THE AMERICAN PHYSIOLOGICAL SOCIETY

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The Physiologist

A Publication for Physiologists and Physiology
Orr E. Reynolds, Editor

Volume 23, No. 5, October 1980

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Fall

Note: Change in time and place of 1981 Fall Meeting

October 11-16, 1981 - Cincinnati, OH
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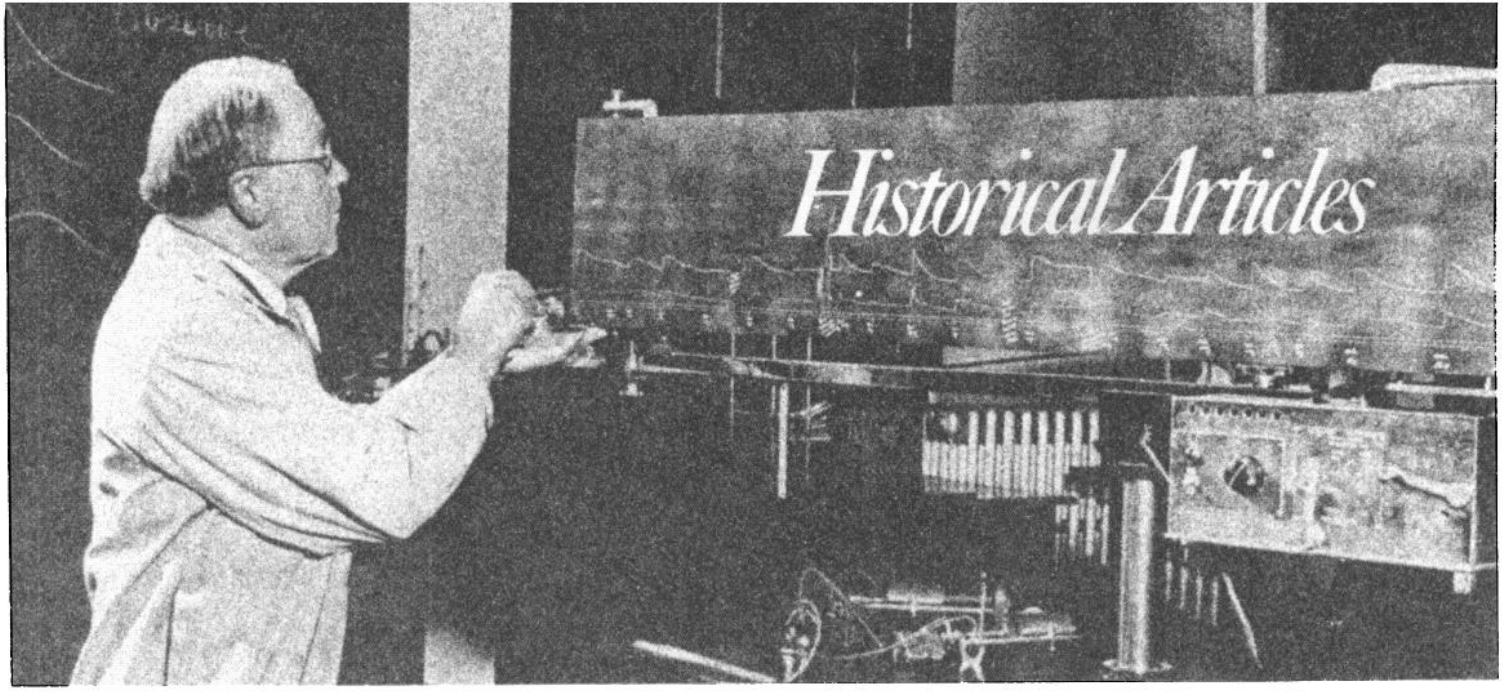

COMPOSITION OF GLOMERULAR URINE WITH CONCLUSIVE EVIDENCE OF REABSORPTION IN THE RENAL TUBULES

A Vignette

Joseph T. Wearn

After serving a year as an interne and two years as an assistant resident on the service of Dr. Henry A. Christian at the Peter Bent Brigham Hospital and a year in the army on the medical service of Major Francis W. Peabody, I was convinced that the field of academic medicine would be the one of my choice if I could qualify for it. Peabody not only encouraged me in this decision but added some advice which I gladly accepted, and for which I have been ever grateful. "Before you decide on your next step, I would advise you to pay a visit to Professor A. N. Richards at the University of Pennsylvania. He is doing some very interesting work which you should see, and if by any chance you could get a position in his laboratory for the coming year, you would be most fortunate." I got an appointment and an invitation from Professor Richards to come to Philadelphia and spend a day with him in his laboratory. Richards and Carl F. Schmidt were engaged at that time in their direct observations of the circulation in the living frog's kidney, and Richards was kind enough to demonstrate the preparation and give me the opportunity to observe it at length. It was an interesting and exciting day; and, before it was over, I had already decided that I had found the person with whom I would like to work. I had a delightful conference with him before leaving and, as I rose to go, he said, "Don't hurry, there is one other little matter we might talk about. How would you like to come and work with me this coming year?" I accepted so quickly that it could leave no doubt in his mind as to how pleased I was. In retrospect, then and there began a lifelong friendship that I treasure and cherish.

On reporting for duty at the beginning of the following academic year, Richards assigned me work assisting with the teaching experiments in preparation for the class in pharmacology. With his assistance, I also learned the technique of preparing the living frog for observation of the circulation in the kidney. He also gave me Cushny's Monograph on "Secretion of Urine" and suggested that I read it with care to familiarize myself with the literature on urine formation. After that, he said, "Come back and we will discuss plans for your future work."

Richards had recently visited the laboratory of Professor Robert Chambers where he witnessed Chambers' injection of red blood cells using a minute glass pipette. This procedure gave Richards the idea he might use such a pipette to inject minute amounts of epinephrine and pituitrin into a glomerulus and observe the effect of these substances on the afferent and efferent vessels of the glomerulus. Previous experiments by Richards and Plant and Richards and Schmidt gave indirect evidence that the efferent vessels might be selectively constricted by these substances. He asked me to think about the possibility of joining him in such a problem.

In the meantime in reading the voluminous literature and the arguments pro and con filtration, reabsorption and secretion, it occurred to me that if one could puncture the capsule of a glomerulus with a pipette and withdraw some of the glomerular fluid, it could be analyzed for protein, sugar, chlorides, urea, dyes and other substances and comparison of these results with the results of similar analyses of bladder urine and blood plasma, and the answers to some long standing important questions might be found. I countered Richards' suggestion, therefore, with my idea that we tackle the problem of trying to get sufficient glomerular fluid for analysis and comparison with analyses of bladder urine and blood collected simultaneously. He accepted the idea instantly with the heartiest approval.

That afternoon, he assigned me a laboratory in the basement where it would be quiet. I spent the next few days in assembling

available equipment, but we soon realized that we would have to construct most of it ourselves. Richards and Schmidt had constructed an adequate lighting system for illumination of the frog's kidney. A binocular microscope with paired objectives was obtained. The glass pipettes presented no difficulty. Using a glass tube of 1 mm. diameter and holding it perpendicular with a weight attached to the lower end, it was passed through an oxygen flame which melted it immediately, allowing it to drop into a bed of cotton. By this method, the lumen was drawn to a diameter of 3 or 4 mu. and one could cut the tube at the level of any diameter desired. We cut the tube where the lumen at the point of the pipette was 10 to 20 mu. When the tube was cut the pipette usually had a sharp point protruding, which we found later to facilitate the puncturing of the capsule of the glomerulus.*

The pipette was then sealed into the end of a glass tube, using deKhotinsky cement to hold it in place. The end of the tube holding the pipette was firmly clasped in a stage of Barbour's pattern which could be moved micrometrically in three planes. This, in turn, was firmly attached to a Zimmerman stativ which was capable of coarse adjustments

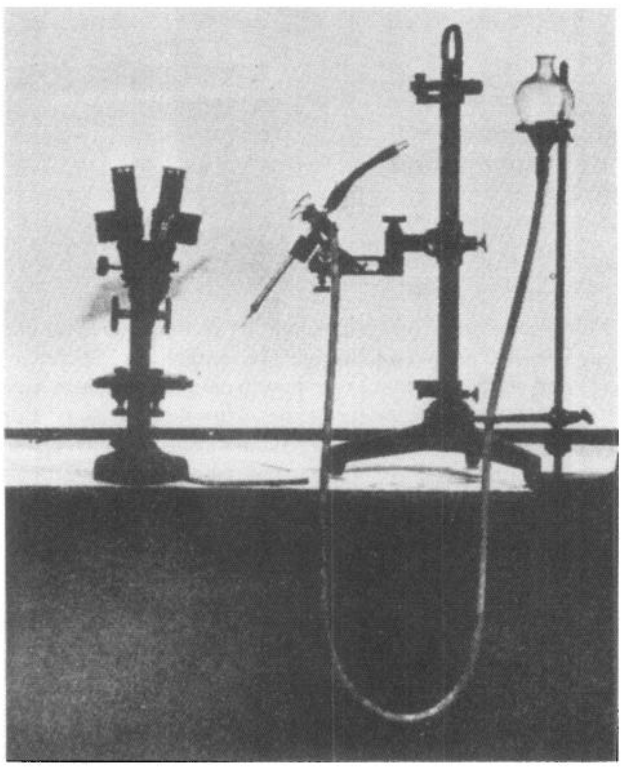

Fig. 1 Photograph of capillary pipette ready for use.

From: AJP, Vol. 71, 1924.

Puncture of Bowman's capsule with a micropipette was carried out as follows: with the kidney preparation in place on the stage of the microscope and the light properly adjusted, the point of the pipette was brought into the center of the microscopic field and placed about 1 mm. directly over the glomerular capsule that had been selected for puncture. Through a small hypodermic needle attached to the microscope, a fine jet of air was played on the surface of the kidney until the area over the glomerulus was dried.** Drying facilitated the insertion of the pipette as it prevented the point from slipping over the wet surface and, at the same time, prevented contamination of the point with the overlying surface fluid. At the time of puncture that area of Bowman's capsule was selected immediately overlying the part filled with fluid and at the greatest distance from the capillary tuft and the capsule wall. After many trials, we were able to insert the pipette without touching either of these structures.

When the pipette was in place inside the capsule the three-way stopcock was turned to connect the levelling bulb and the pipette, and the bulb was then lowered 3 cm. below the level of the kidney in order to create negative pressure and draw in the glomerular fluid.

When the collection of the glomerular fluid was to be terminated, the three-way stopcock was turned to close the connection between the pipette and the levelling bulb. The surface of the kidney in the area of the pipette was dried by means of the air jet, the pipette withdrawn and immediately carefully washed by playing a fine stream of distilled water over it.

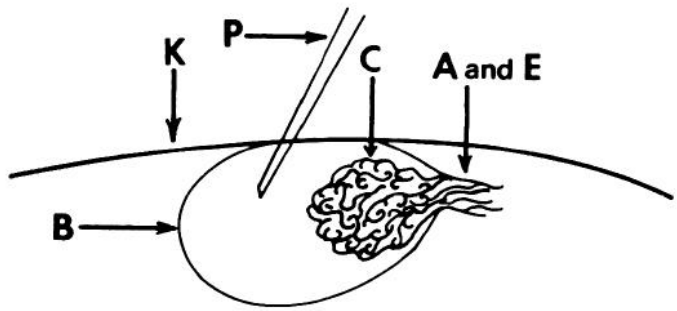

Fig. 2 Diagrammatic sketch of pipette in place in a glomerulus. K surface of kidney. P pipette. A & E afferent & efferent vessels of glomerulus. B capsule of Bowman. C capillary tuft of glomerulus.

The glomerular fluid was then transferred to a capillary tube with a diameter of about 3 or 4 times that of the pipette. This was accomplished by mounting the tube on the stage of the microscope, at an oblique angle corresponding to that of the pipette, and with its upper end in the microscopic field. The pipette containing the glomerular fluid was then brought into the microscopic field and, by use of the Barbour stage adjustments, its tip was inserted into the end of the capillary tube and the contents expelled by raising the levelling bulb.

The column of fluid in the capillary tube was then drawn into the center of the tube and the tube cut at the center of the column of fluid. This procedure was repeated as many times as the volume of fluid permitted. In order to add reagents to the tubes with the individual samples of glomerular fluid, it was only necessary to touch the end of the tube to the reagent fluid surface to have capillarity force the reagent into the tube. Then by moving the reagent and the glomerular fluid back and forth by alternate gentle suction and pressure, it was possible to mix them. The ends of the tubes were sealed in a flame and, thereafter, they could be immersed in boiling water.

Urine that had been collected in the bladder during the collection of the glomerular fluid was then taken and submitted to identical tests as used with the glomerular fluid. A blood sample was also taken at the end of the collection.

* We soon learned that the glass pipettes were not strong enough and frequently broke when pressure was exerted to force them through Bowman's capsule. We therefore switched to quartz tubing from which we made the pipettes, and they proved to be entirely satisfactory.

** The layer of fluid normally over the surface of the kidney had been a troublesome problem by contaminating the pipette and blocking its entrance by clotting. We were indebted to Dr. Wm. Pepper, then dean of the medical school, who suggested that we try blowing a fine jet of air on the area we wished to dry. It worked beautifully.

After a good deal of practice I could, with reasonable certainty, insert a pipette into a glomerulus without touching the capillary tuft or the wall of the capsule. Then, early one afternoon, I prepared a frog and inserted the pipette into the glomerulus without touching the capillary tuft or interrupting the blood flow in it. In a little less than an hour's time, the end of the pipette began to show fluid below the mercury. The circulation in the glomerular tuft was rapid and the fluid in the pipette rose steadily. Richards and I literally tiptoed around the laboratory lest we shake the preparation. It was our first sight of such a "copious" amount of glomerular fluid. Late in the afternoon I terminated the collection, transferred the fluid successfully to a capillary tube, and then by dividing the fluid, ended up with four samples of glomerular fluid for testing. We stored the tubes in the refrigerator, adjourned to Richards' house, had a couple cocktails and then went to a burlesque show.

The next morning we performed tests on all the samples with the following results:

Protein. The acetic acid-potassium ferrocyanide test was used. The glomerular fluid and the bladder urine taken at the end of the collection were tested and in neither was a precipitate formed. This result also indicates that our methods used to avoid contamination with tissue fluid were successful. As a control, fluid which normally covers the surface of the kidney was collected, diluted one hundred times with water and tested. An unmistakable flocculent precipitate was obtained. Frog's plasma diluted one hundred times also yielded a flocculent precipitate. These control tests show the delicacy of the method and prove that there was no significant contamination of the pipette during its entry or withdrawal, also that there was no leakage of tissue fluid into the capsule of Bowman during the collection.

Sugar. Benedict's qualitative solution was introduced into the capillary tubes in volume five to ten times that of the glomerular fluid or bladder urine to be tested. The ends of the tubes to be tested were sealed in a flame and the tubes immersed in boiling water for five minutes. Control tests showed no precipitate or discoloration with distilled water. Glucose solutions of 0.02 per cent and upward, on the other hand, showed unmistakable reduction. These tests on glomerular and bladder urines were made simultaneously and under the same conditions. A control test of the reagent with distilled water was made at the same time. No reaction was obtained with either glomerular or bladder urine. Sugar estimations were then made on the blood of several frogs using McLean's method,[1] with the result that no sugar was detectable. In subsequent experiments, therefore, glucose was injected in varying amounts under the skin of the thigh before beginning the collection of glomerular and bladder urine. In all of these experiments in which the blood sugar was 0.05 per cent or lower, glomerular urine reduced Benedict's solution; bladder urine did not.

Chlorides. The test used was silver nitrate and nitric acid. When performed in capillary tubes, it produced visible turbidity with NaCl concentrations as low as 0.01 percent. It has been shown by van der Heyde[2] that the urine of fasting frogs is nearly chloride free. The glomerular fluid collected in our first experiment yielded a heavy white precipitate, while the bladder urine showed only a small amount. In later experiments when the frogs were kept in distilled water for 24 hours before collection, glomerular fluid gave a definite reaction for chloride; bladder urine gave none.

We had had several interruptions at crucial points in our experiments so I decided to work in the evenings. It proved to be ideal--never an interruption--but after a few evenings Richards came into his office and seeing a light in my laboratory, investigated. "What a superb idea" he said, and from that time on we worked mostly in the evenings. He went to considerable trouble in rearranging his schedule, but it meant a great deal to me to have the privilege of working so closely with him.

We proceeded with a series of experiments, each one carried out as described in the one above. Rather than attempt to describe our series of experiments that followed, with their results and the conclusions we drew, I shall quote the essential points from our original paper.[3]

TABLE 1

NUMBER OF EXPERIMENT	WEIGHT AND PREPARATION OF FROG	TIME OF COLLECTION OF GLOMERULAR URINE	GLOMERULAR URINE			BLADDER URINE			BLOOD	
			Protein	Sugar	Cl	Protein	Sugar	Cl	Sugar	NaCl
		hours							*per cent*	*per cent*
1	55 grams. 2 cc. 5 per cent glucose in stomach during operation		0							
2	2 cc. 1 per cent glucose + 3 cc. H_2O subcutaneously immediately before operation	3	0			0				
3	Same frog as in experiment 2. Another capsule punctured	3		+			0			
4	1.3 cc. 1 per cent glucose + 3 cc. H_2O subcutaneously immediately before collection began	2		++			+		0.065	
5	0.4 cc. 1 per cent glucose + 3 cc. H_2O subcutaneously 15 minutes before operation.	3¼		++					0.022	
	Another capsule punctured	½		+			0			
6	Small frog. 1.5 cc. 1 per cent glucose 12 hours before operation. 4 cc. H_2O subcutaneously after pithing	2	0	+	+	0			0.033	
7	45 grams. 0.3 cc. 1 per cent glucose 5 hours before operation	4	0	++	+	0	0	0	0.05	
8	48 grams. No injection		0	0	+	0	0	0		0.21
9	35 grams. 4 cc. 0.05 per cent NaCl subcutaneously immediately before operation	4¾	0	+	++	0	0	+		0.215
10	48 grams. 0.3 cc. 1 per cent glucose + 3 cc. H_2O 15 minutes before collection began	10*	0	+	++	0	0	±	0.0175	
11	In distilled water 20 hours before experiment 0.3 cc. 1 per cent glucose immediately before operation	5	0	++	++	0	0	0	0.045	
12	48 grams. 0.6 cc. 1 per cent glucose + 4 cc. H_2O immediately before collection began		0	++	++	0	+	0		
13	54 grams. 0.4 cc. 1 per cent glucose + 3 cc. H_2O subcutaneously immediately before operation	3		+	++		0	0		
14	32 grams. 0.4 cc. 1 per cent glucose + 2 cc. H_2O. Excessive diuresis and very rapid collection of glomerular urine	4†		++	+		+	0		
15	2 cc. 0.4 per cent NaCl subcutaneously before operation	3		+			0		0.025	
16	No injection	2		+			0		0.037	

* 2.4 mgm.
† 10 to 12 mgm.

From: AJP, Vol. 71, 1924.

In due time we extended our tests to other substances including urea, potassium, indigo-carmine and other dyes as well as to the reaction of the glomerular fluid.

Urea. Using the Xanthydrol test as described by Oliver[4] we found typical crystals, as described by Oliver, in both glomerular and bladder urine, but much more abundantly in bladder urine. We accepted this as evidence that urea is eliminated through the glomerular membranes, but discontinued the tests until more reliable methods could be developed.

Dyes. Indigo-carmine is of special interest in the study of the kidney because it is the dye chosen by Heidenhain for tracing the path of elimination from blood into urine. In sections of the kidney he found it in the tubules and not in the glomerulus; hence, he revived the Bowman theory of tubular secretion and denied the filtration hypothesis.

Indigo-carmine, because of its visibility in the blood vessels, offered an unusual opportunity for direct observation of the sequence of events during its elimination in the kidney. Consequently, arrangements were made for injection of the dye into the anterior abdominal vein while an observer was looking at the kidney through the microscope. At the same time, the capillary pipette was inserted into the capsule of Bowman so that both glomerular fluid and bladder urine were collected during elimination of the dye. The sequence of changes which was seen to follow the injection of 0.5 cc. of 0.5 percent indigo-carmine in water or salt solution is as follows: Within the first thirty seconds after the start of the injection the visible arteries became blue; immediately the capillary tuft in the glomerulus becomes intensely blue; then the colorless, transparent, fluid-filled space between the tuft and the capsular wall takes on a light blue tinge; then all of the vessels, including veins, take on the color so that the whole kidney is opaque; finally the color fades rapidly so that the original state of the kidney is restored. This sequence is complete in three to five minutes following the injection.

Within ten to thirty minutes later another change is seen. The tubules, which are seen with difficulty in the unstained kidney because of their transparency, become more clearly visible owing to the collection of blue granules in their walls. Presently thread-like collections of dye can be seen apparently in the lumina of some tubules; what appears to be a stippling of the inner border appears in others.

The glomerular fluid which was collected during this series of events was blue; so also was the bladder urine. When approximately equal amounts of the two fluids were discharged upon white filter paper, the stain produced by the glomerular urine was distinctly blue, but less intense than that produced by the bladder urine.

While complete interpretation of these changes cannot be made out with certainty at this time, one fact is clear: indigo-carmine is eliminated by the glomerulus.

The character of the distribution of the dye in the tubules as described in this experiment is in harmony with von Sobieranski's[5] belief that the staining of the tubule cells occurred as a result of the presence of the dye in the lumen of the tubule in more concentrated solution than that in which it exists in the blood.

Phenol red and methylene blue were injected in similar experiments and were eliminated by way of the glomerulus.

Other Observations. The choice of a glomerulus for puncture and collection of fluid was determined on the basis of accessibility and the rate of blood flow through its vessels. It was assumed that the more rapid the blood flow the greater would be the rate of glomerular elimination. If the tip of the pipette on entering the capsule of Bowman touched the capillary tuft, flow of blood through the tuft ceased for an interval of from a few seconds to several minutes and sometimes much longer. When the blood flow ceased, fluid did not rise in the pipette; a fact which not only indicates that formation of glomerular urine ceases when glomerular blood flow ceases, but also the fluid drawn from the capsule of Bowman in these experiments did not originate in the tubule.

The length of time during which collection of fluid from a single glomerulus could be continued was surprising. In one preparation, collection lasted for eighteen hours and the total fluid collected was 10 milligrams. In another experiment following an injection of glucose, 6 milligrams of glomerular fluid were collected in four hour's time.

Discussion

Direct testing of the fluid eliminated by the frog's glomerulus proves that a protein-free fluid is separated from the blood stream as it passes through the glomerular capillaries.

The discovery that two substances, sodium chloride and glucose, both normal constituents of blood plasma, are not to be found in bladder urine under the conditions of these experiments, but are to be found in considerable concentration in the fluid taken from the glomerulus, proves beyond doubt that the reabsorption of these substances must take place in the renal tubules. Proof is also at hand in these experiments that the threshold of reabosorption of these two substances is not the same. The conception of a differential reabsorption in the tubules, therefore, receives support of the most direct character.

Finally, after two happy years of exciting work without a semblance of a disagreement, one arose while we were writing up the results of our work for publication. It involved whose names should appear as authors. Cecil Drinker, who had worked with Richards previously, came to visit him at that time. He came to see me with the information that Richards was planning to have the paper appear under my name as the sole author. He justified his decision, Drinker said, on the fact that I had the original idea of puncturing the glomerulus to withdraw fluid for analysis and for comparing the analysis with that of the bladder urine, and that I had performed practically all of the glomerular punctures and collection of glomerular and bladder urine. I was so upset by this that I went to see Richards immediately; and, when he confirmed Drinker's report, I told him there would be no paper published unless he agreed to be the senior author. I told him that I never would have had the idea of withdrawing glomerular fluid if he had not told me of his observations in Chambers' laboratory and of his plan to inject substances into the glomerulus. I also reminded him of his invaluable guidance throughout the investigation, especially his major role in selecting and overseeing the microchemical methods. And finally I reminded him that I had come to Philadelphia to work with him and that I couldn't be happier at having enjoyed that privilege.

He finally reluctantly agreed to have his name appear as an author, but was adamant in his decision to have my name appear first. His generosity was ingrained. The years I spent working with him were not only the most profitable, but two of the happiest, as they resulted in a close lifelong friendship.

REFERENCES

1. McLean. *Biochem. J.* XIII, 135, 1919.
2. van der Heyde. *J. Biol. Chem.* XIVI, 421, 1921.
3. Wearn and Richards. *Am. J. Physiol.* LXXI, No. 1, 1924.
4. Oliver. *J. Exptl. Med.* XXXIII, 177, 1921.
5. von Sobieranski. *Arch. Exptl. Pathol. U. Pharm.* XXXV, 144, 1895.

INVITATION TO JOIN CARDIOVASCULAR SECTION

Dear APS Member:

The American Physiological Society is forming sections representing the various areas of physiology, and we would like to invite you to join the Cardiovascular Section.

Presently the Cardiovascular Section's activities include a symposium at the spring APS meeting, a dinner meeting following the symposium where the Lamport and Wiggers awards are made, and the appointment of a Cardiovascular representative to the APS - FASEB program committee.

The Cardiovascular Section recognizes meritorious research in cardiovascular physiology by the election of a limited number of fellows from the APS membership.

If your work concerns any aspect of the cardiovascular system, and you would like to participate in our activities, you may join the Cardiovascular Section of the APS simply by writing the APS Executive Secretary, Dr. Orr E. Reynolds.

Sincerely,

James Davis
Eric Feigl
Kiichi Sagawa
Steering Committee
APS Cardiovascular Section

STATEMENT OF ORGANIZATION AND PROCEDURES FOR THE CARDIOVASCULAR SECTION

(Adopted April 15, 1980 - Anaheim, California)

ARTICLE I. *Name*

The name of this organization is THE CARDIOVASCULAR SECTION of the AMERICAN PHYSIOLOGICAL SOCIETY.

ARTICLE II. *Purpose*

The purpose of this organization is: (1) to advise the American Physiological Society on matters of interest to cardiovascular physiologists, and (2) to assist the American Physiological Society in organizing and presenting scientific sessions, symposia, and other programs of interest to cardiovascular physiologists. These activities include sponsoring an annual meeting of the Section.

ARTICLE III. *Membership*

Membership is open to any member (student, associate, regular, emeritus, corresponding) of the American Physiological Society who wishes to be a member. Membership in the Cardiovascular Section is automatic upon application to the Executive Secretary of the American Physiological Society.

