspects, the reader should have no concerns about the universal nature of the book, the quality of its contents, or the attractiveness of its style. Finally, book collectors may be interested to learn that the book was printed in limited edition and that its price is eminently reasonable.

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Acetylsalicylic Acid: New Uses for an Old Drug.

H. J. M. Barnett, J. Hirsh, J. P. Mustard (Editors)

New York: Raven, 1982, 278 pp., illus., index, $39.00

Acetylsalicylic Acid is a compilation of review articles from the proceedings of a Canadian conference on acetylsalicylic acid (ASA) in 1980. Major emphasis is given to reviewing the role of prostaglandis (PGs) and PG synthetase inhibitors in inflammation, hemostatis, and thrombosis. The overviews are brief but authoritative and complete. The controversy and rationale behind the therapeutic applications of high and low doses of ASA in regulation hemostasis, affecting the development of coronary artery disease, and in stroke prevention are presented in several chapters. An interesting and novel chapter on coronary prostacyclin and its relationship to platelet function rounds out the section on inflammation. The effects of ASA and related compounds on PG enzyme systems is reviewed in various chapters, with one chapter devoted to the mode of action of ASA on processes such as oxidative phosphorylation, glycolysis, and fibrinolysis. There are clinically relevant and instructive presentations of the use of PG synthetase inhibitors in altering patency of the ductus arteriosus and the effect of PGs on uterine function and abortion. A much needed review is the timely, knowledgeable, helpfully illustrated, research-oriented discussion of the mechanisms for the antialgesic action of ASA. The chapter correlates PG and PG synthetase inhibitor effects on peripheral nerve endings and the central nervous system. The beneficial and adverse effects of ASA, its pharmacokinetics, as well as unresolved methodological problems are presented. Enlightening conference-participant discussion has been included for many chapters. The text is easy to read and will prove a valuable reference source and teaching aid for medical educators and pharmacologists.

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