ARTICLE IV. *Fellows*

Section 1. *Purpose.* The purpose of fellows in the Cardiovascular Section is: a) to recognize meritorious research in cardiovascular physiology, b) to serve as a candidate pool for officers of the Cardiovascular Section, c) to serve as a candidate pool for the Wiggers Award.

Section 2. *Election of Fellows.* A prospective fellow shall: a) be a *regular* member of the American Physiological Society, b) have published meritorious physiological research in the cardiovascular field. Nomination for fellows will be made by two Cardiovascular Section fellows submitting letters of nomination to the secretary of the Cardiovascular Section. Election of a fellow will be by a majority of the Cardiovascular Section Steering Committee. Once elected, an individual remains a fellow of the Cardiovascular Section so long as he/she is a *regular* member of the American Physiological Society. When a fellow becomes an emeritus member of the A.P.S., he/she relinquishes his/her fellowship and becomes a retired member of the Cardiovascular Section.

Section 3. *Limited Number of Fellows.* The total number of Cardiovascular Section fellows shall not exceed 5% (1/20) of the total number of *regular* A.P.S. members.

Section 4. *Initial Fellows.* Upon formation of a Cardiovascular Section, all the members and Distinguished Members previously elected to the Circulation Group of the A.P.S. (founded in 1933) shall become *Fellows* of the Cardiovascular Section of the American Physiological Society.

ARTICLE V. *Officers*

Section 1. *Steering Committee.* The responsibility for management and supervision of the affairs of the Cardiovascular Section shall be vested in the Steering Committee. The members of the Steering Committee shall be the Chairman, Treasurer, and Secretary.

A quorum for conducting official business of the Cardiovascular Section shall be two of the members of the Steering Committee. Such business may be conducted at meetings of the Society or by conference or telephone call, or by mail.

Section 2. *Term and Sequence of Office.* The term of office for the Chairman, Treasurer, and Secretary shall be for one year, beginning July 1. The Secretary newly elected at the annual Spring meeting will begin to serve on July 1, when the previous

Secretary becomes Treasurer, and the previous Treasurer advances to Chairman. Thus an officer serves three years, one year each as Secretary, Treasurer, and Chairman. In the event that the annual Cardiovascular Section meeeting is in the Fall, the terms of office will begin January 1.

Section 3. *Election of Officers.* A Secretary shall be elected each year at the annual Spring meeting. Officers must have been a fellow of the Cardiovascular Section for at least one year. Nominations shall come from the floor.

ARTICLE VI. *Committees*

Section 1. *Committees.* The Chairman may appoint committees that are necessary for the proper conduct of the affairs of the Section.

Section 2. *Program Committee Representative.* The Program Committee Representative to the American Physiological Society will be appointed by the steering committee to serve a two-year term.

ARTICLE VII. *A.P.S. Relationship*

Nothing in this Statement of Organizational Procedures shall be construed as contradictory to the Constitution and Bylaws or Operational Guidelines of the American Physiological Society.

THE RESPIRATION SECTION

The following Statement of Organization and Procedures was approved by Council at its April 1980 meeting:

ARTICLE I. *Name*

The name of this organization is THE RESPIRATION SECTION of the AMERICAN PHYSIOLOGICAL SOCIETY.

ARTICLE II. *Purpose*

The purpose of this organization is: (1) to advise the American Physiological Society on matters of interest to respiration physiologists; (2) to assist the Program Committee of the American Physiological Society in organizing and presenting scientific sessions, symposia, and other programs of interest to respiration physiologists. These activities include sponsoring an annual dinner; (3) to coordinate activities with physiologists working primarily in other organ systems that are related to the respiratory system.

ARTICLE III. *Membership*

Membership is open to any member of the American Physiological Society who has indicated respiration physiology as a primary or secondary interest.

Membership is open to those members of FASEB with an interest in respiration physiology but who are not members of the American Physiological Society. Candidates for Sectional Membership who are not members of the American Physiological Society are nominated by two Regular Members of the Section who send their written nomination and the candidate's curriculum vitae to the Secretary. The Steering Committee will approve membership. If disapproved, letters are sent to the nominators telling of the disapproval and the reasons.

ARTICLE IV. *Officers*

Section 1. *Steering Committee.* The responsibility for management and supervision of the affairs of the Respiration Section shall be vested in the Steering Committee. The members of the Steering Committee shall be the Chairman (Chairperson), the Secretary-Treasurer, two Councillors, and the representative of the Respiration Section to the Program Committee of the American Physiological Society.

A quorum for conducting official business of the Respiration Section shall be three of the five members of the Steering Committee. The Steering Committee will meet twice yearly at the annual Spring meeting of FASEB and the Fall meeting of the APS.

Section 2. *Councillors.* There shall be three councillors elected to the Steering Committee, each for a term of three years, but with only one being selected in any one year, and each such Councillor to serve as chairman of the Steering Committee during the third year. The newly elected Councillor will serve as Chairman of the Respiration Dinner.

Section 3. *Secretary-Treasurer.* There shall be a Secretary-Treasurer elected for a term of three years.

Section 4. *Program Committee Representative.* There shall be a Program Committee Representative elected for a term of three years.

Section 5. *Election of Officers.* One Councillor shall be elected each year, and the Secretary-Treasurer and Program Committee Representative shall each be elected every third year, with the Secretary-Treasurer being elected in the year preceding the election of the Program Committee Representative.

Nominations shall be made annually, as appropriate, by the Nominating Committee to fill forthcoming vacancies. The names of the nominees shall be announced by mail to the members two months in advance of the annual meeting. Additional nominations may be made by three or more members submitting the name of a candidate who has agreed in writing to serve if elected. Nominations must be submitted by February 1 of the election year.

Election of officers shall be by mail ballot sent to all members concurrently with the announcement of the annual meeting.

ARTICLE V. *Standing Committees*

Nominating Committee. The Chairman, in consultation with the other 4 members of the Steering Committee, will appoint annually two at large members to serve with a Councillor (serving as Chairman) as the Nominating Committee. The Committee nominates two members as candidates for the election of the new Councillor, and for Secretary-Treasurer and Program Committee Representative when appropriate.

ARTICLE VI. *Duties of Officers*

Section 1. The Program Committee Representative is responsible for performing the functions defined by the Society Operational Guide for members of the Program Advisory Committee.

Section 2. The Chairman, in consultation with the other 4 members of the Steering Committee, will annually choose a topic to be presented in symposium form at the annual FASEB meeting. The Committee will also choose a person to be responsible for the organization, funding and presentation of the Symposium.

Section 3. The Chairman may appoint committees that are necessary for the proper conduct of the affairs of the section.

ARTICLE VII. *Dues*

Dues will not be assessed.

ARTICLE VIII. *Meetings*

The Respiration Section will meet at the time of the annual dinner and at other times determined by the Steering Committee. Members must be notified in writing at least one month before the meeting.

ARTICLE IX. *General*

Section 1. *Amendments.* Amendments to these procedures must be proposed in writing to the Steering Committee by five members, at least two months before the annual meeting. The proposal must then be sent to the members at the time of the announcement of the annual meeting. An amendment requires the approval of two-thirds of the entire membership for adoption.

ARTICLE X.

Nothing in this Statement of Organizational Procedures may be construed as contradictory to the Constitution and Bylaws or Operational Guidelines of the American Physiological Society.

HONORS AND AWARDS

Two APS members were selected by the Awards Committee of the American College of Chest Physicians to receive special recognition at the ACCP's 46th Annual Scientific Assembly in Boston, October 26-30, 1980. The recipients presented a state-of-the-art lecture during the five-day medical meeting.

Dr. **Edward A. Gaensler,** M.D., FCCP, was selected as the 1980 Distinguished Lecturer in Physiology. A professor of surgery and physiology at Boston University School of Medicine, Dr. Gaensler also lectured at the Harvard Medical School and Tufts University School of Medicine. He is a past consultant to the Department of Health, Education and Welfare serving as a member of the Cardiopulmonary Disease Advisory Committee of the National Heart and Lung Institute, the Pulmonary Training Committee of the NHLI, and a member of the Applied Physiology and Bioengineering Study Section of NIH. Dr. Gaensler's lecture was titled "Adventures in Respiration."

Dr. **Eugene D. Robin,** M.D., presented the Simon Rodbard Memorial Lecture. Dr. Robin is a professor of medicine at Stanford University School of Medicine. His medical career included academic appointments at the Harvard Medical School and the University of Pittsburgh School of Medicine. Dr. Robin's lecture was titled "Some Basic and Clinical Challenges in Pulmonary Circulation."

VISITING FULBRIGHT SCHOLARS

The following material is abstracted from an announcement from the Council for International Exchange of Scholars.

Many of the visiting scholars welcome opportunities to lecture or participate in special programs on campuses other than their principal location. The Council encourages direct contact with the visitors but is also willing to assist in identifying appropriate scholars for special projects. The Council for International Exchange of Scholars is located at 11 Dupont Circle, Washington, D.C. 20036 or telephone (202) 833-4979. Following is a list of scholars who may be of interest to APS members, their home institution and their visiting address:

CHAUCA, Rosaura D. - Assoc. Prof. Vet. Physiol., Inst. High Altitude and Tropical Research, Univ. San Marcos, Lima, Peru. Lecture on high altitude physiology; Univ. of Alaska, Div. Life Sci., Fairbanks.

GANDER, Phillippa H. - Ph.D. Candidate, Univ. Auckland, New Zealand. Research in mammalian circadian rhythms; Harvard Med. Sch., Dept. Physiol., Boston, Mass.

GOLDSPINK, Geoffrey - Prof. Zoology, Univ. Hull, United Kingdom. Lecture and research in muscle locomotion; Harvard Univ., Cambridge, Mass.

MOSER, Hans - Asst. Zoophysiology, Inst. Zoology, Innsbruck Univ., Austria. Research in electrophysiological measurements; Univ. Utah Coll. Med., Dept. Physiol., Salt Lake City.

REDDY, Nallu S. - Scholar, National Dairy Res. Inst., Karnal, India. Research in ruminant digestion; Univ. of Wisconsin Dept. Dairy Sci., Madison.

SHANKARAIAH, K. - Lecturer in Zoology, Osmania Univ., Hyderabad, India. Research in chronobiology; Univ. of Minnesota, Dept. Ecology & Behavioral Biol., Minneapolis.

FORMATION OF THE SECTION ON ENDOCRINOLOGY AND METABOLISM OF THE AMERICAN PHYSIOLOGICAL SOCIETY

At its meeting in New Orleans in September, 1979 the Council of the American Physiological Society mandated the development of sections in various areas of physiology. One of the areas selected for sectionalization was endocrinology and metabolism. This section will include endocrinology, neuroendocrinology and metabolism.

The overall objective of the section will be to enhance the quality of research and promote interaction among scientists working in these areas. In order to accomplish this purpose the section will advise the American Physiological Society on matters of interest in this area and will assist the American Physiological Society in organizing and presenting scientific sessions, symposia and other programs of interest to physiologists in these areas. A primary purpose of this section will be to improve the quality of the program both at the Federation Meetings and the Fall Meetings.

Membership in this section is open to any member of the American Physiological Society who submits a statement to APS signifying that they wish to become a member. No change in APS dues will be made because of membership in the section.

When the constituency of the section has been established, the management and supervision of the affairs of the Endocrinology and Metabolism Section shall be handled by a Steering Committee which will be elected by the membership of the section. The Steering Committee will consist of a chairperson and councilors. One of the councilors will be selected as a representative to the program advisory committee of the American Physiological Society and it will be through this mechanism that the program will be improved. The Steering Committee will play a role in recommending members for appointment to the Editorial Board of the Section on Endocrinology and Metabolism of the American Journal of Physiology.

The section on Endocrinology and Metabolism will meet at least once a year and at other times as determined by the Steering Committee. Initially, we visualize that these meetings would take place at the Federation Meetings since this is the meeting which is most attended by members with interest in endocrinology and metabolism within the Society.

Organizing Committee - Robert E. Fellows
Henry G. Friesen
Howard E. Morgan
Edward J. Masoro
Jimmy D. Neill
S.M. McCann, Chairman

ENDOCRINOLOGY AND METABOLISM SECTION

Statement of Organization and Procedures

ARTICLE I. *Name*

The name of this organization is the ENDOCRINOLOGY & METABOLISM SECTION of the AMERICAN PHYSIOLOGICAL SOCIETY.

ARTICLE II. *Purpose*

The purpose of this organization is: (1) to advise the American Physiological Society on matters of interest to these areas, and (2) to assist the American Physiological Society in organizing, and presenting scientific sessions, symposia, and other programs of interest to physiologists in these areas.

ARTICLE III. *Membership*

Regular Membership is open to any member of the American Physiological Society who signs a statement declaring the wish to be a member. To accomplish this, the entire membership of the American Physiological Society will be polled during the first year that this Statement is in effect. Thereafter, only new members of the organization will be polled to ascertain their interest.

Intersociety Membership is open to those with an interest in endocrinology and metabolism but who are not members of the American Physiological Society. Intersociety Members share all of the rights and responsibilities of Regular Members. Candidates for Intersociety Membership are nominated by 2 Regular Members who send their written nomination and the candidates curriculum vitae to the Secretary-Treasurer. If approved by the Steering Committee, membership is granted. If disapproved, letters are sent to the nominators telling of the disapproval and the reasons.

ARTICLE IV. *Officers*

Section 1. *Steering Committee.* The responsibility for management and supervision of the affairs of the Endocrinology and Metabolism Section shall be vested in the Steering Committee. The members of the Steering Committee shall be the Chairman, the Secretary-Treasurer, two Councillors, and a representative of the Endocrinology and Metabolism Section to the Program Advisory Committee of the American Physiological Society.

A quorum for conducting official business of the Endocrinology and Metabolism Section shall be three of the five members of the Steering Committee.

Section 2. *Councillors.* There shall be three Councillors elected to the Steering Committee, each for a term of three years, but with only one being selected in any one year, and each such Councillor to serve as

chairman of the Steering Committee during his/her third year.

Section 3. *Secretary-Treasurer.* There shall be one Secretary-Treasurer who shall be elected for a term of three years.

Section 4. *Program Committee Representatives.* A Program Advisory Committee representative (or representatives) shall be elected for a term of three years. The number of such representatives will be as authorized by the APS Council. The representative to the APS Program Advisory Committee shall also be a Councillor. If more than one such representative is authorized, one of these shall be identified as the Councillor.

Section 5. *Election of Officers.* One Councillor shall be elected each year, and the Secretary-Treasurer and Program Committee Representatives shall each be elected every three years with the Secretary-Treasurer being elected in the year preceding the election of the Program Committee Representative.

Two nominations shall be made annually, as appropriate, by the Nominating Committee to fill forthcoming vacancies. The names of the nominees shall be announced by mail to the members two months in advance of the annual meeting. Additional nominations may be made by three or more members submitting the name of a candidate who has agreed in writing to serve if elected. Nominations must be submitted by February 1 of the election year.

Election of officers shall be by mail ballot sent to all members concurrently with the announcement of the annual meeting.

ARTICLE V. *Standing Committees*

Section 1. *Nominating Committees.* The Chairman, in consultation with the other 4 members of the Steering Committee, will appoint annually two members to serve with a Councillor (serving as Chairman) as the Nominating Committee. The Committee nominates two members as candidates for election to each office.

Section 2. *Publications Committee.* The Chairman, in consultation with the members of the Steering Committee, will recommend to the Publications Committee, American Physiological Society, and to the Editor, AMERICAN JOURNAL OF PHYSIOLOGY: ENDOCRINOLOGY AND METABOLISM, section members for appointment to the Editorial Boards and Editorships, as vacancies occur. A minimum of five members from the Editorial Board appointed by the Editor will serve as the Publications Committee for the Section Endocrinology and Metabolism. Its Chairman will be appointed annually by the Steering Committee from among Editorial Board members who hold sectional membership. Terms of service of sectional Associate Editors normally shall be three years with possible reappointment for additional terms as determined by the Editor, and subject to ratification by the Publications Committee of the American Physiological Society in conformity with Bylaws of the Society. Duties of the Sectional Publications Committee will be to assist the Editor in identifying, inviting, and attracting manuscripts of interest to the Section of Endocrinology and Metabolism and to advise the Editors as appropriate on publication policies of the AMERICAN JOURNAL OF PHYSIOLOGY: ENDOCRINOLOGY AND METABOLISM, in relation to sectional interests.

ARTICLE VI. *Duties of Officers*

Section 1. The Program Committee Representative(s) is (are) responsible for performing the functions defined by the Society Operational Guide for members of the Program Advisory Committee.

Section 2. The Chairman, in consultation with the other 4 members of the Steering Committee, will annually choose topics to be submitted to the APS Program Committee for annual meetings of the Society. They will also choose a person who will organize each approved endocrinology or metabolism symposium and be responsible for its presentation.

Section 3. The Chairman may appoint committees that are necessary for the proper conduct of the affairs of the Section.

ARTICLE VII. *Dues*

Dues may be assessed annually in an amount established by the Steering Committee.

ARTICLE VIII. *Meetings*

The Section on Endocrinology and Metabolism will meet at least once a year and at other times determined by the Steering Committee. Members must be notified in writing at least one month before the meeting. Meetings are for transacting the business of the Section on Endocrinology and Metabolism and are governed by Roberts Rules of Order Newly Revised.

ARTICLE IX. *General*

Section 1. *Amendments.* Amendments to these procedures must be proposed in writing to the Steering Committee by five members at least two months before the annual meeting. The proposal must then be sent to the members at the time of the announcement of the annual meeting. An amendment requires the approval of two-thirds of the entire membership for adoption.

Section 2. *Quorum.* The quorum required for all membership business meetings is no less than 30 percent of the total members of the Section.

ARTICLE X.

Nothing in this Statement of Organizational Procedures shall be construed as contradictory to the Constitution and Bylaws or Operational Guidelines of the American Physiological Society.

1981 FEDERATION MEETING

The meeting will be held in Atlanta, Georgia from April 12 through 17, 1981. The call for abstracts was mailed in September and the deadline for receipt of abstracts is December 1, 1980.

APS will act as host to the Biomedical Engineering Society and the Society for Experimental Biology and Medicine. The call for abstracts was sent to members of these societies as well as the members of the American Society of Biological Chemists who were also invited to submit their abstracts to APS.

APS had approved 19 symposia for the 1981 Spring Meeting. Of these, five for the Nervous System Section and one on Epithelial Function were transferred to FASEB sponsorship as part of the "thematic" portion of the meeting. (The Nervous System Section dropped one of their other planned symposia). The selected "thematic" elements of the meeting are "Neurobiology and Behavior," "Atherosclerosis" and "Membranes." These theme elements are being organized across society lines by a specially appointed ad hoc committee and the resulting sessions will be programmed to avoid conflicts in the scheduling of related subjects.

The *following symposia* are currently being planned with the organizer for each shown:

Clinical Science Topic on Receptor Mechanisms. Francois Abboud.

What Roles Do Nerves Play in Renin Release? A. Clifford Barger and John W. Manning.

*Thermoregulatory Effects of the Newer Putative Central Neurotransmitters. Clark M. Blatteis.

Cellular Dynamics of Insulin Action. Michael P. Czech.

Pathogenic Mechanisms in Hypertension. James O. Davis.

Use and Misuse of Skinned Muscle Fibers. Alexandre Fabiato.

Role of Calcium in Controlling Renal Functions. John C. S. Fray

Dehydration Induced Thirst. John Greenleaf.

Genetic Polymorphism and Regulation of Gene Expression. (SEBM sponsored) Paul A. Marks.

*Fast Axoplastic Transport in Mammalian Nerve. Sidney Ochs.

Prostoglandins and the Digestive System. Andre Robert.

Physiology of the Mammalian Gastric Mucosa. Linda L. Shanbour.

The Role of Hormones in Phosphorylation-Dephosphorylation in Metabolic Regulation. Thomas K. Soderling.

*Physical Probes of Epithelial Function. Ken Spring.

*Pepditergic Neurons in Invertebrate and Vertebrates. Felix Strumwasser.

*New Understandings of Motor Units. Douglas G. Stuart.

Comparative Studies on the Control of Renal Function. Bruce P. K. T. Pang, B. Umminger, H. Nishimura.

Neuroendocrine Cells, Peptide Hormones, Purinergic Nerves in Lung (cosponsored with AAP). James Will.

Cardio-Pulmonary Dynamics. D. T. Weber. Legal and Engineering Interfaces of Surgical Implants (BMES sponsored). C. F. Smith, A. Weinstein, W. E. Johansen.

* thematic sessions

In addition to those listed above, Helene Cecil, Chairman of the Animal Care and Experimentation Committee, is organizing a FASEB symposium on The Ethics of Animal Care. Walter Randall, Chairman of the Career Opportunities in Phsyiology, is organizing a session on Careers in Physiology. The careers session is tentatively scheduled for the late afternoon of Wednesday, April 15, 1981, and the animal care session in the evening of the same day.

TORONTO TO HOST AAAS ANNUAL MEETING 3-8 JANUARY 1981

Washington, D.C.... "Science and Technology: Bridging the Frontiers" will be the theme for the 147th national meeting of the American Association for the Advancement of Science (AAAS) to be held in Toronto, 3-8 January 1981. The many facets of science, including medicine, engineering, ecology, physics, anthropology, chemistry, and psychology, will be presented.

Several thousand scientists, engineers, and others interested in science and technology are expected to attend the meeting, which will be headquartered at The Sheraton Centre and the Royal York Hotel.

Among over 150 diverse symposium subjects will be: the age and size of the universe; psychological bases of morality; Mount St. Helen's; biological energy conversion; contamination trends in the Great Lakes; religion and food; science for handicapped students; science and secrecy; the laser revolution in chemistry; and development of a shark repellant.

The program also features nine (9) public lectures by prominent persons dealing with popular aspects of science, and the AAAS Science Film Festival, with 50 of the best short science films produced over the last year.

The AAAS Annual Meeting Exhibit, displaying new scientific instruments and publications, will run from 4 January through 7 January at The Sheraton Centre Exhibit Hall.

Through its Project on the Handicapped in Science, AAAS will again make its national meeting fully accessible to disabled individuals. A "Handicapped Resource Center" will be operated throughout the meeting.

Further information about the meeting is available from the AAAS Meetings Office, 1776 Massachusetts Avenue, N.W., Washington, D.C. 20036. A preliminary program for the meeting appeared in the 12 September 1980 issue of SCIENCE, the weekly journal of the AAAS.

APS SYMPOSIUM AT AAAS MEETING

The APS will sponsor a symposium on January 7, 1981 at the AAAS Meeting in Toronto, Canada, January 3-8, 1981. The subject of the symposium "Role of Cell Surface Receptors in Human Diseases" was suggested by the APS representative to Section N (Medical Sciences) Dr. Hadley L. Conn, Jr., Chairman of the Department of Medicine, College of Medicine and Dentistry of New Jersey.

The symposium will be held at 9:00 AM on January 7, 1981 in the Royal York Hotel. It is being organized by Jesse Roth (NIAMD). The tentative program includes the following presentations:

Receptors and Disease. JESSE ROTH, *NIAMD, NIH, Bethesda, MD*

Autoantibodies to ß-Adrenergic Receptors in Allergic Respiratory Disease. J. CRAIG VENTER, *Dept. Pharmacol. and Therap., SUNY at Buffalo.*

Myasthenia Gravis: An Auto-Immune Disorder of Acetylcholine Receptors. DANIEL B. DRACHMAN, *Dept. Neurol., Johns Hopkins Univ., Baltimore.*

Lipoprotein Receptors and Atherosclerosis. JOSEPH L. GOLDSTEIN, *Chrmn., Molecular Genetics, Univ. of Texas Hlth. Ctr., Dallas.*

Androgen Receptor Effects as a Cause for Steroid Sensitivity. C. WAYNE BARDIN, *Ctr. for Biomed. Res., Population Council, Rockefeller Univ., New York.*

MEMBER CONTRIBUTIONS

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.

We gratefully acknowledge the contributions received from the following Emeritus Members:

Franz X. Hausberger
John C. Lilly
Walter S. Wilde, in memory of Richard Ashman

Other Members:

Eugene Ackerman
Mario Atamirano
Francisco Alvarado
Nicholas R. Anthonisen
Octavio Q. Aprigliano
William McD. Armstrong
J. Howland Auchincloss
Marvin B. Bacaner
Praphulla K. Bajpai
William M. Balfour
A. Clifford Barger
Samuel B. Barker
Ann-Lisa Barofsky
Frank Barrera
J.B. Bassingthwaite
D.V. Bates
Paul M. Beigelman
Francis L. Belloni
Kathleen H. Berecek
Richard D. Berlin
Robert W. Berliner
Beverly P. Bishop
Joseph R. Blair
Victor P. Bond
Nicholas H. Booth
Thomas A. Boyd
Robert A. Brace
William A. Brodsky
Alfred W. Brody
Jerome S. Brody
Baruch Bromberger-Barnea
Nancy L.R. Bucher
Ian E. Busch
Robert A. Butler
Peter R.B. Caldwell
Leon Cander
Drew E. Carlson
Jose L. Cangiano
Drew E. Carlson
Kenneth L. Casey
Helene C. Cecil
Cornelia P. Channing
Francis P. Chinard
Paul C. Churchill
Richard L. Clancy
Hazel M. Coleridge
John Coleridge
Jose A. Colina-Chourio
Robert W. Colman
James Conway
John S. Cook
Keith E. Cooper
LaVal N. Cothran
Benjamin G. Covino
Larry I. Crawshaw
Louis G. D'Alecy
Mary F. Dallman
Brian G. D'Aoust
Robert L. DeHaan
William D. DeHart
Francisco Del Greco
Duane Denney
David E. Donald
Philip Dow
Michael J. Durkot
Walter Ehrlich
Robert Elsner
Howard H. Erickson
Solomon D. Erulkar
Leon E. Farhi
John A. Faulkner
Larry P. Feigen
Vladimir Fencl
James L. Ferguson
Benjamin G. Ferris
Joseph D. Fondacaro
Irwin J. Fox
Henry H. Freedman
Melvin J. Fregly
Robert H. Furman
Ronald A. Gabel
Walter J. Gambel
William F. Ganong
Apostolos P. Georgopoulos
Daniel L. Gilbert
Roger M. Glaser
Robert C. Goode
Robert S. Gordon
Robert W. Gore
Alejandro E. Grassino
Joseph Greenberg
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Fred S. Grodins
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Joseph H. Hafkenschiel
Howard B. Haines
James C. Hall
Robert L. Hamlin
Edith L. Hardie
Carolyn M. Hardin
Lura A. Harrison
Aslam Hassan
Franklin W. Heggeness
Richard M. Herman
Julian I.E. Hoffman
Carl R. Honig
Leif Horn
Barbara J. Howell
Panayotis G. Iatridis
Roland H. Ingram, Jr.
Ernst R. Jaffe
John A. Johnson
Paul C. Johnson
Gabor Kaley
Madhu Kalia
Merrill B. Kardon
Frederick W. Kasch
Michael J. Katovich
Ronald L. Katz
William C. Kaufman
Hiroshi Kawamura
Ralph H. Kellogg
Paul A. Kelly
Theodore M. King
Leon K. Knoebel
Thomas I. Koike
Samuel N. Kolman
Robert L. Kroc
Ladislav Krulich
Kiyoshi Kusano
Martin J. Kushmeric
Hau C. Kwaan
Ardelle C. Lane
Stanley Lang
Leroy L. Langley
N. Leroy Lapp
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W. Harold Lawson, Jr.
John K. Leach
Jacob Lemann, Jr.
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Marshall A. Lichtman
Frederick M. Liebman
Samuel L. Liles
Thomas P.K. Lim
Julian H. Lobard
William G. Lotz
James H. Ludens
Julian B. Marsh
Manual Martinez-Maldonado
Leo C. Massopust, Jr.
Donald K. Mathews
Earl Mayeri
H.S. Mayerson
Charles H. McGinnis, Jr.
James J. McGrath
Ivan F. McMurtry
Jere Mead
Richard A. Meiss
William L. Mengebier
Elliott Mills
Vu-Dinh Minh
Charlotte M. Mistretta
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Kenneth M. Moser
Campbell Moses
David R. Mouw
Syed J. Mustafa
Joseph B. Myers, Sr.
Robert M. Nerem
Thomas E. Nightingale
Hiroko Nishimura
Sarah A. Nunneley
John J. O'Neil
Daniel H. Osmond
Arthur B. Otis
John R. Pappenheimer
Juan C. Penhos
Jack H. Petajan
Barry T. Peterson
Irwin J. Pincus
Frank L. Powell, Jr.
Michael R. Powell
Freeman H. Quimby
Wilfrid Rall
Henry J. Ralston
Lawrence W. Raymond
Martin D. Rayner
Thomas J. Reeves
Davis M. Regen
Orr E. Reynolds
Benjamin M. Rigor
James S. Robertson
Terence A. Togers
Albert J. Romanosky
Donald O. Rudin
Elena-Ruiz Ceretti
Herbert A. Saltzman
Hisashi Sanui
Toshino Sato
Michael N. Sawka
Alfonso Schettini
Milton J. Schiffrin
Lawrence P. Schramm
Gordon W. Searle
Ewald E. Selkurt
John W. Severinghaus
Alan W. Sexton
Aaron B. Shaffer
Richard H. Shepard
A.P. Shepherd
Jim L. Shields
Virgie G. Shore
William W. Sleator
Theodore C. Smith
Jan W. Snellen
Joseph F. Spear
Walter M. St. John
Sidney J. Stolzenberg
Robert E. Swanson
Robert B. Tallitsch

Roy V. Talmage
Catherine S.H. Tan
Stephen M. Tenney
Paul E. Teschan
Robert E. Thurber
Donald F. Tierney
Richard B. Tobin
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James H. Veghte
Herman Villarreal
Karlman Wasserman
Shizuo Wanatabe
Billy E. Welch
Hugh G. Welch
J. Henry Wills
Mary E. Wohl
Earl H. Wood
Ernest B. Wright
Edward L. Yellin
Martin A. Zade-Oppen
Thomas W. Ziegler
Douglas P. Zipes
Claire E. Zomzely-Neurath

EIGHTH INTERNATIONAL SYMPOSIUM ON GASTROINTESTINAL MOTILITY

The 8th International Symposium on Gastrointestinal Motility will be held at Konigstein near Frankfurt am Main, F.R. Germany, from September 7 to September 11, 1981. The organizers of this interdisciplinary conference invite papers on the nature, the function, and the control of the movements of the alimentary tract in health and disease. Clinically relevant papers are particularly sought. Papers to be presented on the program will be selected by the International Steering Committee from abstracts submitted. Abstracts, not to exceed 250 words in length, should be sent to Dr. Martin Wienbeck, Department of Internal Medicine D, University Hospitals, Moorenstr. 5, D-4000 Duesseldorf, F.R. Germany. The deadline for receipt of the abstracts is March 1, 1981.

A BRIEF HISTORY OF THE TASK FORCE ON WOMEN IN PHYSIOLOGY (APS)

In 1970, at the Federation meetings in Atlantic City, a small group of women physiologists met informally and decided it was time to do something in behalf of their women colleagues. Esther Hardenberg, Louise Marshall, Florence Millar, Willie Smith, Elizabeth Tidball and Marion Webster, all of Washington, DC, began to meet regularly and to plan ways to increase the visibility of women within the Society.

Their first project focussed on encouraging members to nominate a woman to Council. After explaining their plan to Bodil Schmidt-Nielsen, they combined their personal monetary and time resources to send a letter to all Society members, including signatures from their member colleagues at the National Academy of Sciences, NNMRI, NIH and George Washington University, suggesting that Dr. Schmidt-Nielsen be nominated on the write-in ballots. She was. Indeed, she received more nominations by mail than any previous candidate for Council or President of the Society! Then, at the spring business meeting, she was elected to Council by the members present and subsequently, in 1975, she became the first woman President of the Society.

The second project of this lively *ad hoc* group was to encourage the establishment of an official body within the APS for the benefit of women. A proposal was presented to Council in January 1973 during the Presidency of Robert Berne, and was acted upon favorably. The Task Force on Women in Physiology thus came into being. Its stated goals were: to increase the visibility of women physiologists; to develop a reference file of pertinent journal articles on women scientists; to assist in the incorporation and utilization of women's talents into all APS activities; and to make recommendations to the Society of structures and policies that would facilitate this inclusion process. Its members were Elizabeth Tidball, Chairperson; June Barker; Ray Daggs; Virginia Fiske; Elizabeth Gerst; and Florence Millar. Orr Reynolds provided generous support and Mary Dittbrenner of the APS office served as a contact person for the Task Force.

The Task Force held its organizational meeting in March 1974 in Washington with all members present as well as APS President Dan Tosteson, Orr Reynolds and Mary Dittbrenner. The first action taken by the Task Force was to develop a postcard questionnaire in order to acquire names and addresses of persons who identified themselves as women physiologists. Color-coded according to site of distribution (eg., FASEB meeting, *Physiologist, Physiology Teacher,* etc.), the cards were headed "Do you know a woman Physiologist?" and brought hundreds of replies. A report of the initial meeting and planned activities of the Task Force was made at the April 1974 business meeting in Atlantic City and is recorded in the *Physiologist,* 17(2): 135-137, 1974.

The Task Force as a group made its formal debut before the Society at the fall 1974 meeting in Albany, where a Round Table on Women in Science was held as part of the regularly scheduled events. Participating for the Task Force were Drs. Barker, Gerst, Fiske and Tidball. It was a first for the Society, well attended by both men and women, and the beginning of increased visiblity and awareness vis-a-vis women in physiology. One outcome of the impetus provided by the Round Table was an article in the *Physiologist* (18(1): 1-36, 1975) entilted "Women in the Biosciences - A Brief Primer." Subsequently, at the spring 1975 meetings in Atlantic City, displays of literature and photographs of women physiologists occupied a prominent place at Convention Hall; and small group discussions were led by Task Force members in the informal setting of the lounge at various times during the FASEB meetings. These provided opportunites for women and men to share their interests, concerns and ideas with respect to the participation of women in the natural sciences

But the Task Force did not take the matter of women's position narrowly. There were areas of concern within the Society's structure that the Task Force felt could be improved for *all* participants, including women. One such area related to the means by which members were elected to Council and to the Presidency. Working with the *ad hoc* Committee on Election Procedures which was reviewing these procedures, the Task Force provided the suggestion and documentation for the method presently in use by the Society. (See the Report of the Ad Hoc Committee on Election Procedures in the *Physiologist,* 17(1):2, 1974). In a further initiative, the Task Force recommended that Council

establish a Committee on Committees to facilitate a more orderly and broad representation of members on APS committees. This new standing committee was voted by Council in 1974, and women have always been among its membership. One result has been the inclusion of more women, minorities and young physiologists on a variety of APS committees.

The Task Force was also instrumental in encouraging Council to undertake a questionnaire to all members of the APS. While the final product did not contain many of the items desired by the Task Force, it nonetheless provided a current database for the Society in 1977, the first update in almost 30 years. There is still hope that some of the information acquired may be used in further studies of women and men physiologists.

Finally, recognizing that the ultimate objective of the Task Force was greater *inclusion* in APS activities rather than isolation, the Task Force recommended to Council that a new APS committee be established on Career Opportunities in Physiology which would incorporate many of the original goals of the Task Force. This new committee was voted by Council at its spring 1979 meeting, and thus the official work of the Task Force on Women in Physiology was brought to a close. In a letter to the Chairperson in June 1979, APS President David Bohr wrote:

> This letter is for the purpose of discharging the Task Force on Women in Physiology with gratitude for your work in guiding the Society's approach to career planning.....a Committee on Career Opportunities in Physiology was established in line with one of the recommendations of your Task Force.....I wish to extend my personal thanks to you for having brought the Society's attention to this need and having stayed with it through the vicissitudes of the decision process.

Thus, some 10 years of productive, deliberate and constructive activities were formally concluded. And progress surely has been made in practical as well as attitudinal realms. Although their representation is still low, women have become more active in many areas of APS work. And, behind the scenes, the Task Force has been able to advocate and effect a number of changes in governance which have benefitted not only individuals of both sexes but also the Society by opening up new avenues for participation.

M. Elizabeth Tidball
Member, Ad Hoc Group of Women Physiologists,
1970-1973
Chairperson, Task Force on Women in Physiology,
1973-1979

Professor of Physiology
George Washington University Medical Center
Washington, DC

September 1980

"WATCH THIS SPACE"

In order to plan effectively for the greater participation of women physiologists in their chosen discipline during the next decade, the PHYSIOLOGIST will feature a new, regular article in future editions. A caucus of Society members interested in these issues was formed at the FASEB, 1980 meeting in Anaheim, California. In the future, they will provide important and timely information on key legislative, education, employment and research opportunities and directions as they pertain to women scientists and those interested in their professional development. The participation of Society members in this effort is earnestly solicited and all ideas are welcome.

INTERNATIONAL SYMPOSIUM

DIETARY FIBRE IN HUMAN AND ANIMAL NUTRITION

An International Symposium on Dietary Fibre in Human and Animal Nutrition is to be held in Palmerston North, New Zealand from 23 to 28 May, 1982. The Symposium is being sponsored by the Royal Society of New Zealand and the International Union of Nutritional Sciences. The major purpose of the Symposium will be to review and to integrate the research being carried out in the broad areas of Dietary Fibre in Human Animal Health and Nutrition. The Symposium will bring together people with an up to date knowledge in such scientific disciplines as: Medicine, Physiology, Nutrition, Microbiology, Botany, Agronomy, Forestry, Biochemistry, Food Technology, and Epidemiology. The Organizing Committee will help participants in every way to get most value from the leisure time they have available during their visit to New Zealand and the South Pacific.

Interested persons are asked to write to: Secretariat, International Symposium on Dietary Fibre in Human and Animal Nutrition, University Extension, Massey University, P.O. Box 63, Palmerston North, New Zealand.

THIRTY-EIGHTH ANNUAL MEETING

AMERICAN PSYCHOSOMATIC SOCIETY

This meeting will be held on March 26-29, 1981 at the Hyatt Regency, Cambridge, Massachusetts. The Program Committee invites abstracts of original work to be considered for presentation. The deadline for submission of abstracts is November 14, 1980. The Committee would like contributions from the entire spectrum of the basic and clinical sciences related to psychosocial issues in the psychosomatic area, in the broadest sense of the word.

The program will also include a section of Brief Communications of 10 minutes each, reporting up-to-date findings. The deadline for these is February 2, 1981.

Please contact Dr. Franz Reichsman, Chairman, American Psychosomatic Society, 265 Nassau Road, Roosevelt, N.Y. 11575. Tel.: (516) 379-0191

From the Publications Desk

HANDBOOK OF PHYSIOLOGY
1959 - 1978

Through its *Handbook of Physiology* series, the American Physiological Society has undertaken to provide students, teachers, and investigators with "a critical, comprehensive presentation of physiological knowledge and concepts." As far as we can tell, this venture and its success are unique accomplishments: no other society of about 5000 members has published a large series (27volumes to date) on a self-supporting unsubsidized basis. Moreover, the series is continuing actively, not only with new topics but also with fresh new editions of the first three sections of the *Handbook of Physiology* currently in preparation. Therefore, now, about twenty years after the first volume appeared, it seems appropriate to review the components of this series to evaluate their worth, and to set goals for the next cycle.

The first volume in the *Handbook of Physiology* series was published in 1959. In its preface, goals for the series were defined:

> This *Handbook of Physiology,* like its predecessors from von Haller on, is designed to constitute a repository for the body of present physiolgical knowledge, systematically organized and presented. It is addressed primarily to professional physiologists and advanced students in physiology and related fields. Its purpose is to enable such readers, by perusal of any Section, to obtain a working grasp of the concepts of that field and of their experimental background sufficient for initial planning of research projects or preparation for teaching.
>
> To accomplish this purpose the editors have planned a book which would differ from textbooks in being more complete, more analytical and more authoritative. It would differ from a series of monographs in being organized on a consistent plan without important gaps between topics and with as nearly as possible the same relation of intensity of coverage to importance of topic throughout. It would differ from publications emphasizing new developments in that the background of currently accepted or classical concepts would be set forth, new ideas receiving not more than their due proportion of emphasis relative to the whole body of knowledge in the field. Finally it would differ from a collection of original papers on a series of topics in that it would provide an integrated condensation and evaluation of the material contained therein. Moreover, the overall plan provides that the key experimental findings in the development of each field of investigation be described and discussed in sufficient detail (with appropriate illustrations, quantitative data and adequate documentation) to make clear their nature, validity and significance for the fundamental concepts of the field. The success of this endeavor must be left to the reader's judgment.

The topics that have been covered to date are neurophysiology, circulation, respiration, adipose tissue, endocrinology, and renal and environmental physiology (Table 1). During the next ten years, most additions to the Handbook series will probably be revisions of present volumes. But, new volumes, e.g., skeletal muscle, are also in prospect.

Maurice B. Visscher initiated the idea of the Handbook project while a member of the Board of Publications Trustees (predecessor to the present Publications Committee). He and the other members of the Publications Trustees guided the Handbooks through the first round (Section 1). Beginning with Section 2, editorial responsibility for the series was delegated by the Publications Committee to a subcommittee, "the Handbook Editorial Committee" (Table 2). In 1979, the Publications Committee resumed direct responsibility for the Handbooks.

Although each Section has had a Section Editor and Executive Editor, the editorial arrangements have been far from uniform (Table 1). Different editors have varied their demand for preliminary outlines, draft manuscripts, and the formality of the review process. Until now, no indication has surfaced that one editorial arrangement works better than the others. The commitment of the editors and their editorial skills is undoubtedly more critical than any administrative arrangements either conceived by the Publications Committee or dictated by the editors.

The key element in the scientific quality of the Handbook series has been the selection of qualified contributors by the editors. The essential qualifications are expert knowledge of a particular area and writing skill. Once the editor is satisfied, the manuscript is turned over to the Publications office of the American Physiological Society for final revision. The copyediting of the *Handbooks* is given special care. Great effort is taken to provide consistent use of abbreviations, symbols, and the like throughout each volume and to produce a book that has a unity, and is more than a collection of articles. To ensure against any inadvertent changes in meaning, the author is given two opportunities to examine the text before it is published, one before the manuscript is sent to the printer to be set in type and a second time in the galley proof stage.

TABLE 1. Handbooks Published 1959 -1978

SECTION 1: *Neurophysiology*
Editor-in-Chief: J. Field
Section Editor: H. W. Magoun
Executive Editor: V.E. Hall
Volume I, 1959; Volume II, 1960; Volume III, 1960

SECTION 1: *The Nervous System* (formerly *Section 1: Neurophysiology*)
Section Editors: J. M. Brookhart and V. B. Mountcastle
Executive Editor: S. R. Geiger
Volume I, Parts 1 and 2-*Cellular Biology of Neurons,* 1977
Volume Editor: E. R. Kandel

SECTION 2: *Circulation*
Section Editor: W. F. Hamilton
Executive Editor: P. Dow
Volume I, 1962; Volume II, 1963; Volume III, 1965

SECTION 3: *Respiration*
Section Editors: W. O. Fenn and H. Rahn
Volume I, 1964; Volume II, 1965

SECTION 4: *Adaptation to the Environment,* 1964
Section Editor: D. B. Dill
Associate Editor: E. F. Adolph
Executive Editor: C. G. Wilber

SECTION 5: *Adipose Tissue,* 1965
Section Editors: A. E. Renold and G. F. Cahill, Jr.

SECTION 6: *Alimentary Canal*
Section Editor: C. F. Code
Executive Editor: W. Heidel
Editorial Committee: J. R. Brobeck, R. K. Crane, H. W. Davenport, M. I. Grossman, H. D. Janowitz, C. L. Prosser, T. H. Wilson
Volume I - Control of Food and Water Intake, 1967
Volume II - Secretion, 1967
Volume III - Intestinal Absorption, 1968
Volume IV - Motility, 1968
Volume V - Bile; Digestion; Ruminal Physiology, 1968

SECTION 7: *Endocrinology*
Section Editors: R. O. Greep and E. B. Astwood
Executive Editor: S. R. Geiger
Volume I - *Endocrine Pancreas,* 1972
Volume Editors: D. F. Steiner and N. Freinkel
Volume II, Part 1 and 2 - *Female Reproductive System,* 1973
Volume Editor: R. O. Greep
Volume III - *Thyroid,* 1974
Volume Editors: M. A. Greer and D. H. Solomon
Volume IV, Parts 1 and 2- *The Pituitary Gland and its Neuroendocrine Control,* 1974
Volume Editors: E. Knobil and W. H. Sawyer
Volume V - *Male Reproductive System,* 1975
Volume Editors: D. W. Hamilton and R. O. Greep
Volume VI - *Adrenal Gland,* 1975
Volume Editors: H. Blaschko, G. Sayers, and A. D. Smith
Volume VII - *Parathyroid Gland,* 1976
Volume Editor: G. D. Aurbach

SECTION 8: *Renal Physiology,* 1973
Section Editors: J. Orloff and R. W. Berliner
Executive Editor: S. R. Geiger

SECTION 9: *Reactions to Environmental Agents,* 1977
Section Editor: D. H. K. Lee
Associate Editors: H. L. Falk and S. D. Murphy
Executive Editor: S. R. Geiger

Table 2. Members of Editorial Committee

1958-1959	M. B. Visscher, Chairman; J. Field, A. B. Hastings, H. Rahn
1960	M. B. Visscher, Chairman; A. B. Hastings, H. Rahn
1961-1966	M. B. Visscher, Chairman; A. B. Hastings, J. R. Pappenheimer, H. Rahn
1967-1972	A. P. Fishman, Chairman through June 30, 1972; J. M. Brookhart, G. F. Cahill, Jr., C. L. Prosser, L. D. Carlson
1972-1978	J. R. Pappenheimer, Chairman through June 30, 1978; G. F. Cahill, Jr. (term expired June 30, 1974); H. W. Davenport (resigned August 12, 1974); T. H. Bullock (appointed January 1, 1977), R. E. Forster (appointed January 1, 1973), W. F. H. M. Mommaerts (appointed July 1, 1974)

When the project was begun, $250,000 was set as the limit of indebtedness that the American Physiological Society could afford, i.e., of costs over income. Despite inflation, this ceiling has not been reached (Figure 1). Indeed, for a while (1969 and 1970) income even exceeded costs. This positive balance occurred because no new volumes were published during those years. It has taken four to nine years to recover the costs of producing a section. The number of books printed of each edition is set to avoid excessive inventories. If the series were to be discontinued, it seems likely that sale of the inventory would more than defray the indebtedness.

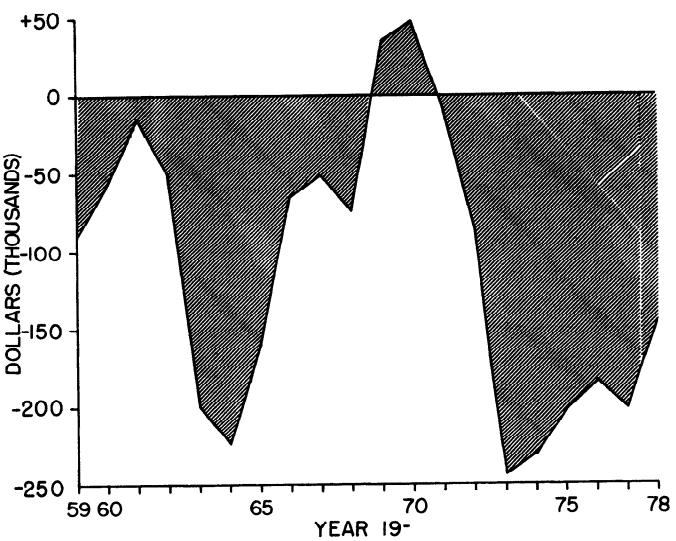


Fig. 1. Income to cost relationship of *Handbook of Physiology* +, income over cost; -, income below cost.

Through the end of 1978, 141,880 copies of the *Handbook of Physiology* had been sold, about half outside of the United States. Sales promotion and distribution have been handled by the Williams & Wilkins Company. Direct mail, advertising in journals, and displays at meetings, libraries, and schools have been utilized to increase sales. Copies are available at a discount to members of the American Physiological Society by direct order from the headquarters of the Society in Bethesda.

Type size and format have been selected to give excellent legibility; photographs are printed at fine resolution and with good tonal gradation on quality paper; and the bindings have been selected so that the volumes will withstand the heavy use to which they are subjected.

The period in which the *Handbook of Physiology* has been published has been a period in which major changes have occurred in the printing industry. The original volumes were composed by monotype and printed by letterpress. Monotype composition was used until the *Endocrinology* section was completed in 1976, although the books were printed by offset. This bastard system used negatives from illustrations rather than metal engravings. From 1976-1978 the pages were photocomposed and printed by offset. Electronic (cathode ray tube) composition has now replaced photocomposition.

The original volumes used a fine clear Baskerville typeface, with wide spacing between lines and broad margins. Halftones were prepared with a 133 line screen and printing was on quality 70 pound paper. With the switch to offset printing, finer resolution 150 line screen was introduced and the paper weight was reduced to 60 pound paper. (The next volume will utilize a still finer 200 line screen.) Although Baskerville was an excellent choice for monotype, its fineness often results in poor reproduction when photocomposition systems are used. Therefore, when the Handbooks were changed to photocomposition, the typeface was changed to the wider heavier Century typeface. With the beginning of the *Endocrinology* series, the number of words on a page was increased by decreasing the space between lines and the width of margins and the space between columns of text. Much automation has been introduced, for example, hyphenation and justification is now done by computer. Without the changes in printing technology and economics of spacing that have been introduced, the price of the volumes would be greater by far than it is.

In the twenty years that the series has existed, despite the great changes in printing technology, the legibility of the type, the quality of the illustrations, and the durability of the paper have not suffered.

Subject indexes for the first four Sections were prepared by Williamina A. Himwich. A subject index was not prepared for Section 5, *Adipose Tissue.* Instead, a single bibliography was prepared for all chapters and a subject and an author index were prepared for this biliography. Since Section 6, *Endocrinology,* the subject indexes have been prepared by Constantine J. Gillespie.

A constant concern of the Handbook Editorial Committee and Publications Committee is additions to and revisions of the sections. The problem is to identify areas of physiological interest that are sufficiently developed to warrant the extensive, in-depth coverage intended for the Handbook series. New developments in environmental physiology led to a new volume, *Reactions to Environmental Agents,* rather than a revision of *Adaptation to the Environment.* As new revisions come on to the horizon, a key question has been whether an update or a complete overhauling is in order. For example, when the time came for revisions of *Neurophysiology* and *Circulation,* one suggestion was that only one or two updating volumes were needed. However, this notion was rejected. Instead, the decision was reached that for the Handbooks to serve their purpose, they should provide a balanced overview of a field and not take the form of a state-of-the-art update.

The first three sections of the *Handbook of Physiology* dealt with *Neurophysiology, Circulation,* and *Respiration.* Each section was divided into two or three volumes. Later sections (*Alimentary Canal* and *Endocrinology*) were subdivided into more volumes. The revisions of the three original sections are following the later pattern with more individual volumes, each devoted to a particular subfield, (*The Nervous System* - Volume I: *Cellular Biology of Neurons,* Volume II: *Motor Control,* Volume III: *Sensory Processes,* etc.). Each volume has its own volume editor or editors. This gradual switch in the organization of the Sections may influence future revision and buying patterns. Thus, from the point of view of the Publications Committee, it will now be easier to update a single volume if the rest of the field does not warrant a reappraisal in the Handbook series. For the consumer, the change makes available a single volume of special interest rather than the entire section. The latter option may have important implications in the years ahead as increasing publishing costs make the purchase of a complete large section prohibitive for some individuals.

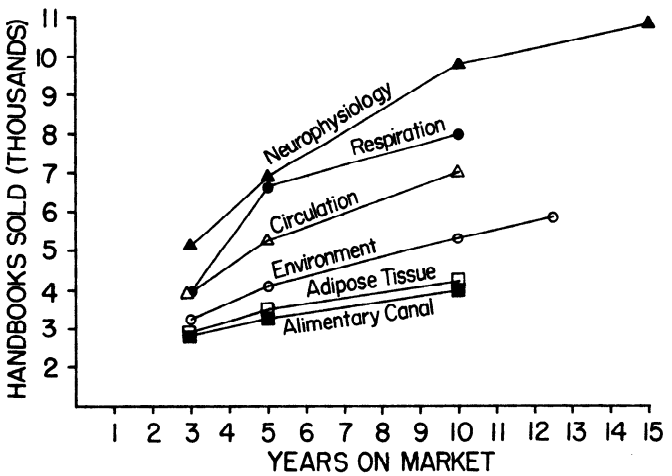


Fig. 2. Average sales per volume of sections more than 5 years old at 3, 5, 10, and 15 years after completion of section.

Against this background, we return to the question of the future direction of the Handbook series. As indicated above, according to sales, the series is well off. But, sales are not the total answer for a learned society. Sales (Figure 2) are a function of the size of a scientific discipline, quality of the publication, length of time since publication, price, and the availability of competing volumes. It is difficult to measure the success (use) of a volume from sales figures alone, although continued demand for the books is a healthy sign. Book reviews are another useful evaluation. Well-worn library copies are encouraging qualitative indices of use. Unfortunately, all of these criteria do not dictate the optimal direction for future Handbooks.

We direct you to the questionnaire and look forward to hearing from you.

SURVEY OF DEPARTMENTS OF PHYSIOLOGY

Association of Chairmen of
Departments of Physiology

ANALYSIS OF ACDP QUESTIONNAIRE - 1979

TOTAL QUESTIONNAIRES	1974	1975	1976	1977	1978	1979
Total Questionnaires Returned	96	91	87	78	102	101
A. Medical School	88	81	81	74	85	89
Other	6	10	6	4	17	12
B. Public	65	65	56	49	63	63
Private	29	29	31	29	34	38

ACADEMIC POSITIONS (Mean/Dept.)	1974	1975	1976	1977	1978	1979	1979 Medical School Only
Professors (Including Chairmen)	4.2	4.7	4.9	4.9	4.4	4.6	4.5
Professors (Excluding Chairmen)	3.3	3.7	3.9	3.9	3.4	3.6	3.6
Associate Professors	3.5	3.6	3.9	5.0	3.4	3.0	3.1
Assistant Professors	4.1	4.5	4.3	4.2	3.6	3.3	3.4
Instructors	0.7	0.7	0.5	0.6	0.5	0.4	0.4

UNFILLED POSITIONS	1974	1975	1976	1977	1978	1979	1979 M.S.	1979 Other
Chairmen						1	1	
Professor	12	17	7	6	4	12	8	4
Associate Professor	23	17	11	14	11	22	20	2
Assistant Professor	39	43	39	42	55	58	54	4
Instructor	2	4	4	8	2	4	2	2

FACULTY STATISTICS (Mean/Dept)	1976	1977	1978	1979 M.S.	1979 Other
Full time paid positions	12.9	12.4	12.0	12.6	8.3
Part-time paid positons	1.0	1.1	1.1	0.5	2.7
Joint appointments	1.2	1.1	1.1	0.7	0.8
Joint appointments paid by other sources	.8	.7	4.7	5.1	2.2
Total Faculty Positions	18.6	15.8	18.6	19.2	14.2
Tenure Positions[1]				10.6	8.3
Non-tenure Positions				7.4	8.6

FRINGE BENEFITS[2]	1976	1977	1978	1979 M.S.	1979 Other
Percentage rate of fringe benefits (n = 65)	16	13	---	--	--

SPACE[3]	1978
Non-teaching space (mean, n = 81)	15,230

[1]New question in 1979
[2]Not asked in 1978 or 1979
[3]Only asked in 1979

GRADUATE PROGRAMS AND POSTDOCTORAL FELLOWS

	1975	1976	1977	1978	1979 Medical School	1979 Other
Ph.D. degrees granted	189	152	134	232	138	29
Mean	3.2	1.8	1.7	2.3	1.6	2.4
Ph.D. candidates enrolled	1124	1046	832	1040	856	101
Mean	14.4	12.6	10.6	10.2	9.6	8.4
Postdoctoral Fellows (Current)	299	404	323	482	454	22
Mean	5.4	4.8	4.3	4.7	5.1	1.8
Postdoctoral Fellows (completing training before June 30)	132	100	111		101	8
Mean	1.6	1.3	1.1		1.1	0.7
Vacant postdoctoral positions	45	51	59		76	2
Predoctoral Training Grants - YES	35	23	32		32	2
NO	47	54	65		55	10
[1]Postdoctoral Training Grants- YES			34		31	3
NO			63		56	9

[2]DEPARTMENTS OFFERING COURSES IN ALLIED HEALTH

Dentistry	16
Pharmacy	11
Nursing	30
Other (Physical Therapy, Occupational Therapy Medical Technology, Dental Hygiene, Radiation Technology, Nuclear Medicine, etc.)	29

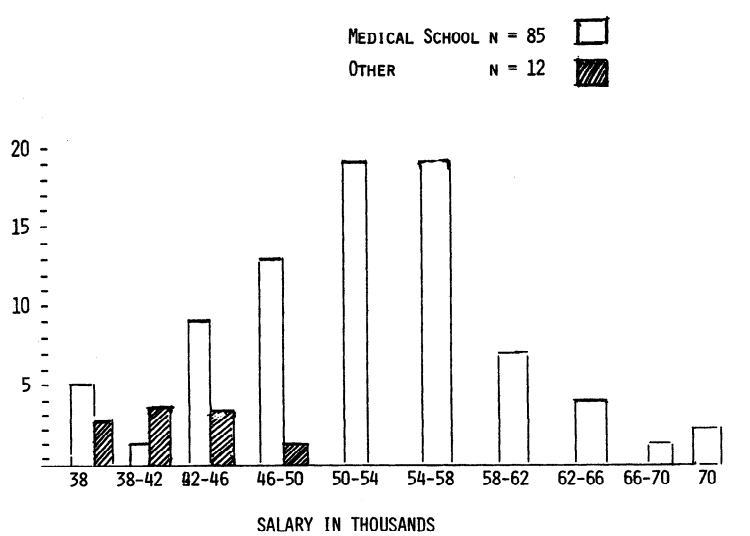
BUDGET (Nearest Thousand - Mean)

	1975	1976	1977	1978	1979	n
Institutional Sources	351	378	420	456	459	97
Research Grants	392	502	438	541	627	94
Training Grants	38	44	37	100	133	40
Budget support other than above	40	26	22	123	141	45
TOTAL	821	950	917	1065	1175	97

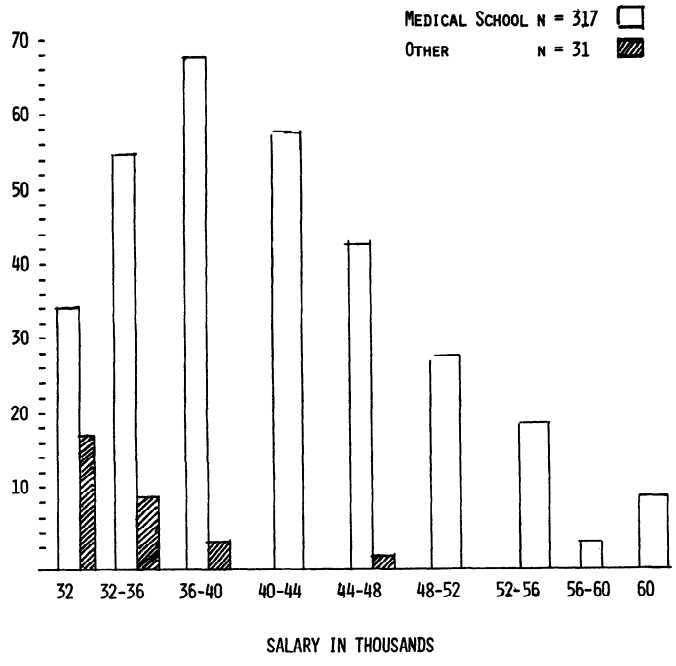
SALARIES (Mean/Thousands)	1977	N	1978	N	1979	N	Starting Range[3]	N
Chairman	43.3	73	47.5	95	51.1	95	--	--
Professors	31.2	296	36.6	346	40.0	348	31.9	70
Associate Professors	26.3	273	29.6	349	30.2	299	25.9	72
Assistant Professors	21.1	280	23.6	363	24.4	327	20.3	74
Instructors	16.0	30	16.5	48	17.5	41	15.5	40

[1]New question in 1978
[2]Not asked in 1978 or 1979
[3]New question in 1979

CHAIRMEN - 1979

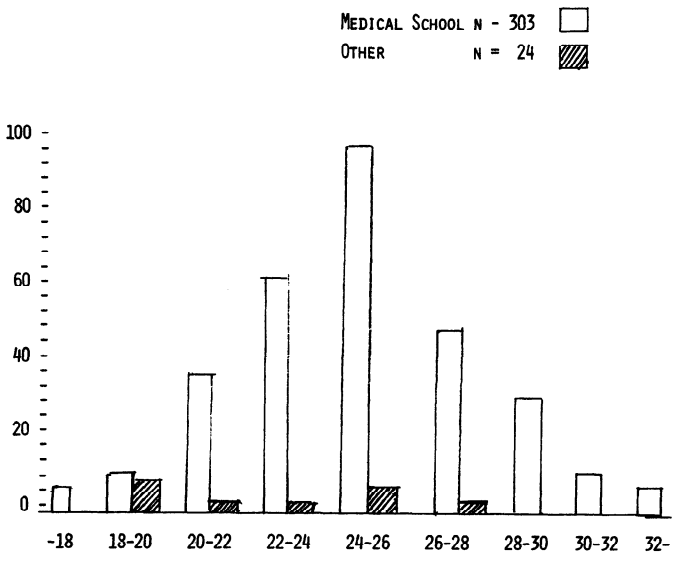


PROFESSORS - 1979



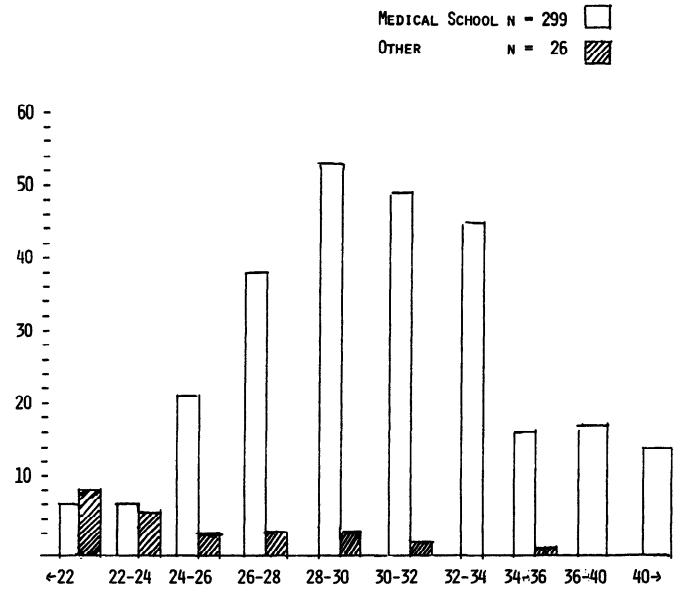
SALARY IN THOUSANDS

ASSISTANT PROFESSORS - 1979



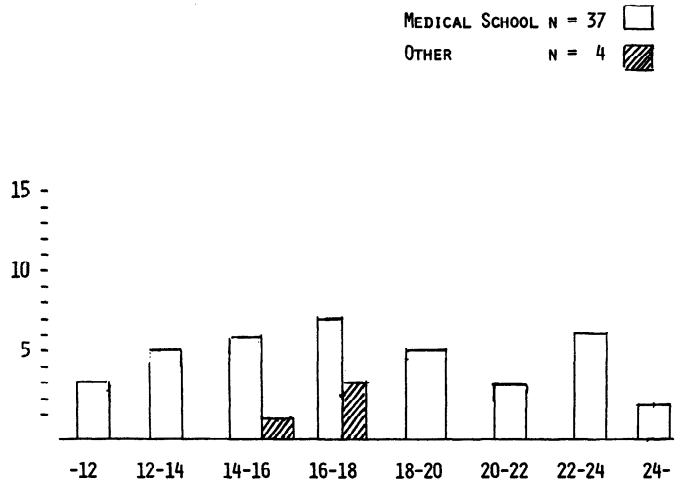
SALARY IN THOUSANDS

ASSOCIATE PROFESSORS - 1979



SALARY IN THOUSANDS

INSTRUCTORS - 1979



SALARY IN THOUSANDS

RETIRED PHYSIOLOGISTS: AN UNTAPPED RESOURCE

Donald M. Miller

The Department of Physiology at Southern Illinois University has always been rather small, oscillating somewhere around nine faculty members for approximately fifteen years. In 1978, we had just completed the search process and hired a new department head when we lost three faculty members. One was an expected retirement, a second loss was due to an unfortunate illness and a third was due to a resignation. In addition to these three vacancies, relationships with the newly formed SIU School of Medicine was somewhate critical and our administration expressed extreme concern over the reduced staffing of the Department. To heighten the dilemma, these events occurred at the beginning of the fall semester.

The time required for a second search process would have been intolerably long to have helped with that school year. In addition, it was felt that it would be advantageous in the long run if we could have waited out the evolving interactions with the Medical School and then conduct a careful search process for new staff members. Nevertheless, at the same time the immediate needs of the curriculum and graduate program had to be met.

In the course of a meeting between faculty and administration to discuss the problems, I suggested SIU capitalize on the skills of retired physiology members and hire them for a one-year period. At the time I had in mind a senior statesman of APS, who I knew had retired and thought he might be willing to accept a one-year appointment. "That's an excellent suggestion but won't that be difficult this late in the game," someone said to which I answered, "Not at all." I had no sooner finished when I heard the reply, "Good Don, why don't you try to get us someone as soon as possible." I usually follow the old army adage of keeping my mouth shut and never volunteering for anything, but there I was sitting with my mouth open and nodding my head yes.

I thought that I would make short shrift of this affair and immediately put in a long distance call to my senior colleague recently retired. After an exchange of amenities, he informed me that he had already accepted a position in the southwest. Now I was back to where I started and I had myself a predicament.

What does one do I thought, when one would like to find those physiologists who have recently retired and whether or not they are in the market for a one-year position. While sitting and musing over this pillow problem, my thoughts wandered back to earlier days when F.R. Steggerda would say, "Students, you must keep up with the news about the great physiologists by reading *The Physiologist.*" This fond remembrance jarred my mind and I immediately wrote to the Director of FASEB's Life Science Research office, Ken Fisher, whom I had known several years and explained my problem.

He put me in contact with the APS Executive Secretary and Treasurer, Dr. Orr E. Reynolds. Not long after that I received a list of physiologists who were retiring along with information on their areas of interest and present address. On that list was the name of Dr. Warren Rehm. I provided the administration with the data on Dr. Warren Rehm, found he was both interested and available. Subsequently he was hired for a one-year position.

As things turned out, Dr. Rehm was an excellent choice: he taught two courses and gave many guest lectures during his stay and brought to SIU-C a fresh perspective. Being an ex-department head, he also demonstrated great finesse and administrative skill in dealing with both the University officials and department faculty. In addition he had a very fresh view of several current physiological concepts. Certainly we all speak with a certain degree of reverence when we discuss acid secretion by the stomach and many of us *think* that we understand Mitchell's Chemio-osmotic hypothesis.

The moral to this short story is that the retired physiologists form a large pool of potential help. They are an under-utilized resource of APS which is available in all areas of expertise, available for adaptable periods of time, and requiring no training or warm-up period. If you find yourself in such a position, I recommend that you contact Dr. Reynolds at APS headquarters and request information on recently retired physiologists. With the new computerized facilities of FASEB available to APS, a list of expert senior scientists is yours for the asking. Retired members of APS have immeasurable skills and expertise that should not be overlooked.

Editor's Note: For about twenty years APS has maintained a biographical index on its members. First initiated by Ray Daggs in 1961, with guidance by a committee chaired by James D. Hardy, the index was carried on McBee cards. As technology of data processing has grown, and the membership numbers as well, the index has become more accessible and useful for a variety of purposes. One of these uses is portrayed in the foregoing article. Other uses have been the make up of society committees, producing specifically oriented mailing lists, providing lists of potential candidates for governmental peer review committees and others.

The index however is only as useful as the biographical information is accurate and up to date. Members who have not done so recently, or who have experienced recent changes in the nature of their work or interests are urged to complete the Membership Records Questionnaire printed on page 21.

To expedite entry of the data into the computer, please affix, in the space provided on the questionnaire, the mailing label used for mailing this publication or; write in that space the first six digits appearing in the upper left corner of the label.

THE AMERICAN PHYSIOLOGICAL SOCIETY
9650 Rockville Pike, Bethesda, MD 20014

MEMBERSHIP RECORDS QUESTIONNAIRE

PLEASE MARK ALL ENTRIES IN RED.

CURRENT MAILING LABEL OR
PRINT NAME & ADDRESS

DATE _____

DATE OF BIRTH
Month Day Year

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

OPTIONAL PERSONAL DATA
SEX
☐ Female ☐ Male
A ☐ American Indian or Alaskan Native
B ☐ Asian or Pacific Islander
C ☐ Black
D ☐ White E ☐ Hispanic

POSITION TITLE CODE (SEE REVERSE) ☐☐

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

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

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

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

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

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

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

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

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

☐☐ MAJOR AREA ☐ SPECIFIC INTEREST

SECONDARY INTEREST AREA (If appropriate)

☐☐ MAJOR AREA ☐ SPECIFIC INTEREST

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

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

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

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

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

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

POSITION TITLE CODES (use most closely related description)

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

EARNED DEGREE CODES

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

INTEREST AREA CODES

01. Anesthesia

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

03. Anthropology

04. Biochemistry
A. General
B. Clinical

05. Biophysics

06. Biomedical Engineering

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

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

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

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

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

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

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

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

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

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

17. General Physiology

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

19. Immunology

20. Liver and Bile

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

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

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

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

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

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

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

27. Pathology

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

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

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

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

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

99. Other
Z. Other

INSTRUCTIONS FOR APPLYING FOR APS MEMBERSHIP

CURRENT APPLICATION FORMS

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

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

GENERAL INSTRUCTIONS

FOR ALL CATEGORIES:

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

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

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

Send no reprints.

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

QUALIFICATIONS (Except Students):

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

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

SPONSORS:

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

Each sponsor should write an independent confidential letter about the candidate using the five categories listed above to evaluate the candidate.

CHECK LIST:

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

Executive Secretary
American Physiological Society
9650 Rockville Pike
Bethesda, Maryland 20014

SPECIAL INFORMATION AND INSTRUCTIONS

FOR REGULAR MEMBERSHIP

Bylaws of the Society:

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

IF ALIEN: Please attach a letter and 7 copies stating visa status and type of passport and giving evidence of intent to stay in North America.

Duties and Privileges:

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

FOR CORRESPONDING MEMBERSHIP

Bylaws of the Society:

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

Duties and Privileges:

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

FOR ASSOCIATE MEMBERSHIP

Bylaws of the Society:

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

Duties and Privileges:

Same as for Regular Members except for the privilege of:

1. Holding Executive Office, or membership on certain committees.
2. Voting at Society Meetings.
3. Sponsoring New Members.
4. Receiving the Daggs Award.
5. Selection as Bowditch Lecturer.
6. Sponsoring papers of which he/she is not an author.

FOR STUDENT MEMBERSHIP

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

Bylaws of the Society:

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

Duties and Privileges:

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

Submit original and 7 copies of application and supporting documents.

APPLICANT'S LAST NAME _____

Date _____

THE AMERICAN PHYSIOLOGICAL SOCIETY
9650 Rockville Pike, Bethesda, MD 20014

MEMBERSHIP APPLICATION FOR:

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

CURRENT MEMBERSHIP
CATEGORY; YEAR ELECTED _____

See Instructions

Name of Applicant: _____
First Middle Last

Mailing _____ Birth Date: _____

Address _____ Citizenship: _____

_____ Country of Permanent Residence:* _____

_____ Telephone No.: _____

*Alien residents of North America attach 8 copies of Alien Registration Card or other evidence of intent to remain in North America.

1. EDUCATIONAL HISTORY

Dates	Degree	Institution	Major Field	Advisor

Doctoral Dissertation Title:
(if any)

Postdoctoral Research Topic:

2. OCCUPATIONAL HISTORY

Present Position:

Prior Positions:

Dates	Title	Institution	Department	Supervisor

SPONSORS

#1. Name: _____

Mailing Address: _____

_____

_____

_____

Telephone No. Zip Code

#2. Name: _____

Mailing Address: _____

_____

_____

_____

Telephone No. Zip Code

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

#1 Signature _____ #2 Signature _____

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

(over)

APPLICANT'S LAST NAME _____

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

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

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

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

List other scientific societies of which candidate is a member:

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

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

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

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

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

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

Editor: Orr E. Reynolds, Education Office, APS
Associate Editors: Edward M. Eisenstein, Dept. Biophys., Michigan State Univ.
Robert E. Fellows. Dept. Physiol. & Biophys., Univ. of Iowa
Mary Forsling, Middlesex Hosp. Med. Sch., London, U.K.
Ann E. Kammer, Div. Biol., Kansas State Univ.
Charles S. Tidball, Dept. Physiol., George Washington Univ. Med. Ctr.
Executive Editor: M.C. Shelesnyak, A.P.S.

THE PHYSIOLOGY TEACHER

COPING WITH COMPUTER TERMINOLOGY

Charles S. Tidball
Dept. of Physiology
The George Washington University Medical Center
Washington, D.C.

Computer science, like other disciplines, has evolved a language of its own. Some of this development consists of words in general use which have taken on restricted meanings when used in a computer related context; more often, totally new expressions have emerged. Many of the new terms are acronyms which means pronounceable words formed from the letters of other words, for example: FORTRAN, the name of a computer language which accomplishes mathematical FORmula TRANslations; other terms consist of the initial letters of compound terms, for example: TV which is easier to say than TeleVision, or CRT than Cathode Ray Tube. In order to enable persons approaching the subject for the first time to acquire a sense for computer terminology as rapidly as possible, a Glossary has been developed. Many of the definitions in the Glossary contain other terms from the Glossary in context. The terms most frequently used are considered a Basic Vocabulary and are presented in the three paragraphs which follow. These are the terms printed in bold-faced type; it should be possible to derive their meaning from the way they are used in the paragraphs. Definitions for these terms are also contained in the Glossary at the back of the volume.

Computers are machines which have been designed to perform complex tasks with a minimum of human intervention. Because of their speed, their retention power, and their ability to perform tasks like human beings, computers are occasionally personified; but it should be emphasized that they remain machines. There are two general varieties of computers: **analog** and **digital. Analog** computers utilize continuously variable physical quantities, such as electrical voltages and different electronic units, to represent the elements in a problem to be solved. The process of measurement is used to arrive at a final answer which can often be read directly from a meter or other **analog** device. By contrast, **digital** computers utilize **binary,** a discontinuous numerical system consisting only of zeros and ones, to represent the elements in a problem. The way in which the numbers must be manipulated to arrive at a solution is **programmed** into the machine and the process of counting is used to obtain intermediate and final answers. Both **analog** and **digital** computers have been used to solve problems of interest to physiologists; but when the word computer is used without a modifier, it generally refers to a **digital** computer.

An important distinction is made between that part of a computer physically present as equipment, referred to as **hardware,** and that part of a computer representing **instructions** to the equipment and designated **software.** Major subdivisions of each of these parts are recognized. **Hardware** exists either as a central processing unit, called **CPU** for short, or as **peripheral devices.** The **CPU** contains elements which keep track of what the computer is doing, store intermediate results, and perform calculations. Some of the storage is done in the **CPU** in electronic units called **memory** which can be **accessed** very quickly. Less expensive retention, with somewhat slower retrieval capabilities, is contained in **peripheral devices** known as **mass storage units.** Another example of a **peripheral device** is a computer **terminal** which consists of a keyboard and a display device similar to a television screen. A **terminal** may be used either to **access** data which are stored in the computer or to generate **instructions** to the computer, a process known as **programming.** Because of miniaturization and advances in electronics, a complete **microcomputer** can now be contained in the same space as a portable television set.

Software exists in three main categories: **operating systems, computer languages,** and **application programs. Operating systems** contain utilities which automatically perform repetitive tasks that would be tedious for a human operator to undertake. In some instances because computers are able to **execute** millions of **instructions** per second, human operators would be unable to accomplish system tasks rapidly enough to insure satisfactory computer utilization. Therefore, **computer languages** have been developed to improve the communication between human beings and these machines. For reliability and to maintain high operational speed the internal manipulations of computers are carried out in a **binary** language, consisting only of zeros and ones. Some **computer languages** are close to **binary** language but the so-

called **high-level languages** have been designed to facilitate **programming** the solution of different kinds of **computer applications.** An **application program,** such as the **instructions** to generate a payroll, is the specific solution to a **computer application** as it has been **programmed** in the most appropriate **computer language.** Just as one does not need to know how to build an automobile in order to drive it, the user of a computer does not need to know how **programming** is accomplished or how the different elements of **software** collaborate to make computer utilization efficient. Because of the multiplicity of intricate tasks performed, especially for larger and more complex **computer applications, programming** has become a substantive intellectual activity.

This completes the presentation of the Basic Vocabulary which has introduced you to twenty terms. A summary of these concepts and a complete listing of the Basic Vocabulary in alphabetical order is provided below. For those interested in the techniques used to develop the Glossary and the Basic Vocabulary, a description is provided in an Appendix to the Glossary along with a few references to other sources of computer definitions.

SUMMARY

Two kinds of computers: **analog** and **digital**

Two parts of a digital computer: **hardware** and **software**

Two subdivisions of hardware: **CPU** and **peripheral devices**

Two kinds of retrieval units: **memory** (fast but expensive) and **mass storage** (of larger capacity and capable of being removed from the machine)

Three kinds of software: **operating systems, computer languages** and **application programs**

Two kinds of computer languages: **binary** (the machine's own language) and **high-level languages** (optimized for undertaking specific human tasks)

Two tasks which can be **executed** on computers: **access** to data stored in the computer and **programming** (generating **instructions** to the machine for the solution of a **computer application**)

Two different units that look similar: **terminal** (a **peripheral device** which must be connected to the computer to perform useful work) and **microcomputer** (a small, full-capability, **digital** computer)

ALPHABETICAL LIST OF TERMS IN BASIC VOCABULARY

(The terms in the Basic Vocabulary are used so frequently in the Glossary definitions that it will be a distinct advantage to readers to master this list of terms before attempting to use the Glossary.)

access
analog
application program
binary
computer application
computer language
CPU
digital
execution
hardware
high-level language
instruction
mass storage
memory
microcomputer
operating system
peripheral device
programming
software
terminal

AN ANNOUNCEMENT

This message, sandwiched between two articles on computer science by Professor Charles S. Tidball, *Coping with Computer Terminology* and *Overview of Computer Hardware,* is to alert the reader of a forthcoming publication:

FRONTIERS IN THE TEACHING OF PHYSIOLOGY: COMPUTER LITERACY AND SIMULATION

A series of articles was started in *The Physiology Teacher* Section of *The Physiologist,* Vo. 21, No. 6 under the Guest Editorship of Dr. Tidball. As the series developed and some other material appeared in *The Physiology Teacher,* it became clear that issuing a reprint of the collected papers with some additional articles and a glossary of terms relevant to the field was warranted. The volume is the product of the original articles, added matrix material, and some thoughts on the general subject of computers and laboratory teaching.

The collection has also stimulated a plan to consider development of other "reprint series" on various teaching (and historical) subjects. Precedence for reprinting collected papers from *The Physiologist* was made in 1973. Interestingly, the subject was "Computer Assisted Education" and Dr. Tidball played a leading role. This collection of articles initiates a new series which we plan to pursue on the general subject of physiology teaching. It has also stimulated some contemplation on current problems associated with the teaching of physiology to future physiologists who will engage in teaching and research, and to medical students who will a) practice medicine or b) engage in medical research or c) undertake both.

The contents of *Frontiers in the Teaching of Physiology: Computer Literacy and Simulation* include:

An affirmation of Conventional Physiology Laboratory Exercises - C. S. Tidball
Coping with Computer Terminology - C. S. Tidball
An Overview of Computer Hardware - C. S. Tidball
Doctors, Digits and Disks - C. S. Tidball
The Analog (Computer) as a Physiology Adjunct; Part 1 - P. A. Stewart
Teaching Computer Literacy and Physiological Simulation - C. S. Tidball
The Analog (Computer) as a Physiology Adjunct; Part 2 - P. A. Stewart
Teaching by Simulation with Personal Computers - J.E. Randall
A computer Model of the Cardiovascular System for Effective Learning - C. F. Rothe
Computer Simulation in the Physiology Laboratory - S. Katz, R. G. Hollingsworth, J. G. Blackburn, and H. T. Carter
A Digital Computer Simulation of Cardiovascular and Renal Physiology - C. S. Tidball
Physiological Simulation: An Assessment of its Advantages as Well as its Limitations - R. A. Standing and C. S. Tidball
The volume is edited by Charles S. Tidball and M. C. Shelesnyak.

The format is based on *The Physiologist.* The volume is approximately 64 pages, including an extensive bibliography and an index. It will be available from the American Physiological Society, Education Office, 9650 Rockville Pike, Bethesda, MD 20014 for $7.50 prepaid.

called **high-level languages** have been designed to facilitate **programming** the solution of different kinds of **computer applications.** An **application program,** such as the **instructions** to generate a payroll, is the specific solution to a **computer application** as it has been **programmed** in the most appropriate **computer language.** Just as one does not need to know how to build an automobile in order to drive it, the user of a computer does not need to know how **programming** is accomplished or how the different elements of **software** collaborate to make computer utilization efficient. Because of the multiplicity of intricate tasks performed, especially for larger and more complex **computer applications, programming** has become a substantive intellectual activity.

This completes the presentation of the Basic Vocabulary which has introduced you to twenty terms. A summary of these concepts and a complete listing of the Basic Vocabulary in alphabetical order is provided below. For those interested in the techniques used to develop the Glossary and the Basic Vocabulary, a description is provided in an Appendix to the Glossary along with a few references to other sources of computer definitions.

SUMMARY

Two kinds of computers: **analog** and **digital**

Two parts of a digital computer: **hardware** and **software**

Two subdivisions of hardware: **CPU** and **peripheral devices**

Two kinds of retrieval units: **memory** (fast but expensive) and **mass storage** (of larger capacity and capable of being removed from the machine)

Three kinds of software: **operating systems, computer languages** and **application programs**

Two kinds of computer languages: **binary** (the machine's own language) and **high-level languages** (optimized for undertaking specific human tasks)

Two tasks which can be **executed** on computers: **access** to data stored in the computer and **programming** (generating **instructions** to the machine for the solution of a **computer application**)

Two different units that look similar: **terminal** (a **peripheral device** which must be connected to the computer to perform useful work) and **microcomputer** (a small, full-capability, **digital** computer)

ALPHABETICAL LIST OF TERMS IN BASIC VOCABULARY

(The terms in the Basic Vocabulary are used so frequently in the Glossary definitions that it will be a distinct advantage to readers to master this list of terms before attempting to use the Glossary.)

access
analog
application program
binary
computer application
computer language
CPU
digital
execution
hardware
high-level language
instruction
mass storage
memory
microcomputer
operating system
peripheral device
programming
software
terminal

AN ANNOUNCEMENT

This message, sandwiched between two articles on computer science by Professor Charles S. Tidball, *Coping with Computer Terminology* and *Overview of Computer Hardware,* is to alert the reader of a forthcoming publication:

FRONTIERS IN THE TEACHING OF PHYSIOLOGY: COMPUTER LITERACY AND SIMULATION

A series of articles was started in *The Physiology Teacher* Section of *The Physiologist,* Vo. 21, No. 6 under the Guest Editorship of Dr. Tidball. As the series developed and some other material appeared in *The Physiology Teacher,* it became clear that issuing a reprint of the collected papers with some additional articles and a glossary of terms relevant to the field was warranted. The volume is the product of the original articles, added matrix material, and some thoughts on the general subject of computers and laboratory teaching.

The collection has also stimulated a plan to consider development of other "reprint series" on various teaching (and historical) subjects. Precedence for reprinting collected papers from *The Physiologist* was made in 1973. Interestingly, the subject was "Computer Assisted Education" and Dr. Tidball played a leading role. This collection of articles initiates a new series which we plan to pursue on the general subject of physiology teaching. It has also stimulated some contemplation on current problems associated with the teaching of physiology to future physiologists who will engage in teaching and research, and to medical students who will a) practice medicine or b) engage in medical research or c) undertake both.

The contents of *Frontiers in the Teaching of Physiology: Computer Literacy and Simulation* include:

An affirmation of Conventional Physiology Laboratory Exercises - C. S. Tidball
Coping with Computer Terminology - C. S. Tidball
An Overview of Computer Hardware - C. S. Tidball
Doctors, Digits and Disks - C. S. Tidball
The Analog (Computer) as a Physiology Adjunct; Part 1 - P. A. Stewart
Teaching Computer Literacy and Physiological Simulation - C. S. Tidball
The Analog (Computer) as a Physiology Adjunct; Part 2 - P. A. Stewart
Teaching by Simulation with Personal Computers - J.E. Randall
A computer Model of the Cardiovascular System for Effective Learning - C. F. Rothe
Computer Simulation in the Physiology Laboratory - S. Katz, R. G. Hollingsworth, J. G. Blackburn, and H. T. Carter
A Digital Computer Simulation of Cardiovascular and Renal Physiology - C. S. Tidball
Physiological Simulation: An Assessment of its Advantages as Well as its Limitations - R. A. Standing and C. S. Tidball
The volume is edited by Charles S. Tidball and M. C. Shelesnyak.

The format is based on *The Physiologist.* The volume is approximately 64 pages, including an extensive bibliography and an index. It will be available from the American Physiological Society, Education Office, 9650 Rockville Pike, Bethesda, MD 20014 for $7.50 prepaid.

OVERVIEW OF COMPUTER HARDWARE

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The development of the digital computer has stimulated one of the more dramatic growth industries known. This however would not have been possible without an equally impressive development in electronics technology. It is not easy to describe briefly these two rapidly moving developments which have brought about The Age of Technology. At the insistence of my co-editor, I have made the attempt, with an apology at the outset, to readers involved in this development and who may have preferred a different presentation.

The first modern computer, the Mark I, was developed at Harvard University starting in 1939. It took five years to assemble and was physically quite bulky. Because the electromagnetic relay was the basis for storing information, calculations were slow and power requirements were substantial (1). A successor, the ENIAC, built at the University of Pennsylvania utilized the vacuum tube as a storage and switching device and became the first electronic computer. It was developed in only three years because of military urgency and a perceived need for such a computational device by the Services. The vacuum tube acted so much faster than the electromagnetic relay that ENIAC could perform computations about a thousand times more rapidly. However, this machine was limited because it took several people several days to set up a problem for calculation. This process involved making hundreds of wired connections (2). The next stage in the development was the ability to store the instructions to the machine in the computer's memory and to obviate the complex set up procedure. Such machines included the first commercial stored-program computer built by Sperry-Rand, UNIVAC, and were put in operation in the early 1950's (1).

Two other features were crucial to the rapid development and improvement of this technology. The first of these was the introduction of binary number representation; and the second was increasing miniaturization of electronic components. Numerical representation is discussed in Chapter Four. Miniaturization made possible significant advances because it permitted simplicity of design, increased speed of operation, and decreased power requirements with subsequent reduction in heat generation. This progress in electronics which led from the vacuum tube, to the transistor, to the integrated circuit, and now to large scale integration, or LSI technology, has brought spectacular improvements in cost, speed, and size of storge in less than 30 years. The following tabulation, based on IBM products (3), dramatically reveals these improvements.

TABLE I

Year	Model	Cost*	Speed+	Storage#
1952	701	$221,867	2,193	400
1959	1401	105,600	4,166	100
1964	360	28,800	12,000	8
1976	370	3,800	43,000	0.3
1979	4341	430	239,120	0.03

* Rental cost per month for one megabyte of storage
\+ Processor speed in multiplications per second
\# Number of cubic feet required for one megabyte of storage

There are many different kinds of computers. The range encompasses the smallest units which are used in wrist watches to the so-called super computers that may cost tens of millions of dollars. In addition to cost and space requirements there are various convenient measures of computer size which enable certain distinctions to be made. One of these is memory capacity. Another, more fundamental measure, is the length of the computer word. Most computers have a fixed word length which means that the registers in the machine and the individual locations in memory can only store as many items, (called bits), of binary information as the length of the computer word in that particular computer. Smaller, less powerful, computers tend to have shorter computer words. The extent of memory and mass storage can also be used to describe the size of a computer. Memory and mass storage are measured in bytes. The standard byte contains 8 bits; and since this is usually the amount of information needed to code a number or a letter, the term byte can be equated to character. Using information from Weitzman (4) and other sources, the following table has been derived to show the interrelationships among some of these variables.

TABLE 2

Verbal Description	Number of Bits in Computer Word	Number of Bytes* of Memory	Number of Megabytes of Mass Storage	Approximate Cost
Microcomputer	4 - 8	4K - 64K	1	$10,000
Minicomputer	12 - 24	32K - 256	10	$ 10,000 - 100,000
Midicomputer	16 - 36	64K - 1,2M	100	$100,000 - 1,000,000
Maxicomputer	32 - 60	0.5M	1,000	> $1,000,000

* The letters K and M are used to designate thousand or bytes or millions of bytes (megabytes) respectively.

The table above should be taken only as an approximation because development is proceeding so rapidly that the microcomputer of tomorrow will have more power and speed than the minicomputers of only a few years ago, and this will be accomplished at continuing decreases in hardware cost. Regrettably, the costs of using computers, which are inherently personnel costs, are growing steadily as more diverse ways are found to make these machines useful to society and as increasing specialization occurs in the various categories of jobs that have been created by this developing industry.

It would be appropriate to characterize ways in which computers are used. Initially, computers were used to compute ballistic trajectories; and later, simple scientific and business-oriented problems. To maximize machine efficiency these jobs were submitted in a sequential batch mode, a technique of data processing which has come to be known as batch-processing. In this style of computing, the job resides in the machine only as long as it is necessary to perform the computations and generate the desired output. An alternative approach permits a number of users to appear to have simultaneous access to the machine and is designated time-sharing. The latter is especially useful for those

categories of computing which require frequent consultation with data or programs stored in the computer. The advent of smaller, less expensive machines occasionally blurs the distinctions between batch-processing and time-sharing. It is possible to indicate the growth in complexity of computer applications in graphic form. Figure 1 is reprinted from Weitzman (4) by permission. As one goes from the center of the figure outward, one encounters the subdivisions of machine operation, and, eventually in the outer circle, the multiplicity of computer applications which are possible under each subdivision. For further details about this figure consult the original source (4).

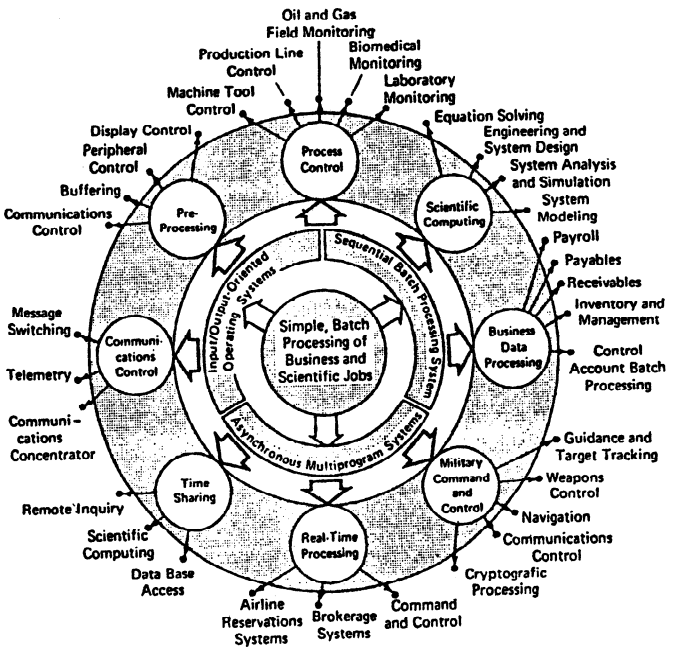

Figure 1 Computer systems application development, starting from sequential batch processing of business and scientific jobs, grew from sequential, asynchronous multiprogramming and I/O-oriented operating systems into time sharing, real-time processing, process control, communications, and several other types of computing systems

Cay Weitzman, Minicomputer Systems, Structure, Implementation and Applicatons, 1974, pp. 7. Reprinted by permission of Prentice-Hall, Inc., Englewood Cliffs, New Jersey.

Finally, it would be worthwhile to comment on which type of computer is appropriate for teaching computer literacy and demonstrating physiological simulation. There is some choice because computers are sufficiently versatile that more than one type of machine can be used to deal with these applications. As developed in this volume, computer literacy refers primarily to the way one communicates with a computer by means of the key board of the conventional computer terminal. Although typing skills are not essential, there are techniques which must be mastered. These include logging-on to the system, gaining access to certain files stored in the computer, correcting errors before they are processed by the computer, and causing the results to appear at the output device in a useful format. Generally, these are the techniques that one uses to communicate with asynchronous multi-program systems operating under time-sharing, but they are not very different from the skills used in obtaining services from the smaller, single-user microcomputers. As far as physiological simulation is concerned, it too can be done on a variety of machines including, in some instances, batch-processing approaches. However, here also time-sharing computers of various sizes as well as stand-alone microcomputers are the machines most likely to be used in the teaching of students.

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3. Linton, D.M., Ed. Price Performance. *Data Processor,* 22 (2), 1979. International Business Machines Corp.
4. Weitzman, C. *Minicomputer Systems.* Prentice-Hall, Eglewood Cliffs, N.J., 1974. pp. 1-8.

POSTDOCTORAL SCIENCE RESEARCH PROGRAMS

Deadline for Applications: January 15, 1981

The National Research Council announces its 1981 Research Associateship Programs for postdoctoral work in the sciences to be conducted in 16 federal research institutions with laboratories located throughout the United States. The programs provide postdoctoral scientists and engineers of unusual promise and ability with opportunities for research on problems largely of their own choosing yet compatible with the research interests of the supporting laboratory. Initiated in 1954, the Associateship Programs have enhanced the career development of over 3500 scientists ranging from recent Ph.D.s to distinguished senior scientists.

Four hundred or more full-time Associateships will be awarded on a competitive basis in 1981 for research in chemistry, engineering, and mathematics, and in the earth, environmental, physical, space, and life sciences. Most of the programs are open to both U.S. and non-U.S. nationals, and to both recent Ph.D.s and senior investigators.

Awards are made for a year with possible extensions through a second year; senior applicants may request shorter tenures. Stipends range from $20,500 a year (approximating GS 11, Step 1 salaries) for recent Ph.D.s to approximately $40,000 a year for Senior Associates. Allowances are made for relocation and for limited professional travel during tenure. The federal laboratory provides the Associate programmatic support including facilities, support services, and necessary equipment.

Applications to the Research Council must be postmarked no later than January 15, 1981. Awards will be announced in April.

Information on specific research opportunities and federal laboratories, as well as application materials, may be obtained from the Associateship Office, JH 610-D3, 2101 Constitution Avenue, N.W., Washington, D.C. 20418, (202) 389-6554.

METHOD AND SIMPLE APPARATUS FOR TEACHING THE AUSCULTATORY METHOD FOR MEASURING HUMAN BLOOD PRESSURE TO LARGE CLASSES*

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Increasing numbers of medical and paramedical students have to become expert in measuring blood pressure indirectly in human subjects. Teaching the technique has traditionally been accomplished on a one-to-one basis; largely because the Korotkoff sounds are so faint, especially to the untrained ear. In order to master the auscultatory method, the student must be able to see the indicator of cuff pressure clearly and hear the auscultatory sounds distinctly. This paper describes teaching aids that meet both criteria.

For many years, Hoff (1) has use an ingenious method of projecting a mercury manometer with a standard 3 ¼" x 4" lantern-slide projector. By constructing a U-tube manometer with arms of different cross-sectional areas, and placing the arm with the larger area in place of the lantern slide, a huge image of the height of the mercury column is visible to a large audience. Excellent as this method is, the manometer is fragile and it is often difficult to keep the mercury clean.

By rearranging a conventional aneroid gauge, it is relatively easy to locate the dial in the lantern for large-screen projection, while the aneroid bellows is external to the lantern. Figure 1 illustrates the assembly in which a frame of the same outer dimensions as the slide carrier is used to support the dial and the aneroid. A clear plastic frame supports the dial gauge portion and a slender rod couples the aneroid bellows to the arm in the indicator assembly that moves the pointer.

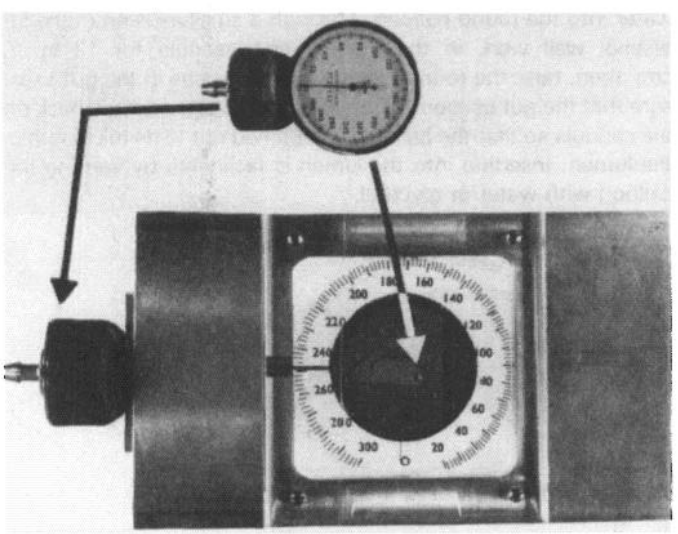

Fig. 1 Aneroid gauge (upper) and its assembly into a slide carrier (lower) The small chamber with the inlet fitting contains the bellows. When mounted in the slide carrier, and extension rod made of brass tubing, (obscurring 250) allows communication of the bellows movement to the indicator assembly.

A standard Tycos model HRI 8014-5090-03 dial gauge was employed. The dial assembly was removed from the cylindrical housing which was cut away from the chamber that contains the aneroid. The dial was removed, photographed and printed with black numbers on clear film. The photographed scale and indicator assembly were mounted on a clear plastic panel and a circular black paper mask was applied to hide the indicator assembly and allow projection of only the pointer and scale. The slender rod used to couple the indicator assembly to the aneroid can be identified at the 250 mm Hg mark in Figure 1. When pressure is applied to the aneroid, the rod pushes on an arm in the dial assembly and the pointer moves around the scale, indicating the applied pressure. When the assembly is placed in the projector, a large bright image of the pressure indication is displayed.

In order to obtain loud and clear strong Korotkoff sounds, we developed (2) a new method for the efficient detection of the auscultatory sounds. The method employs a tiny (5 x 2 x mm) piezoelectric element (Narco Bio-Systems, Houston, Texas) as a microphone. The element is mounted inside the rubber bladder in the cuff. The bladder was opened and the piezoelement was placed in a tiny pocket on the inner wall of the bladder at a level corresponding to one-third of the bladder width, as measured from the lower edge (Figure 2). The pocket was made by using a rubber patch from a bicycle-tube repair kit. After mounting the piezoelectric element, the bladder was closed with another patch. The wires from the piezoelement were brought out through one of the two tubes on the bladder. Room-temperature-vulcanizing (RTV) silicone rubber was used to seal the wires in one tube, leaving the other tube for inflation and deflation of the bladder in the cuff.

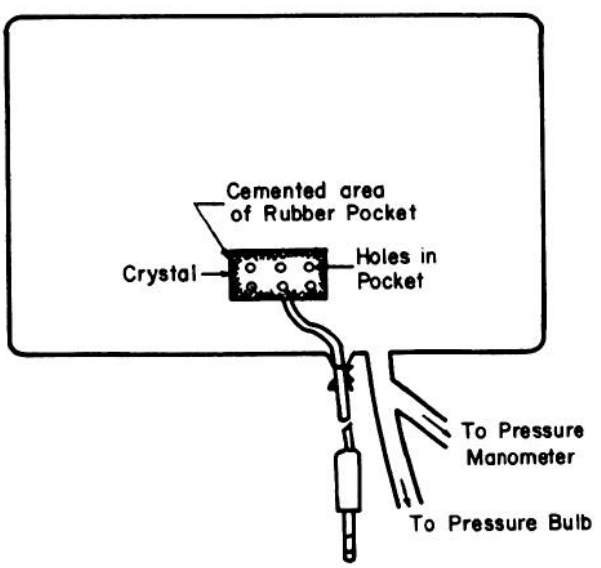

Fig. 2 Location of the piezoelement within the bladder of a blood-pressure cuff.

*Supported by Grant HL18947-03, National Heart, Lung and Blood Institute, Bethesda, MD.

There are three obvious advantages obtained by detecting the Korotkoff sounds from within the cuff. For example, since the piezoelectric element is in direct contact with the bladder surface, it has a large receiving area for sound. Since the element is within the cuff, the bladder surface is smooth and no net force is applied to the piezoelectric element. Finally, since the piezoelectric element is completely surrounded by the cuff, it is acoustically shielded from the environment. Therefore, when the piezoelectric element is connected to an amplifier and loudspeaker, high intensity sounds can be obtained without the presence of acoustic feedback.

In summary, with a standard 3 ¼" x 4" lantern-slide projector in which the slide carrier is replaced by the gauge assembly, a large screen display is available for cuff pressure. With a standard blood-pressure cuff containing a piezoelectric element applied to the arm with the element over the brachial artery, high intensity Korotkoff sounds can be heard by a class of 200 or more. The equipment described herein has been in routine use by the author for five years.

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2. Geddes, L.A., and Moore, A.G. The efficient detection of Korotkoff sounds. *Med. Biol. Eng.* 1968, 6:603-609.

A SIMPLE, INEXPENSIVE METHOD FOR THE MEASUREMENT OF IN VIVO INTESTINAL ACTIVITY

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Introduction

Measurement of the properties of smooth muscle, usually using intestine as a typical example, is one of the most variable and least predictable experiments in student mammalian physiology laboratories. Manipulation of the tissue, change in temperature, and variation in the electrolyte composition of the surrounding medium are but three causes for muscle to become inactive, producing student disinterest in these labs.

Intestinal motility is usually measured either in vivo, using a pressure transducer, or in vitro; however, both of these methods often are fraught with difficulty and failure. Pressure transducers rugged enough to be used in student laboratories are relatively insensitive and noisy so that the usual intestinal pressure changes are not detected. In vitro determinations of motility require excision of the tissue, subjecting it to a great deal of trauma, and placing it in a water bath which is variable in both temperature and nutrient milieu. The gut section is attached to a force transducer, and an evaluation of its function estimated by the tension developed by the longitudinal muscle layer. This preparation is usually even less successful than the in vivo preparation using pressure transducers, and certainly cannot demonstrate the functional activity present under physiological conditions.

We have devised a very simple system to monitor intestinal motility in vivo which is very sensitive, minimally injurious to the tissue, and inexpensive since standard physiological recording equipment is used. It uses two balloons, a length of P.E. tubing, and a force transducer and physiological recorder such as the Narco Physiograph and myograph A or B to detect volume changes in a gut segment.

Procedure

The following procedure has been developed using mongrel dogs under pentobarbital anesthesia. Other animals and anesthetics may be used if appropriate changes in balloon dimensions are made.

A balloon with dimensions of approximately 30 mm by 50 mm or other appropriate dimension for the intestinal lumen, is attached to one end of an 80 cm length of P.E. 280 tubing, snugly tied, and the system filled with water. Another balloon, round, about 30 mm in diameter, is filled to about 25% of its volume with water and attached to the other end of the tubing (Fig. 1). The long balloon is inserted into the intestinal lumen in the following manner: slip the long balloon back over the cannula, and drain the water into the round balloon. Through a small incision in the intestinal wall work in the balloon and cannula for 12 to 15 cm; then, raise the round balloon above the one in the gut to insure that the gut balloon will be filled with water and pull back on the cannula so that the balloon is stretched out to its full length in the lumen. Insertion into the lumen is facilitated by wetting the balloon with water or glycerol.

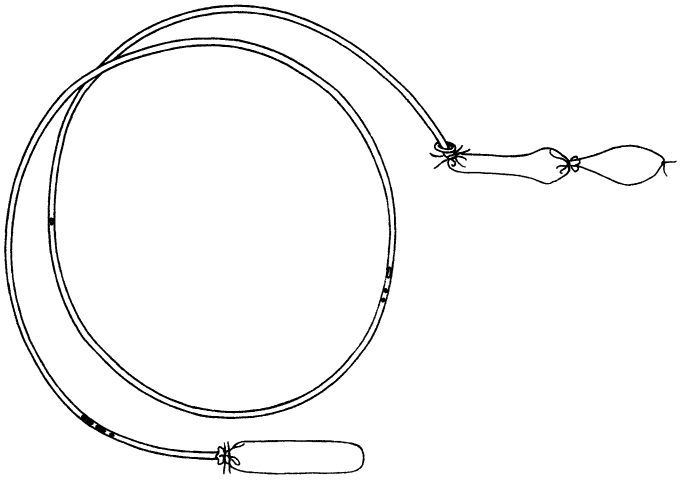

Fig. 1 The balloon tubing system used in the determination of intestinal motility. The longer balloon, approximately 30 by 50 mm, is inserted into the intestinal lumen, and the other balloon is suspended from a force transducer.

The gut balloon is distended, but not stretched, by attaching the round balloon to the force transducer 5 to 10 cm above the level of the gut. This pressure is sufficient to stimulate gut motility by gentle distention without over-stretching the smooth muscle of the wall. It is essential that the gut balloon is large enough to completely fill the intestinal lumen. Now, any contraction of the intestinal segment surrounding the balloon will displace water into the balloon on the transducer, thus increasing its weight. The Narco Bio-Systems myograph B is an excellent transducer for this purpose since its operational range is up to 30 gms. which is sufficient to suspend the weighted balloon without being mechanically limited, but still sensitive enough to detect very slight fluid shifts in the system. The more sensitive myograph A can be used if total load on the transducer is kept very low. Electronic damping to 3 Hz will eliminate higher frequency noise and allow a cleaner record to be obtained.

Results

Figure 2 correlates the changes in intestinal motility (bottom tracing), arterial pressure (middle tracing), and respiration (top tracing) during a control period and following i.v. injections of various pharmacologic agents. The animal was a 20 kg male dog anesthetized with 30 mg/kg sodium pentabarbital.

Figure 2 shows that acetylcholine (Panel A) produces a marked increase in tension of the intestinal wall that lasts approximately one minute following injection.

Epinephrine (Panel B) inhibits the phasic contractions with only a slight change in baseline tensions. This inhibition has a duration similar to the duration of the cardiovascular effects.

Histamine (Panel C) produces a marked inhibition of tone and phasic contractions. The intestine shows prolonged effects on motility even though the baseline tension is regained within 2-3 minutes.

The intestinal response to serotonin (Panel D) is biphasic. Demonstrated is an early inhibition of both tone and phasic contractions, followed shortly by a phase of increased tone and dramatically increased contractions. Another common response is a simultaneuous inhibition of tone and stimulation of phasic contractions.

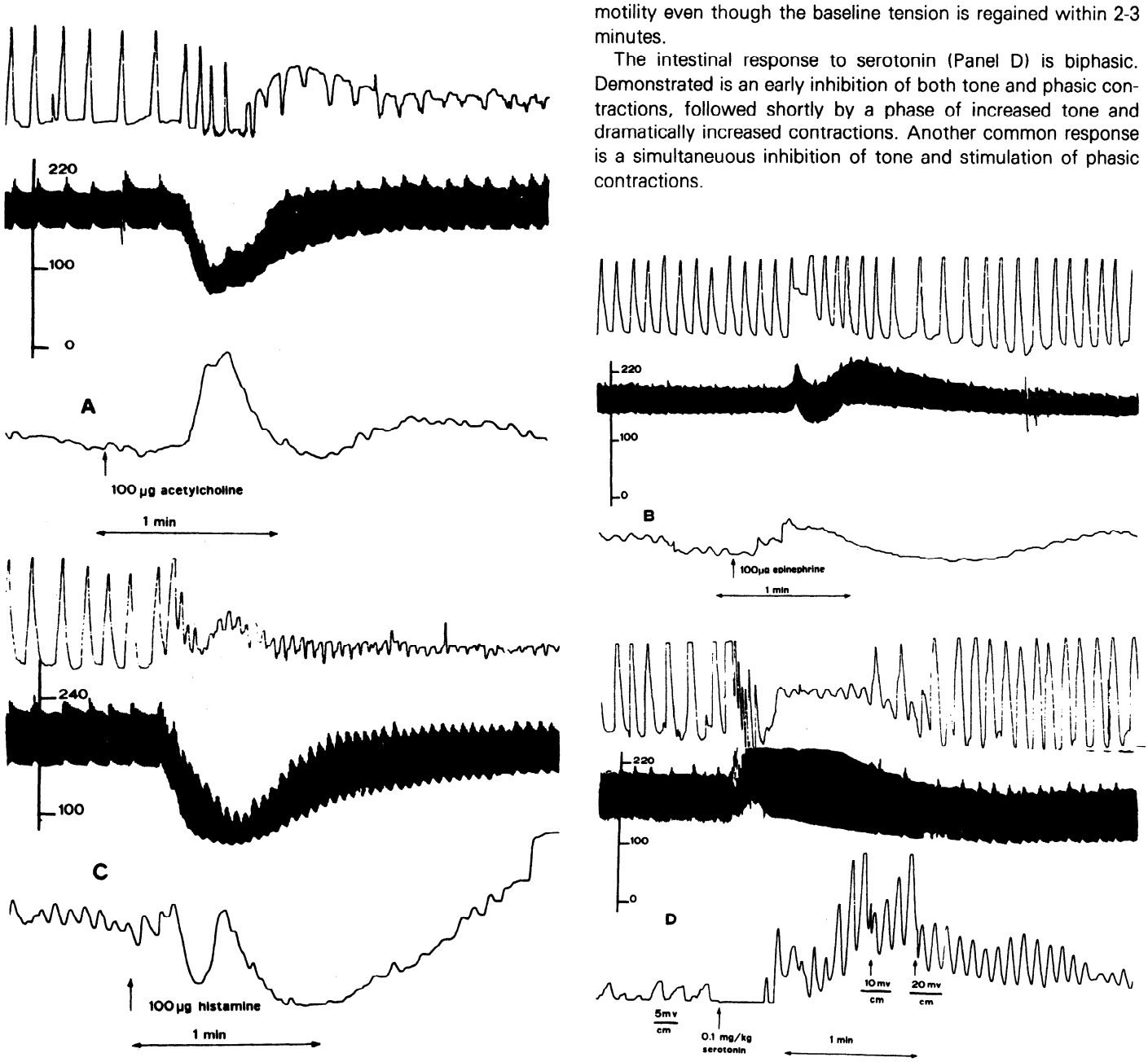

Fig. 2. The effects of various pharmacological agents, administered intravenously, on respiration, blood pressure, and intestinal activity from top to bottom, in a 20 kg male dog. Panel A: 10 µg acetylcholine; Panel B: 100 µg epinephrine; Panel C: 100 µg histamine; Panel D: 2 µg serotonin.

ADIPOCYTES, AGING AND CHOLESTEROL METABOLISM*

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In the not too distant past adipose tissue was considered to be a relatively inert tissue metabolically. In addition to being regarded as a storehouse for excess calories, adipose tissue was thought to serve passive roles as insulation against extreme ambient temperatures and as a cushioning support for certain organs of the abdominal cavity. In more recent years, however, the dynamic aspects of adipose tissue metabolism have been emphasized. Included among these more dynamic functions are: 1) lipolysis or mobilization of the stored triglyceride contained within adipocytes to provide energy in the post-absorptive state; 2) lipolysis of plasma triglyceride-rich lipoproteins via lipoprotein lipase (LPL) in order to direct triglyceride fatty acids (TGFA) of both dietary and hepatic origin into the fat cells for storage; 3) storage site for one of the largest slowly exchangeable pools of cholesterol in the body; and 4) synthesis or lipogenesis of fatty acids from excess carbohydrate in the diet, especially in young animals.

Of these four functions, we shall consider the first three and the relationship of these functions to aging in the male Sprague-Dawley and Fisher 344 rat. The studies to be described resulted from an interest in the relationship between the size of adipocytes and their metabolic function, initially directed toward the problem of obesity and the metabolism of hyperplastic adipocytes. Initially, male Sprague-Dawley rats of varying body weight were chosen in order to obtain a source of adipocytes of varying size from epididymal fat pads. As we shall see shortly, in performing these experiments one cannot rule out the effects of age in most situations, since animals of different body weight which are kept on a stock diet are, by definition, of different ages. Thus, even though the main thrust of the investigations was to study obesity, one could not easily dissociate the metabolic effects exerted by age from those exerted by adipocyte size.

Lipolysis

Throughout the studies to be described, both by these investigators and by others, the isolated adipocyte preparation described originally by Rodbell in 1964 (1) was utilized. Except for the initial study to be described, the remainder of the studies were conducted not only in the epididymal fat pad as had been done previously by most other investigators, but in other adipose depots as well. When investigators first became interested in adipose tissue metabolism, prior to the introduction of the isolated adipocyte preparation, epididymal (Epi) adipose tissue was used in the metabolic studies because the distal portion is very thin and presents a minimal barrier to diffusion of substrates, hormones and nutrients when cut into small pieces and incubated *in vitro*. This could not be done easily with tissue from other depots. Implicit in these early studies was the assumption that this depot was representative of adipose tissue as a whole. One of the important conclusions to be drawn from the studies presented here, is that this is not a valid assumption. The other depots which we have studied include the inguinal subcutaneous (SC), the perirenal (PR) and the mesenteric (M) adipose tissues. The impetus for including these other adipose depots in the studies to be described resulted in part from experiments which showed that hemorrhagic shock differentially affected the ability of cells from different depots to mobilize free fatty acids and glycerol in response to epinephrine (2). The intriguing metabolic differences in the adipocytes from different depots has been a stimulus to continue observation on adipocytes of different depots in the studies to be described.

A series of publications in the late 1960's suggested that obese patients had a defect in their ability to mobilize free fatty acids (FFA) from their fat stores (3-5). The obese patients studied failed to increase their plasma FFA concentrations in response to several stimuli which produced this effect in normal weight persons. These patients also exhibited significantly increased fasting plasma FFA concentrations. Based on these observations it seemed reasonable that one might be able to test the hypothesis of a lipolytic defect in obesity by investiating the effects of norepinephrine (NE) on mobilization of FFA and glycerol from fat cells of different size utilizing the male rat. Norepinephrine was chosen as the lipolytic agent, since it has been regarded as the major lipolytic hormone (6) and the catecholamine which is liberated from post-ganglionic sympathetic nerve fibers.

In our original study, adipocytes of different size were obtained by preparing adipocytes from the epididymal fat pads of rats of different body weights (ages) as shown in Fig. 1 (7). These results of fat cell development with increasing body weight are in agreement with earlier observations (8-11). Since body weight increases as a function of age, there is also an unavoidable direct relationship between age and the size of the fat cells.

At the time these studies were performed it was customary to report adipocyte lipolytic data as a function of the amount of triglyceride present in the incubation. Figure 2 shows representative dose-response curves of glycerol release from adipocytes of different size as a function of the dose of NE (7). This figure demonstrates that with increasing cell size there is an apparent decrease in the amount of glycerol mobilized per unit of cellular triglyceride present, a conclusion which would support the concept that enlarged adipocytes exhibit a lipolytic deficit. This data is misleading, however, since it should be fairly obvious that as fat cells become larger, the number of fat cells present per millimole of triglyceride must necessarily decrease. When glycerol release from these experiments was expressed per million fat cells, the relationship in Fig. 3 for a maximally stimulating dose of NE was observed (7). It can be clearly seen that there is no change in the amount of glycerol released per million cells as a function of cell size when cell size is expressed as triglyceride per cell. A similar relationship was observed when the data for two other doses of NE were plotted in a similar manner.

The NE-stimulated lipolysis in Fig. 3 also contains a component of basal lipolysis which is observed when adipocytes are incubated in the absence of hormone. These data show that total lipolysis is independent of cell size over a wide range of cell sizes.

* Tutorial Lecture presented at APS Fall Meeting, 1979.

Basal lipolysis shown in Fig. 4 (7) is directly related to cell size. This observation suggests the possibility that the increase in FFA in the circulation of fasting obese patients may be related to an increased basal lipolysis in their hyperplastic adipocytes. Indeed, a similar relationship exists with human adipocytes (12); a fact which confirms the use of rat adipocytes as a model in our studies. If basal glycerol release is subtracted from the total release observed in Fig. 3, a decreased sensitivity of large adipocytes to the lipolytic effects of NE is seen. Thus, depending upon how catecholamine-stimulated lipolysis is expressed with regard to basal lipolysis one may see either a decreased sensitivity (11, 13-17) or no change in sensitivity (12, 18-20) with increasing cell size (age). It would appear as though the total response to NE is relatively unaffected by increasing cell size or age, but the basal release becomes an ever increasing percentage of the total stimulated release as cell size (age) increases. Recent studies with specific binding to the β-adrenergic receptor of adipocytes indicate that the number of receptors increases in proportion to cell surface area until rats achieve 8 months of age, whereas glycerol release expressed as a percent above basal gradually decreases (24, 25). Since the catecholamine-stimulated adenylate cyclase activity increased with cell size as well, the decreased responsiveness to lipolysis may, at least in part, be related to an increase in phosphodiesterase with age (26).

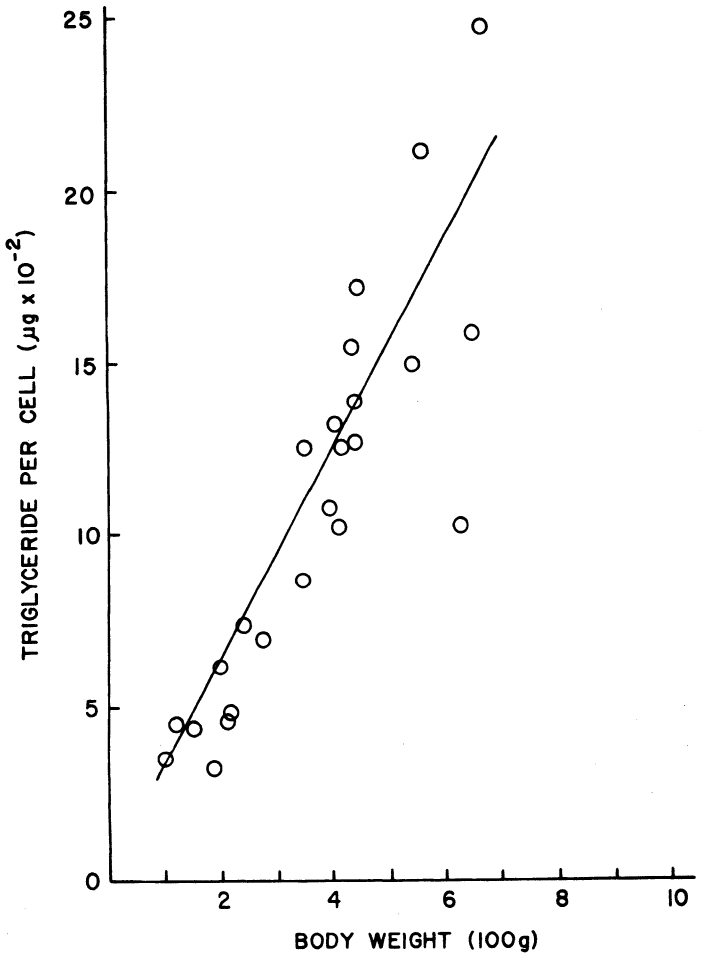

Fig. 1 Relationship between adipocyte triglyceride content and body weight. Each point represents the average cellular content of pooled cells from 2-8 animals.

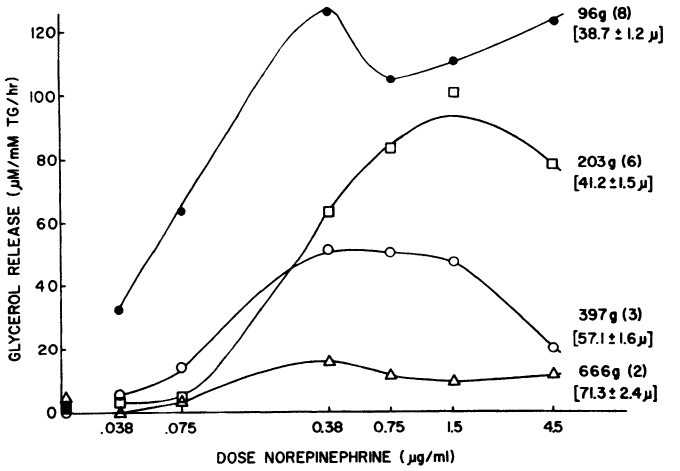

Fig. 2 The influence of cell size on the lipolytic sensitivity to NE. Body weights for the animals used are indicated; the number in parentheses indicates the number of animals from which tissue was pooled to provide cells for the incubation. The numbers in brackets indicate the mean diameter in microns ± standard error of the mean. The isolated cells were incubated in duplicate in Krebs-Ringer bicarbonate buffer for 90 min under an atmosphere of 95% O_2-5% CO_2. In addition, the incubation media contained glucose (1 mg/ml) and fat-free bovine serum albumin (40 mg/ml).

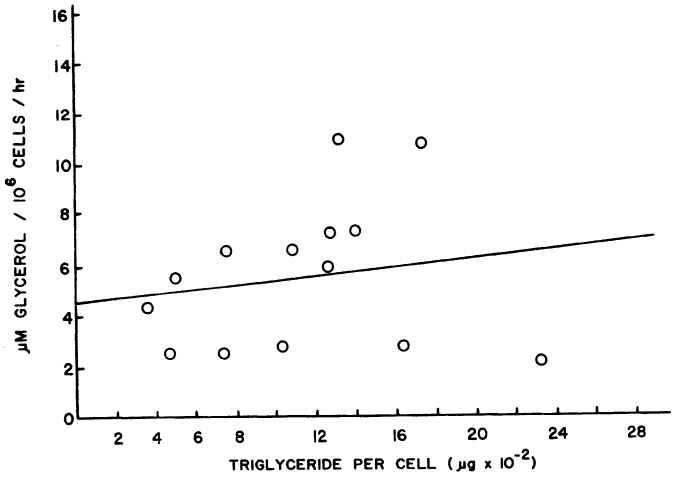

Fig. 3 Lipolytic response per 10^6 fat cells to 0.375 µg/ml NE as a function of cell size. Each point represents the mean of duplicate incubations. Cells at each point were derived from the pooled tissue of 2-8 rats. Incubation conditions were the same as described for Fig. 2. The line drawn is the calculated least squares regression line.

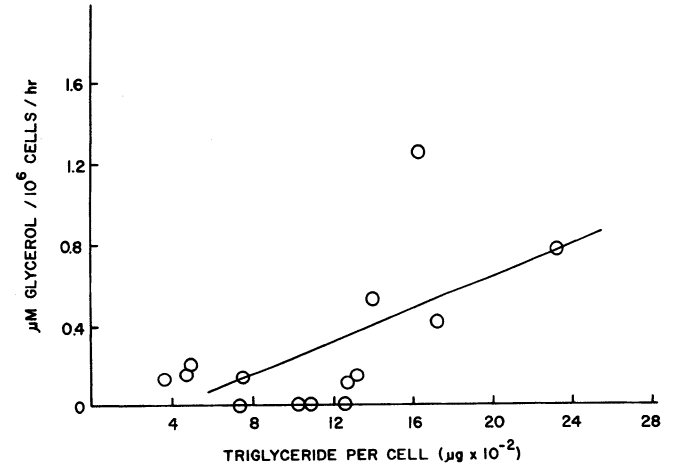

Fig. 4 Correlation between basal glycerol release per 10^6 fat cells and cell size. Each point is the mean of duplicate incubations. Cells at each point were derived from the pooled fat pads of 2-8 rats. Incubation conditions were the same as described for Fig. 2, with the exception that NE was excluded. The line is the least squares regression line of best fit.

The data reviewed here were among some of the first which cast serious doubt on the lipid mobilization defect theory of obesity. *In vitro* studies such as ours and others mentioned were supported by elegant *in vivo* studies on FFA turnover performed by Drs. Harvey Miller, Bela Issekutz and others at Lankenau Hospital in Philadelphia which clearly demonstrated that obese patients had no mobilization defect and in fact for any given plasma FFA level had a higher turnover rate (21-23).

Data from several laboratories have indicated the existence of differences in catecholamine-stimulated lipolysis in man between the subcutaneous adipose depot and adipose tissue found in the omentum (27-29), although this is not a consistent finding (12). There is also evidence that similar types of differences exist between depots in the rat (2) and in the dog (30). A logical question which had not been addressed is the dose-response relationship between NE and lipolysis in various adipose tissue depots of the rat, and secondly, whether this relationship is affected by cell size or age. We therefore addressed this question in the growing (aging) male Sprague-Dawley rat. Figure 5, which depicts the changes in cell size with body weight in the four depots chosen, shows that the depots can be divided into two groups. The first of these groups contains the Epi and PR depots which continue to increase in cell size throughout the life span of the animal. On the other hand, the SC and M depots increase in size until the animals achieve about 400 to 450 gms and then size plateaus.

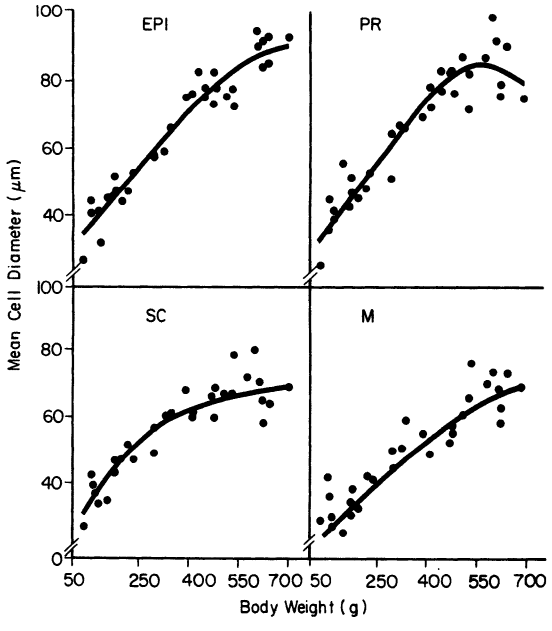

Fig. 5 Relationship between body weight and cell diameter in 4 adipose tissue depots of the rat. Cell size was determined microscopically with aid of a calibrated ocular micrometer on isolated fat cells prepared from depots indicated. Curves were fitted by a weighted least squares method to linear, cubic, and exponential functions. The equations for the lines of best fit are, Epi, $y = 29.85 + .090x + 1.2 \times 10^{-5} x^2 - 2 \times 10^{-7} x^3$; PR, $y = 27.18 + .076x + 2.9 \times 10^{-4} x^2 - 4.3 \times 10^{-7} x^3$; SC, $y = 72.32 - 56.21e^{-.0047x}$; and M, $y = 97.32 - 80.90e^{-.0027x}$.

Based on this cell size data we addressed the two questions described above with regard to dose-response relationships and how age affected these responses in different depots. In order to experimentally approach these objectives, rats of two different ages were chosen. The first group, 7-8 weeks of age, weighed approximately 250 gms. At this age there is very little difference in cell size between the various depots (Fig. 5). The second group of animals weighed about 400 g and were 14-16 weeks of age. At this age the differences in cell size between the depots are well established. This experimental design would not only allow us to compare NE dose-response curves among the different depots at any given age, but also would allow us to investigate the effects of increasing cell size and/or age on the lipolytic response in each depot. Figure 6 shows the dose-response characteristics of adipocytes of different depots from the young group as a function of the dose of NE (31). No differences were found in basal glycerol release between the depots. Likewise, no differences were discernible between glycerol release as a function of the dose of NE between cells of Epi, PR and M depots. In contrast, cells from the SC depot showed significantly reduced responses at doses of .4 and .75 μg of NE/ml. The lipolytic responses between depots were not related to differences in cell size, since cells from the 3 most active depots contain both the largest and the smallest cells in the series, while the cells from the SC depot, which were the least active, fell in the middle of the size range of the others. Likewise, lipolysis was not proportional to surface area by the same line of reasoning. Figure 7 shows the dose-response characteristics for cells isolated from the depots of 400 gm rats (31). Again, no differences were discernible in the rates of basal lipolysis. As previously reported by this investigator (7), there was no alteration in the response of Epi adipocytes, in spite of the fact that they had increased in size about 3-fold. In marked contrast there were significant reductions in response in PR, SC, and M cells, which varied from no significant increase in cell size in the SC depot to a 2.2 fold increase in PR cells when compared to the younger group. Thus, the decrease in responsiveness of these cells to NE is not a function of cell size, but is probably attributable to some undefined effect of age. These data reveal that with regard to lipolysis, Epi adipocytes are the exception rather than the rule. In addition to glycerol, we also measured FFA release in these studies. The most significant observation in this regard was that in the Epi and PR depots there was a decrease in the ratio of FFA/glycerol release with age, but not in the SC and M depots. These data are consistent with an increased re-esterification of FFA in cells from the Epi and PR depots with age. This might account for the increased size of these cells compared to SC and M depots in the adult rats (Fig. 5).

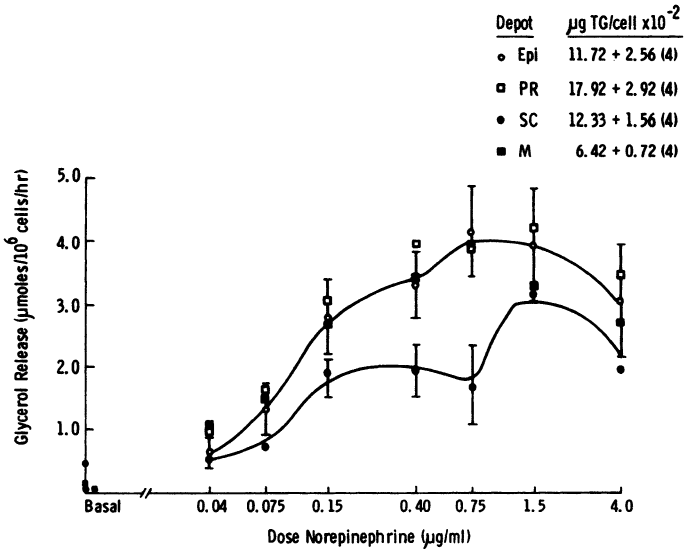

Fig. 6 Effect of norepinephrine concentration on the lipolytic response of 250 g rats. Adipocytes were prepared from the depots shown as described in text. Incubations were performed at 37°C for 90 minutes in Krebs Ringer bicarbonate buffer containing 4 g/dl fatty acid-free albumin, 100 mg/dl glucose and the indicated concentration of NE. Data is presented as the mean ± S.E. (brackets for the Epi and SC depots only).

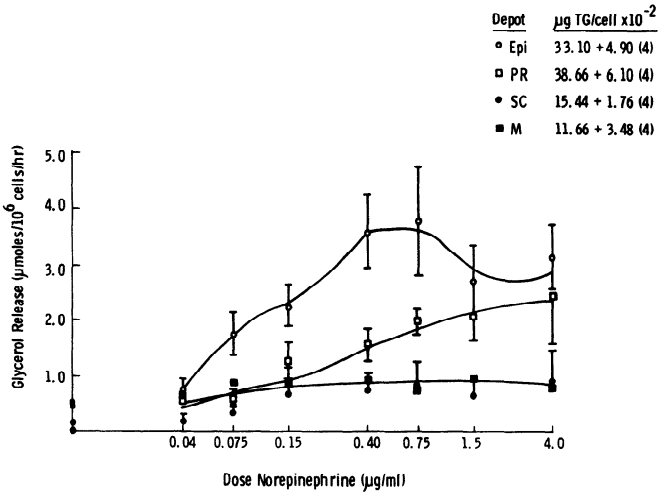

Fig. 7 Effect of norepinephrine concentration on the lipolytic response of 400 g rats. Adipocytes were prepared from the depots shown as described in text. Incubations were performed at 37°C for 90 minutes in Krebs Ringer bicarbonate buffer containing 4 g/dl fatty acid-free albumin, 100 mg/dl glucose and the indicated concentration of NE. Data are presented as the mean ± S.E. (brackets).

In order to test whether these *in vitro* data have any relevance to *in vivo* conditions, we did the following experiment. One would predict from the *in vitro* data that if young rats were forced to mobilize their adipose tissue triglyceride stores by fasting them for 72 hours, that the amount of triglyceride lost per cell should be about the same independent of the depot. conversely, if one were to fast adult animals for the same length of time more triglyceride should be lost from Epi and PR cells than from SC and M. These experiments were performed and the predictions confirmed (data not shown). Such *in vivo* studies lend credence to the validity of the *in vitro* measurements and are consistent with the hypothesis that under the stress of fasting those cells which contain the largest store of triglyceride and the first to empty in the adult. Those cells which contain the least amount of triglyceride empty their stores at a slower rate. This hypothesis was first suggested by Krotkiewski and Björntorp (32) utilizing a slightly different experimental design.

It thus appears that there are minimal differences in adipocyte lipolysis between depots in young animals. As the animals' age, cells in the PR, SC, and M depots become insensitive to the effects of NE. These effects can be demonstrated by *in vivo* studies as well. The reasons for the decreased lipolytic activity in these depots are not known. The decrease in NE sensitivity might occur at any point between hormone-receptor interaction at the plasma membrane to activation of the triglyceride lipase. Further studies are necessary to elucidate these mechanisms.

Lipoprotein Lipase (LPL)

A second major function of adipose tissue relates to the removal of triglyceride from the circulation. Triglyceride is transported primarily in the form of chylomicrons or very low density lipoprotein (VLDL). In the case of adipose tissue, the triglyceride removed from the circulation in the form of FFA is re-esterified back to triglyceride within the adipocyte and stored within the fat droplet. It is known primarily through the work of Robinson (33) that activity within adipose tissue is principally under the control of insulin. In other tissues the primary regulatory hormone(s) is different. For instance, in heart it appears to be either glucocorticoids (34, 35) and/or glucagon (36), and in the lactating mammary gland the regulatory hormone appears to be prolactin (37-39). Rodbell (40) was the first to determine that the adipocyte fraction contains a large proportion of the LPL activity of whole adipose tissue. Later work indicated that the fat cells under appropriate condition were capable of synthesizing LPL (33, 41-44). As a result of these studies the hypothesis has emerged that LPL in adipose tissue is synthesized within the adipocytes, secreted, and transported across the interstitial space and endothelial cells where it is bound to the luminal side of the capillary endothelium. Little or no information exists regarding the regulation of secretion and the means whereby LPL is transported from the adipocyte to the endothelium. It is known, however, from the studies previously cited that high insulin concentrations increase the synthesis and amount of LPL within adipose tissue. Because of this relationship to high insulin levels, LPL in this tissue is elevated following the consumption of a mixed meal and is thought to play a role in directing dietary lipid into the adipose tissue for storage. Following a mixed meal LPL levels in skeletal muscle and heart are reduced, thus directing transport of dietary lipid to adipocytes for storage (33).

A question of critical importance is "*what is the distribution* of LPL between different constituents in the adipose tissue as a function of nutritional state and as a function of the size of the cells within this depot?" This question is readily answered in such tissues as the heart where one can perfuse the tissue with a medium containing heparin which displaces endothelial-bound LPL from its binding site and then measure the total amount of LPL left in the tissue and the amount released in response to heparin and determine how much of the total tissue activity was present at the capillary endothelium. Because of the anatomical locations of the various adipose tissue depots, this type of experiment is not easily performed. As an alternative to this type of study the following experimental protocol was devised to answer this question in adipose tissues of the Sprague-Dawley rat.

Our approach has been to determine the LPL activity in whole adipose tissue and in fat cells isolated from this tissue and compare the activities of both of these when LPL activity is expressed per mmole of triglyceride (45). Fig. 8 shows two examples of how this method may be theoretically applied. The diagram on the left depicts a tissue which contains three units of LPL activity, all of which is localized within the adipocytes and none at the capillary endothelium. In this instance, determination of LPL activity in the whole tissue reveals three units of LPL per unit of triglyceride, all of the triglyceride being contained within the fat cells. When the adipocytes are isolated and LPL activity determined, once again three units of LPL activity are found per unit of triglyceride. The percentage of LPL contained in adipocytes may be calculated by dividing the LPL activity in the adipocytes per unit of triglyceride by LPL activity in whole tissue per unit of triglyceride and multiplying by 100. In this instance the percent LPL in the adipocytes is 100%. In the second diagram, three units of LPL are located within the fat cells and three units of LPL are bound to the capillary endothelium. When LPL is determined on the whole tissue six units of LPL activity per unit of triglyceride are found. In fat cells, we find three units of LPL activity per unit of triglyceride. Therefore, the percent of LPL activity in adipocytes as calculated in Fig. 8 is 50% of the tissue activity.

One of our primary goals was to determine the relationship between adipocyte size and LPL activity within these cells since Nestel, Austin and Foxman (46) in 1969 had reported an inverse relationship between *cell size and lipoprotein lipase* activity.

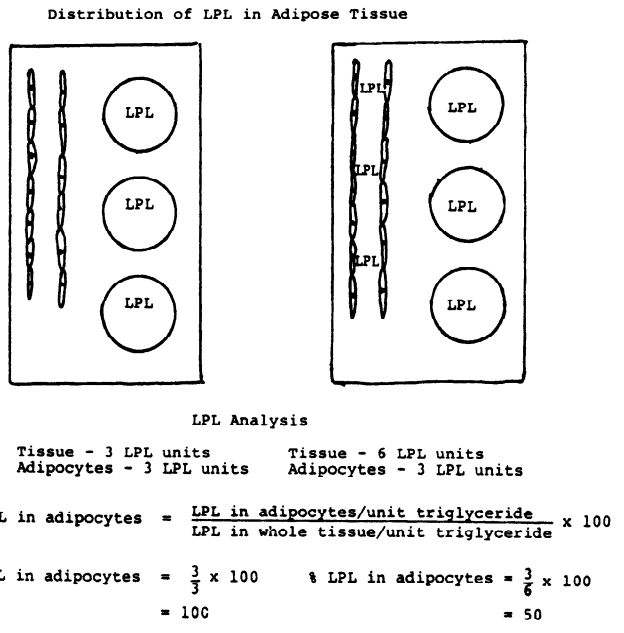

Fig. 8 Calculation of the distribution of LPL in adipose tissue. Details are given in the text.

Preliminary unpublished data on LPL activity in adipocytes by Hartman and Spitzer led the present investgators to question the observations of Nestel et al (46). Data from a large number of experiments relating to this relationship in four different depots are presented in Fig. 9. The top panel of the figures shows results obtained from fasted rats and the bottom panel data from fed animals. Within each nutritional group no difference could be discerned in the regression lines calculated for the regression of LPL activity versus cell size among any of the depots. Thus, a single regression line within each nutritional group described the relationship between cell size and LPL activity. In addition to this observation, there was no difference in the relationship between cell size and LPL activity per million cells between the fed and the fasted state. This was an unexpected finding, which implies that the increase in LPL activity which occurs in adipose tissue following a mixed meal occurs at tissue sites outside of the adipocyte, possibly at the capillary endothelium. In other experiments, LPL activity in adipose tissue was stimulated by the injection into fasted rats of 0.4 units of regular insulin/kg body weight (Hartman and Borenzstajn, unpublished observations). In this study insulin produced a 7-fold increase in LPL activity of epididymal adipose tissue above control levels, but no change in the activity within the adipocytes, confirming this hypothesis.

We next proceeded to pursue the question of the relationship between cell size and the distribution of LPL within the adipose tissues. The results are shown in Fig. 10. The data fall essentially into two groups. One group contains Epi and PR cells, the second contains M and SC. In the M and SC cells, as the cells enlarge, a greater proportion of the total tissue LPL activity is contained within the adipocytes as compared to the Epi and PR cells. This indicates that one of the factors which determines cell size is the availability of LPL at the capillary endothelium since Epi and PR cells in the adult rat are larger than SC and M cells (Fig. 5). The data were all derived from fed rats. In fasted rats, 90-100% of the LPL activity of whole tissue was located in the adipocytes in all depots.

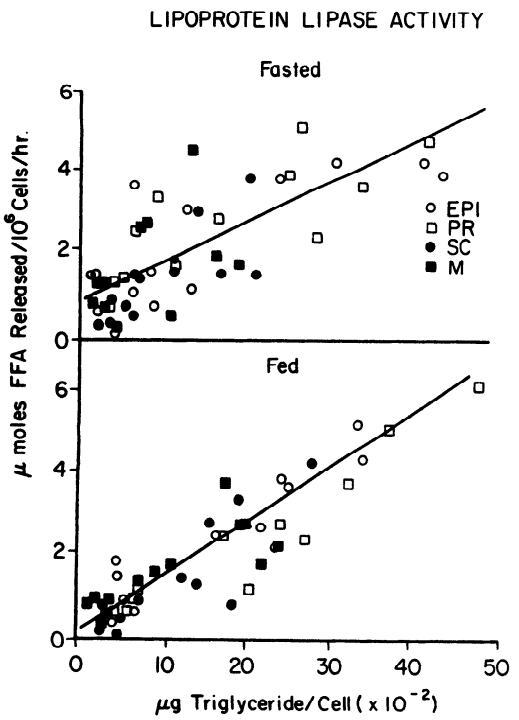

Fig. 9 Relationship between LPL activity per 10^6 cells and cell size in both fed and fasted states. Fat cells were prepared by collagenase digestion and LPL determined on acetone-ether powders of washed cell preparations. Symbols in margin indicate depot from which cells originated.

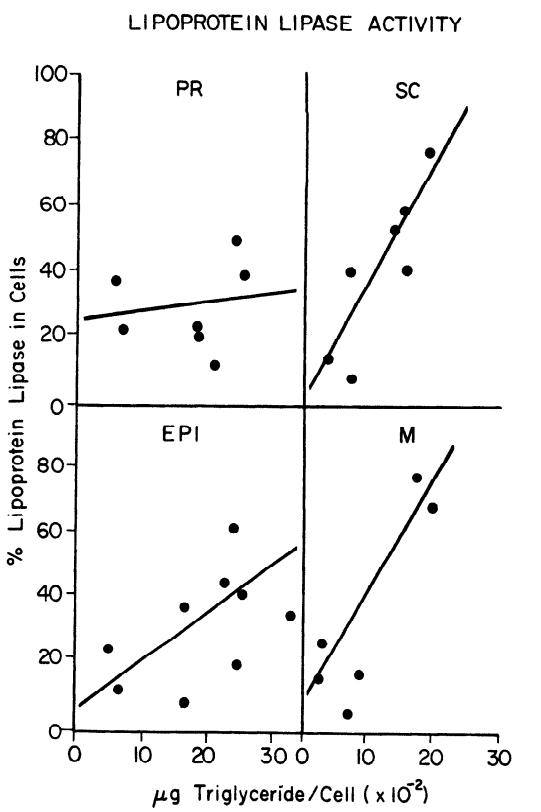

Fig. 10 Relationship between percent of whole tissue LPL contained in adipocytes as a function of cell size in fed rats. LPL activity was determined on acetone-ether powders of both whole adipose tissue and isolated adipocytes and expressed per unit of triglyceride. Percentage of LPL in cells was calculated as ratio of cellular LPL to whole tissue LPL times 100. Curves shown are least squares regression lines of best fit.

From these data, therefore, one could predict that within any given adipose depot the uptake of TGFA from circulating triglyceride-rich lipoproteins should be inversely proportional to cell size. To test this hypothesis we prepared chylomicrons labeled in the triglyceride molecule by intubating animals with 1-C^{14}-palmitate dissolved in corn oil. Chylomicrons collected from thoracic duct cannulas were washed and injected into fed or fasted conscious animals in a dose of 4.5 mg of chylomicron triglyceride per 100 g body weight. The animals were killed 3 to 4 minutes following injection to prevent recirculation of labeled fatty acids from the liver back into the circulation. The extent of uptake of labeled TGFA into adipocytes of each depot was determined and the uptake calculated on the basis of cell number (Fig. 11). In the top panel one can see that within any given depot the uptake of TGFA in the fed state was inversely related to cell size, thus confirming the results which we obtained *in vitro*. In the fasted animals, in every depot studied, the uptake was very low and was independent of cell size.

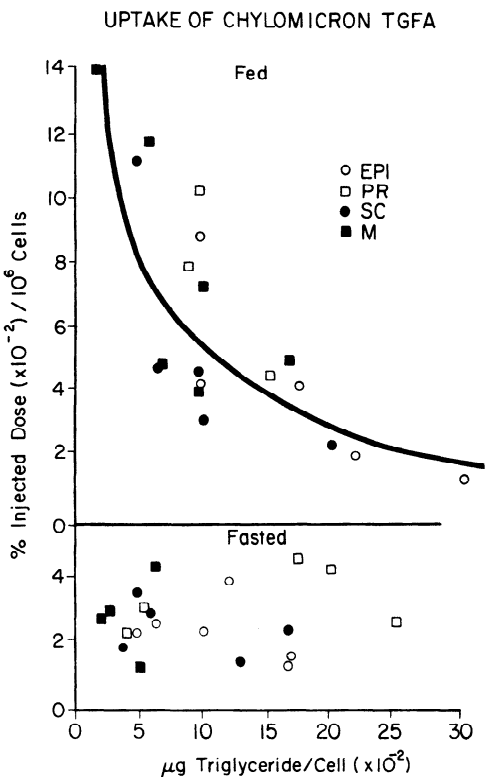

Fig. 11 Relationship between uptake of ^{14}C-labeled chylomicrons and fat cell size in various depots. Chylomicrons labeled with [^{14}C] palmitic acid in triglyceride moiety were injected intravenously into conscious rats previously prepared with indwelling polyethylene catheters in external jugular. Rats were killed by decapitation 3-4 min after injection. Results for fed and fasted animals are presented.

These studies thus indicate that within all of the depots studied, as cell size increased during development, less of the activity found in the tissue in the fed state appeared at the capillary endothelium. This is manifested physiologically by a decreased ability to remove TGFA from circulating lipoproteins. In addition, as cell size increases, there is also an increase in the amount of LPL activity within the adipocytes. These data have led to the hypothesis that in certain types of obesity the distribution of LPL activity within the adipose tissues, may become altered and contribute to the obesity, i.e. there may be an abnormally large amount of LPL located at the capillary endothelium as compared to lean controls. We are presently completing some work in which we have utilized the obese Zucker rat as a model to test this hypothesis (47, 48).

Adipocyte Cholesterol Storage

The final function of adipose tissue to be discussed is the role of adipose tissue as a part of the exchangeable pool of cholesterol in the body. Total body cholesterol behaves as though it is divided into at least two and perhaps three exchangeable pools of cholesterol, depending upon how long the turnover studies are carried out (49). It is generally recognized that plasma cholesterol, which contains less than 10% of the total body cholesterol, is in equilibrium with cholesterol in the various exchangeable pools in the tissues (49-52). If one considers the 2-pool model for simplicity, plasma cholesterol is contained in the first rapidly exchanging pool and adipose tissue composes the largest component of the second slowly turning-over pool. Our interest in this area was aroused by several observations. The first is that there is a direct relationship between body weight and the rate of cholesterol production in man (52). If one considers excess body weight, that is the actual body weight minus ideal body weight, there is also a direct correlation to the rate of cholesterol production (53). These two observations taken together indicate that expansion of adipose tissue, which is the major component of the slowly turning-over pool, results in an increase in cholesterol production rate which is directly related to the total number of adipocytes in the body (53). These data, based on cholesterol turnover studies, and other data derived from direct measurements of adipose tissue cholesterol content (54-56), indicated that there was a direct relationship between the amount of cholesterol within adipocytes in both man and rat as a function of cell size. From the studies on adipocyte cholesterol storage it had been suggested that one of the important determinants of the amount of cholesterol stored within adipocytes was their size. Secondly, it had also been postulated that the adipose tissue might specifically act as a buffer toward limiting plasma levels of cholesterol in the body (55). Since the exact mechanisms which regulate the uptake and storage of cholesterol were unknown at this time, as a first approximation we decided to investigate the storage of cholesterol in adipcytes over most of the life-span of the male Sprague-Dawley rat and, if possible, to correlate this with plasma cholesterol.

Figure 12 shows the relationship between the mass of cholesterol stored in adipocytes as a function of mean cell diameter. In all four depots examined the cholesterol storage was an exponential function of the mean diameter (57). Other investigators (54-56), had shown a direct relationship between cell size and cholesterol storage, however, animals as young as those in our particular experiment were not included. A liner function is apparent in Fig. 12 if one considers only the larger diameter cells. The relationship between plasma cholesterol and body weight is presented in Fig. 13. It can be seen that the plasma cholesterol is a parabolic function of body weight. That is, in very young animals and very old animals plasma cholesterol is elevated compared to 200-500 g rats. As has been seen in very young rats (Fig. 12), cellular cholesterol remains relatively constant while the plasma cholesterol levels are falling, and then later both the cellular and plasma levels increase in parallel (57). Also occurring in young animals is cellular proliferation resulting in an increased fat cell number. These factors may be responsible for the slow rate of cholesterol storage in very young animals.

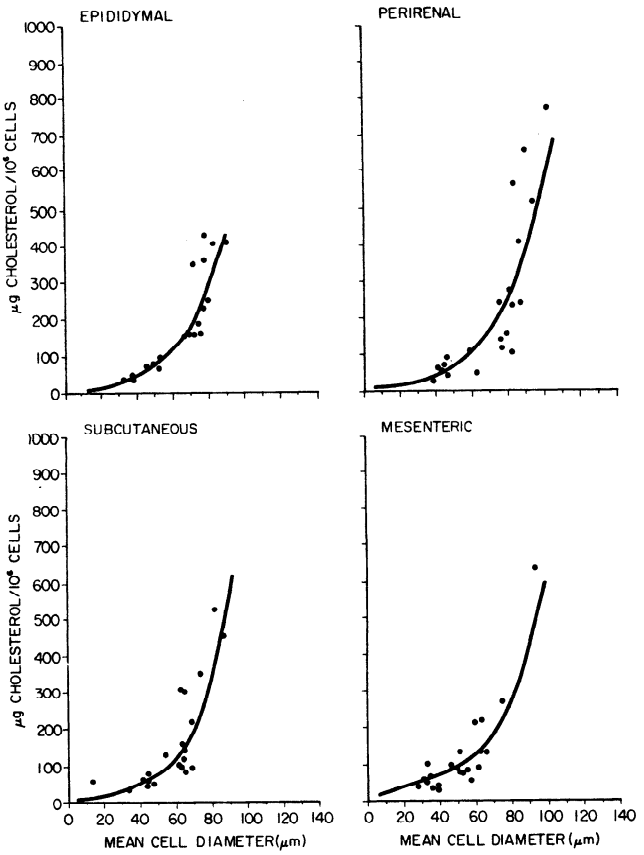

Fig. 12 Relationship between mean cell diameter and the cholesterol content per 10^6 adipocytes from four fat depots of the rat. Cell size was determined microscopically on cells isolated by collagenase digestion.

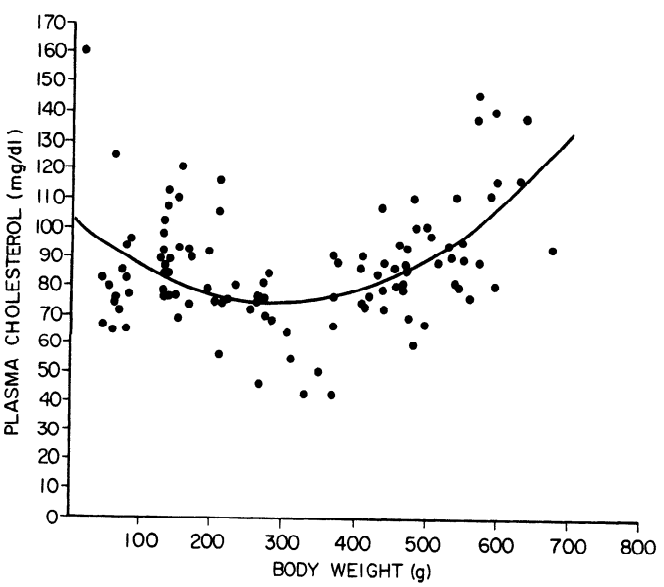

Fig. 13 Relationship betwen body weight and plasma cholesterol in the fasted, male rat.

In the younger animal, cell size is increasing while cholesterol storage is relatively unchanged, and then, at or about the time cell number become fixed, plasma cholesterol begins to rise and cholesterol storage rises also. In order to further understand events occurring within the adipocytes, we determined the ratio of cellular cholesterol to triglyceride and examined cholesterol storage by this relationship as a function of body weight. This is depicted in Fig. 14 for the four adipose tissue depots studied (57). In addition to plotting the cholesterol to triglyceride ratio as a function of body weight, we have also included the plasma cholesterol level as the dashed line for comparison. It may be observed that in all of these depots, with the possible exception of the M depot, the cholesterol to triglyceride ratio in the cell parallels the curve for plasma cholesterol. In the M depot, the increase in cellular cholesterol storage is delayed in the older animals. These latter observations tend to support the concept that the determining factor in cellular cholesterol storage may be the plasma cholesterol and not cell size *per se.* An alternative hypothesis might be that the plasma cholesterol curve exhibits the parabolic shape in response to the amount of cholesterol stored in adipose tissue. These two hypotheses connot be distinguished from the data reported here. Although these data support the concept that plasma cholesterol may be a major determinant of adipocyte cholesterol, the results are not unequivocal since both fat cell size (which has been suggested as a major determinant of storage) and plasma cholesterol are both changing continuously during growth. We thus sought a different model in which to differentiate between these variables in determining cholesterol storage.

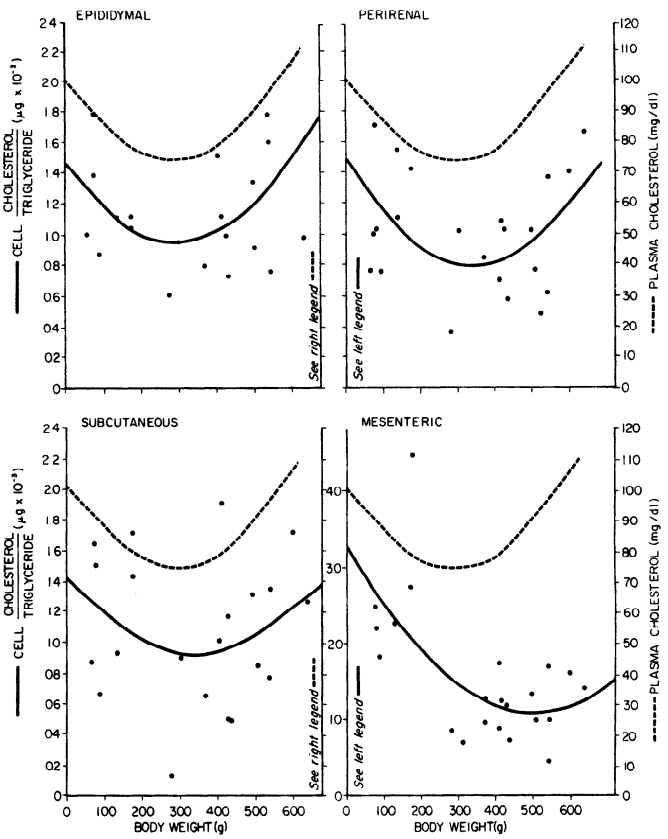

Fig. 14 Relationship between body weight and both plasma cholesterol and the ratio of cholesterol: triacylglycerol within the fat cell. The curve for plasma cholesterol is the calculated curve of best fit from Fig. 13.

A unique model for pursuing this problem was reported by Story *et al* (58). Their data showed that in the Fisher 344 rat body weight and plasma cholesterol plateaued at about one year of age and remained constant for about the next year. In addition, other studies have indicated that fat cell size was also constant in these animals over this period of time (59). We thought, therefore, that

the Fisher 344 rat might be a good model in which to determine the factors regulating adipocyte cholesterol storage. We considered the possibility that by feeding various levels of cholesterol in the diet we might be able to produce animals with varying degrees of hypercholesterolemia for a prolonged period of time and then relate the amount of cholesterol stored in adipose tissue to both the dietary level and to the plasma cholesterol which resulted from these diets. For this study we chose a commercially available semipurified diet which was high in sucrose but which contained no cholesterol and no dietary lipid. To this diet we added varying levels of crystalline cholesterol such that the final concentrations of cholesterol were 0, .05, .5, and 5 percent by weight. In addition, as a control group we included a powdered chow group for comparison. These diets were fed for a period of 90 days which we felt would be sufficient to produce an alteration in the adipocyte cholesterol content. In addition, in analyzing the adipocyte cholesterol level, we also determined how much of the cholesterol was in the free and esterified forms. This analysis was performed by a method specifically designed by us for separating these two forms of cholesterol in adipocyte extracts (60).

Figure 15 shows the body weights of Fisher 344 rats as a function of age and also as a function of the time on the experiment (61). In this figure two experiments are depicted. The protocol outlined above refers only to Experiment 1. At no time during the experimental period did any of the dietary groups differ significantly from each other. Therefore, at all time points data from all dietary groups were pooled. During the first weeks in Experiment 1 there was a significant increase in body weight which then remained constant throughout the remainder of the study. The initial increase in body weight, which also resulted in increased adipocyte sizes, is due to the fact that when the study was initiated, animals were switched from pelleted food to the powdered diets which were used throughout the study. The easy access to the diet probably resulted in the increase in body weight. This is borne out by the results in Experiment 2 in which all animals were allowed to eat powdered food for about two weeks before the experiment was initiated. In this study, the initial increase in body weight and increased adipocyte size seen in Experiment 1 were not observed. The highest plasma cholesterol values obtained were derived from animals which received no dietary cholesterol whatsover. The lowest plasma cholesterols were observed in animals maintained on the Purina diet, and in these animals there was no change in the plasma cholesterol, confirming the observations of Story *et al* (58). The other diets gave plasma cholesterols intermediate between the 0% and the 5% diet. Figure 16 shows the cholesterol content for the four adipose tissue depots investigated and also the effect of dietary cholesterol on storage. Appearing above the bars is the plasma cholesterol concentration. The data is arranged such that data with the lowest plasma cholesterols are on the left and the highest plasma cholesterols on the right. It can be observed that within all of the adipose tissue depots investigated, the groups which had the highest plasma cholesterol also exhibited the highest content of cholesterol in their adipocytes. The increase in adipocyte cholesterol storage was predominantly in the esterified form, similar to the enhanced cholesterol storage found in the livers of these animals. Linear regression analysis was determined on all the depots relating cellular cholesterol content to total plasma cholesterol content; within each depot there was a significant correlation between the plasma cholesterol and the amount of cholesterol per million cells. This would indicate that plasma cholesterol and not the dietary level is a prime determinant in cholesterol storage in adipocytes.

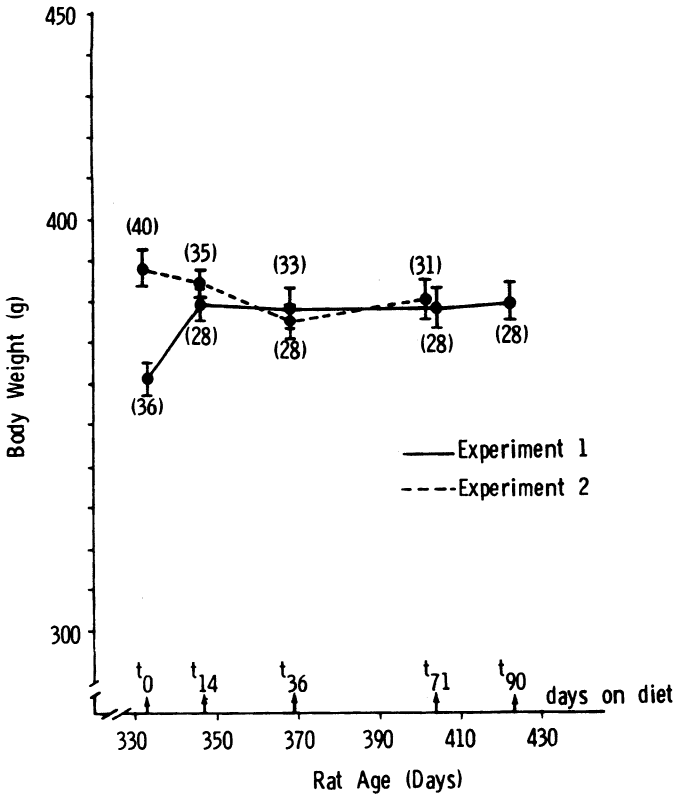

Fig. 15 Pooled body weights of adult Fisher rats fed stock, cholesterol-free and cholesterol-containing diets. Numbers in parentheses are the total number of rats. Values are mean ± SE.

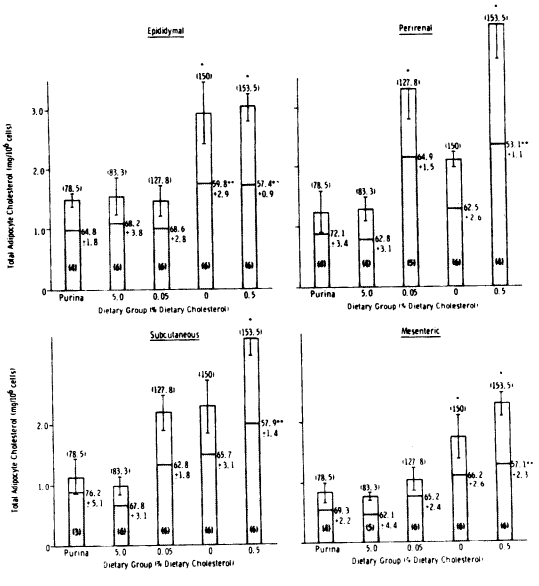

Fig. 16 Adipocyte cholesterol storage as a function of plasma cholesterol level in four adipose tissue depots of adult Fisher rats on day 90 (experiment 1). Bars or numbers not sharing the same superscript are significantly different using Duncan's test for multiple comparisons ($P < 0.05$). Shaded area = free cholesterol fraction and number of animals. Numbers above each bar = mean plasma total cholesterol value for each group. Numbers to the side of each bar = percentage of cellular cholesterol in the free form (mean ± SE).

In conclusion, a number of metabolic parameters have beer assessed in isolated rat adipocytes of varying sizes and from various anatomical locations. Lipolytic data expressed on the basis of cell number reveal that in the Epi depot there is no change in the response to NE as adipocytes increase in size, but basal rates of lipolysis without NE are positively correlated with adipocyte size. Dose-response curves in this depot to NE are identical in young (small cells) and old (large cells) rats. However, in older animals the response to norepinephrine declines in PR, SC and M adipose tissue depots, the latter despite no change in cell size. Thus, in studies on lipolysis, it is possible to delineate an effect of age on hormone sensitivity in this model.

Lipoprotein lipase activity expressed per million cells increases with cell size in all adipose depots in fed and fasted states. By determining LPL activity in both isolated cells and whole tissue, one can calculate the percentage of LPL residing within the cells. As cell size increases, a greater proportion of the total LPL activity is contained within the cells in M and SC depots compared to Epi and PR. Presumably, more LPL activity is available at the capillary endothelium in the latter case, which may explain why Epi and PR cells are larger than M and SC in the adult animal. These calculations are confirmed by the fact that the *in vivo* uptake of labled chylomicrons in the fed state is inversely related to cell size in all adipose depots.

Adipose tissue also participates in the storage of cholesterol as well as triglyceride. But little is known concerning the determinants of cholesterol storage even though on an organ basis adipose tissue contains more cholesterol than the liver in adult animals. As adipocytes enlarge, the amount of cholesterol increases in all depots examined. The changes in the cholesterol/triglyceride ratios in adipocytes with increases in body weight parallel the plasma cholesterol during the entire life span of rats, suggesting that both cell size and plasma cholesterol determine the extent of cholesterol storage in adipocytes. In a strain of rat (Fisher 344) in which one can experimentally alter plasma cholesterol without changing cell size, the influence of plasma cholesterol can be clearly observed. Enhanced cholesterol storage in the experimental hypercholesterolemia in this model is manifest by an increased percentage of cholesterol esters in adipocytes, a phenomena similar to liver but unlike skeletal muscle.

Further studies are in progress to gain more information concerning the distribution of LPL activity in adipose tissues from genetically obese animals. In addition, a series of experiments has been designed to investigate the mobilization of cholesterol from adipose tissue. Finally, a more complete picture of adipose tissue metabolism will be feasible with the inclusion of studies relating lipogenesis in adipose tissue to cell size in adipocytes from the various body depots. Combined, this work will provide insight into many aspects of fat cell metabolism as well as the pathogenesis of obese states.

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PROTECTION OF CEREBRAL VESSELS BY SYMPATHETIC NERVES*

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Introduction

In the midst of continuing controversy (Heistad and Marcus, 1978; Purves, 1978), it is difficult for the physiologist to place in perspective the role of neural mechanisms in regulation of cerebral blood flow (CBF). This tutorial will focus primarily on the role of sympathetic nerves and will attempt to support 3 major conclusions: *First,* cerebral vessels are extremely responsive to changes in metabolism, blood gases, and arterial pressure, but the role of sympathetic nerves is smaller and circumscribed. *Second,* although sympathetic nerves probably have little effect on CBF under normal conditions, there is wide agreement that sympathetic nerves protect cerebral vessels during acute, severe hypertension. *Third,* several factors appear to have contributed to different results obtained by different investigators: species differences, temporal factors, anesthesia, mode of stimulation (reflex or electrical), metabolic state, and most importantly the presence or absence of severe hypertension.

The contribution of cholinergic and peptidergic nerves to changes in CBF has not been studied extensively. Evidence will be presented that, although cerebral vessels are innervated by cholinergic and peptidergic nerves, the physiological role of these nerves is not yet clear.

The complex vascular supply of the brain presents a difficult obstacle to accurate measurement of CBF. Wiggers (1905) wrote 75 years ago "Perhaps no other organ of the body is less adapted to an experimental study of its circulation than the brain." In this light, and with the realization that all of the currently-available methods for measurement of CBF have important limitations, this tutorial should be viewed as a description of our evolving understanding of the role of neural control in regulation of CBF.

Sympathetic nerves: innervation and effects of the neurotransmitter. Cerebral vessels are richly supplied by sympathetic nerves (Figure 1). These nerves originate primarily in the ipsilateral superior cervical ganglion (Nielsen and Owman, 1967; Edvinsson, 1975; Mueller et al., 1977) and innervate small (Edvinsson, 1975) as well as large arteries (Purdy and Bevan, 1977). Because the density of adrenergic innervation tends to correlate with responsiveness of vessels to neural stimuli (Mayer et al., 1968), the extensive innervation of cerebral vessels implies that neural mechanisms potentially may be important.

Responsiveness to the neurotransmitter, however, is unusual in cerebral vessels. J. Bevan (1979) has demonstrated that, at the point that the internal carotid and vertebral arteries enter the skull, the vessels become 30-50 times less sensitive to norepinephrine. Differences in vascular responsiveness may be related to different embryological origins of the vascular segments. Studies of vascular segments *in vitro* indicate that cerebral vessels also are relatively insensitive to transmural nerve stimulation. Electrical stimulation of intramural nerves produces much less constriction of isolated cerebral arteries than of saphenous arteries (Bevan et al., 1975). Thus, although cerebral vessels have dense adrenergic innervation, they are remarkably insensitive to the neurotransmitter and to nerve stimulation *in vitro.*

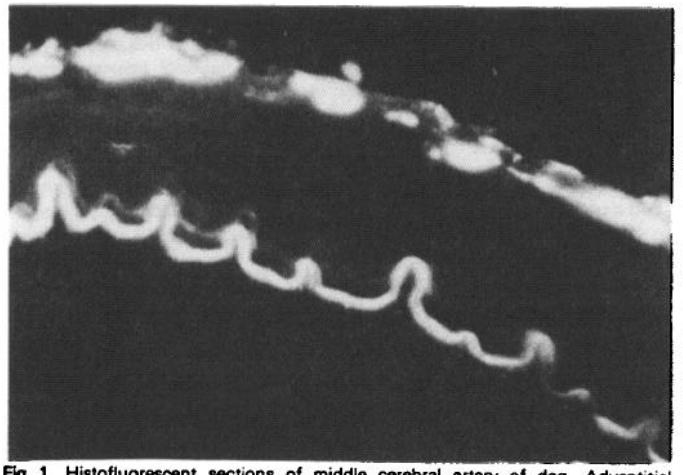

Fig. 1 Histofluorescent sections of middle cerebral artery of dog. Adventitial fluorescence indicates dense adrenergic innervation. Intimal fluorescence is nonspecific. Photomicrograph was prepared by Dr. M.J. Brody.

The most direct method to examine responses of cerebral arteries to neural stimuli *in vivo* is measurement of pial artery diameter. Studies using this method have demonstrated that sympathetic stimulation constricts pial arteries (Wei et al., 1975, Kuschinsky and Wahl, 1975). However, the magnitude of the response was only a 7-12% reduction in vascular diameter and may be confined primarily to large arteries (Wei et al., 1975). Thus, the magnitude of the effect of sympathetic stimulation is small and, if the response is confined to large arteries, it may not produce a detectable change in CBF under normal conditions.

Effects of sympathetic nerves on CBF. Several experiments have demonstrated that sympathetic stimulation decreases blood flow through the internal carotid artery. It is likely, however, that flow through the internal carotid artery is constituted in part by flow to skeletal muscle as well as CBF. Because vessels supplying skeletal muscle are very responsive to neural stimuli, this method is not optimal for examination of neural effects on CBF (Heistad and Marcus, 1978).

Measurement of cerebral venous outflow suggests that sympathetic stimulation does not reduce CBF (Rapela et al., 1967; Traystman and Rapela, 1975). Studies using a modification and simplification of this method, however, have suggested that sympathetic stimulation produces marked decreases in CBF (D'Alecy and Feigl, 1972). Failure to separate completely drainage from intra- and extra-cranial veins may account for the response to sympathetic stimulation (Traystman and Rapela, 1975), although this possibility has been challenged (D'Alecy et al., 1979). It should be emphasized that the complexity of the cerebral circulation makes it difficult to measure CBF accurately with arterial inflow or venous outflow methods.

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Measurements of CBF from clearance of inert gases or with microspheres have led to conflicting conclusions about effects of sympathetic nerves (Heistad and Marcus, 1978; Purves, 1978). It appears that microspheres provide valid measurements of CBF (Marcus et al., 1976; Heistad et al., 1980b) and the ^{133}Xenon method provides valid measurement of CBF, when ^{133}Xenon is injected rapidly into the internal carotid artery of baboons, extracranial contamination of the clearance curves is minimized, and the curves are subjected to stochastic analysis (Marcus et al., 1980). Why, then, have different investigators who have used these two methods observed very different responses to neural stimuli? Several factors may have led to different conclusions (Table 1):

1. **Species differences.** Most experiments using ^{133}Xenon have demonstrated at least modest effects of sympathetic nerves on CBF (Heistad and Marcus, 1978; Purves, 1978); these studies usually were performed in primates. Most experiments using microspheres have demonstrated no effect of sympathetic nerves on CBF under normal conditions (Heistad and Marcus, 1978); these studies usually were performed in dogs or cats. Under normal conditions, cerebral vessels of primates are responsive to sympathetic stimulation but dogs and cats are unresponsive (Heistad et al., 1978) (Figure 2). Thus, there are important species differences in cerebral vascular responses to neural stimuli *in vivo* (Heistad et al., 1978), as well as *in vitro* (Duckles, 1979).

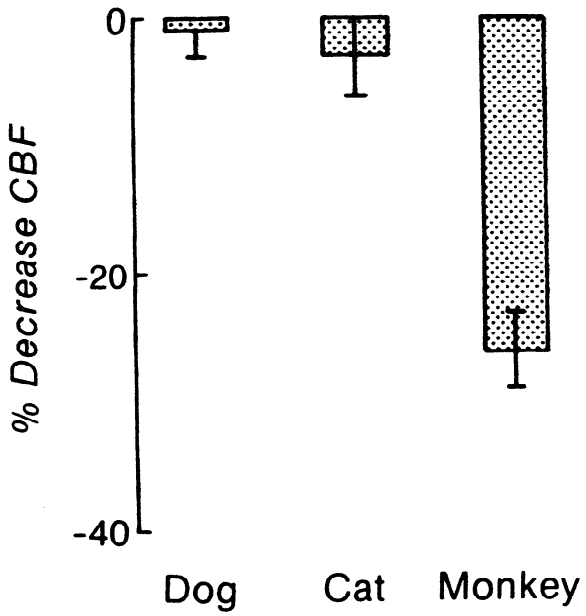

Fig. 2 Effect of sympathetic stimulation on cerebral blood flow. Values (mean ± SE) were calculated from the equation: % decrease in CBF = $(CBF_C - CBF_S) \times 100/CBF_C$ where CBF_C = flow to contralateral (unstimulated) cerebrum and CBF_S = flow to cerebrum ipsilateral to stimulation. From Heistad et al. (1980b).

TABLE I

Determinants of Cerebral Vascular Responses to Sympathetic Stimulation (SS)

Determinant	Conclusion	References
1. Species	There are important species differences in responses to SS	Heistad et al., 1978 Duckles, 1979
2. Temporal factors	Responses to SS are transient	Marcus et al., 1978 Sercombe et al., 1979
3. Regional factors	Responses to SS are greater in cerebral grey matter than white matter	Heistad and Marcus, 1979
4. Anesthesia	Responses to SS are somewhat altered by anesthesia	Marcus et al., 1979 Vatner et al., 1980
5. Electrical vs. Reflex Stimulation.	Reflex SS elicits smaller responses than electrical SS	Gross et al., 1979
6. Metabolic state	Increased metabolism attenuates responses to SS	Mueller et al., 1979
7. Arterial pressure	Responses to SS are much greater during acute hypertension than normotension	Bill and Linder, 1976 Edvinsson et al., 1976 Heistad, et al., 1978 Heistad and Marcus, 1979 MacKenzie et al., 1979 Busija et al., 1980a

2. **Temporal factors.** In species in which sympathetic stimulation reduces CBF, there is recovery of flow to normal levels within 2-5 minutes despite continuation of stimulation (Sercombe et al., 1979; Marcus et al., 1978). In contrast, vasoconstriction is sustained in skeletal muscle (Marcus et al., 1978). Thus, cerebral vessels appear to be unusually susceptible to "escape" from sympathetic stimulation. Because cerebral vessels "escape" rapidly, and because measurement of clearance of inert gases requires several minutes, cerebral vascular responses to sympathetic stimulation may not be sustained for a sufficient time to be detected with this method. Thus, temporal factors may have contributed to conflicting conclusions by several investigators who used inert gases to measure CBF and found that sympathetic stimulation decreases CBF (James et al., 1969) or does not decrease CBF (Harper et al., 1972) in primates.

3. **Anesthesia.** Studies with microspheres indicate that sympathetic denervation does not increase CBF during normotension or hypotension in anesthetized dogs and cats (Mueller et al., 1977; Gross et al., 1979). Denervation produces a slight increase in CBF during hypotension in awake dogs (Marcus et al., 1979) and no increase in awake cats (Heistad et al., 1980a). Thus, there is a modest effect of anesthesia on cerebral vascular responses to hypotension after sympathetic denervation (Figure 3).

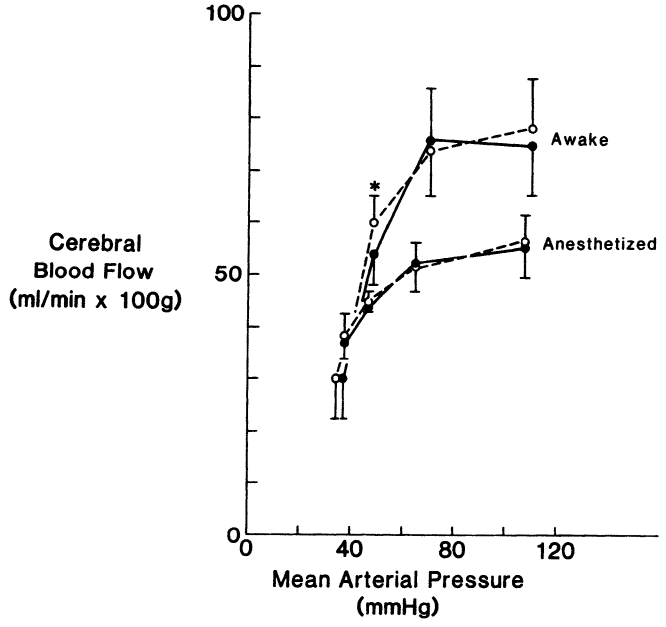

Fig. 3 Effect of hypotension on blood flow to denervated cerebral hemisphere (o----o) and innervated hemisphere (●——●). Values are mean ± SE in 11 awake dogs and 8 anesthetized dogs. * = $p < 0.05$, denervated vs innervated hemisphere. Sympathetic denervation increased CBF only during moderate hypotension in awake dogs. From Mueller et al. (1977) and Marcus and Heistad (1979).

Chemoreceptor stimulation activates sympathetic pathways in awake dogs and prevents an increase in CBF during sudden chemoreceptor-induced increases in arterial pressure (Vatner et al., 1980). In anesthetized dogs, chemoreceptor stimulation does not alter CBF at a time when arterial pressure is not increased (Heistad et al., 1976). Thus, when anesthesia alters the intensity of the chemoreceptor reflex, cerebral vascular responses also are altered.

4. **Electrical vs reflex stimulation.** Most investigators who have studied effects of sympathetic stimulation on CBF have examined responses to electrical, rather than reflex, stimulation. It is difficult, on the basis of cerebral vascular responses to electrical stimulation at 10-20 Hz, to estimate responses to reflex stimuli, which probably do not exceed 6-8 Hz (Folkow, 1952). It appears that during severe hypertension in cats, intense reflex stimulation (Gross et al., 1979) elicits smaller cerebral vascular responses than electrical stimulation (Heistad and Marcus, 1979). Thus, the mode of stimulation, whether electrical or reflex, affects the magnitude of responses of cerebral vessels to neural stimuli.

5. **Metabolic state.** In other vascular beds, constrictor responses to sympathetic stimulation are attenuated during increases in metabolism. A similar predominance of metabolic stimuli over neural stimuli apparently occurs in the cerebral circulation. Reflex sympathetic stimulation attenuates increases in CBF during severe hypertension (Gross et al., 1979) but, during increases in metabolism produced by seizures, reflex sympathetic stimulation has little effect on flow (Mueller et al., 1979) (Figure 4).

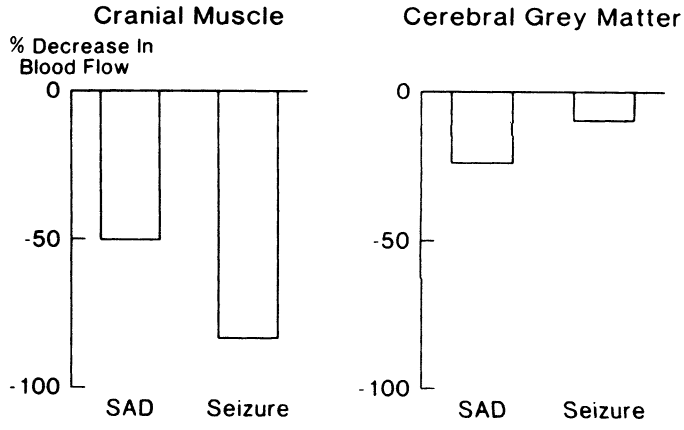

Fig. 4 Effect of reflex sympathetic stimulation on blood flow to cranial muscle and cerebral grey matter. Values for % decrease in flow were calculated as in Figure 2. Values were obtained during reflex sympathetic stimulation and severe hypertension produced by sinoaortic deafferentation (SAD) in 8 cats and seizures in 17 cats. Sympathetic activation probably was greater during seizures than SAD (as indicated by effects in muscle), but neural effects on CBF were smaller during seizures than SAD. These data suggest that effects of sympathetic nerves on CBF are attenuated by increases in metabolism.

6. **Arterial pressure.** An important study in clarifying the role of sympathetic nerves was a report by Bill and Linder (1976). They found that, during severe hypertension with "breakthrough" of autoregulation and a passive increase in CBF, sympathetic stimulation attenuates the increase in flow. This concept has now been confirmed by many investigators (e.g., Edvinsson, et al., 1976; Heistad et al., 1978; Heistad and Marcus, 1979; MacKenzie et al., 1979). Thus, in contrast to the small and transient effect of sympathetic nerves on CBF during normotension (Sercombe et al., 1979; Marcus et al., 1978), responses of cerebral vessels to neural stimuli are much greater during hypertension.

What mechanisms increase cerebral vascular responsiveness during acute hypertension? We have speculated (Heistad et al., 1980) about several possiblities: 1) sympathetic nerves may reduce distensibility of cerebral vessels and restrict passive dilatation 2) stretching of cerebral vessels may increase responsiveness, as suggested by studies *in vitro* (Toda et al., 1978) 3) histamine, which increases cerebral vascular responsiveness (Bevan et al., 1975), may be released during breakthrough of autoregulation.

Several studies have demonstrated responses to sympathetic stimulation during steady-state, extreme hypertension, with mean arterial pressure about 200-250 mmHg. A recent study (Busija et al., 1980a) indicates that sudden increases in arterial pressure, within the physiological range of pressure, produce transient increases in CBF, and that sympathetic stimulation attenuates the transient hyperemia in cats. Thus, during severe, steady-state hypertension and during abrupt increases in arterial pressure within the physiological range, sympathetic stimulation attenuates increases in CBF (Figure 5).

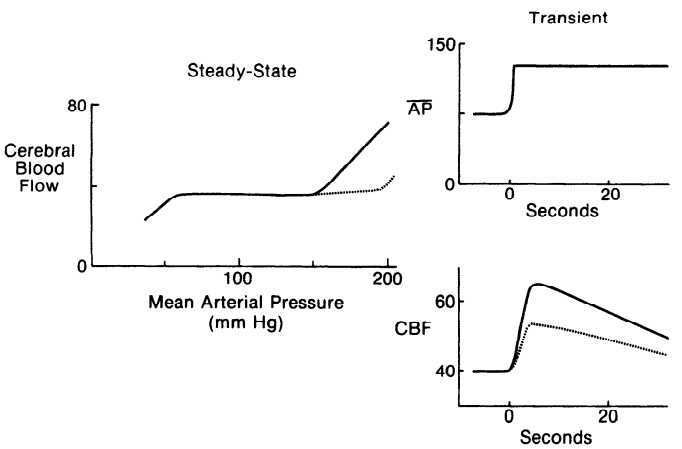

Fig. 5 Schematic of effect of sympathetic stimulation (dotted line) on CBF during steady-state changes in arterial pressure (left) and during sudden increase in pressure (right). In steady-state conditions, sympathetic stimulation attenuates the increase in CBF during severe hypertension. Perhaps of greater importance, sympathetic stimulation attenuates the transient increase in CBF that occurs after a sudden increase in arterial pressure within the physiological range. From Heistad et al. (1980a) and Busija et al. (1980a).

Other Effects of Sympathetic Nerves. Sympathetic stimulation may have important effects on cerebral vessels during hypertension, in addition to their effects on CBF.

First, acute hypertension disrupts the blood-brain barrier to albumin. Sympathetic stimulation not only attenuates increases in CBF during acute hypertension but also reduces disruption of the blood-brain barrier (Heistad et al., 1978; Heistad and Marcus, 1979, Bill and Linder, 1976). (Figure 6).

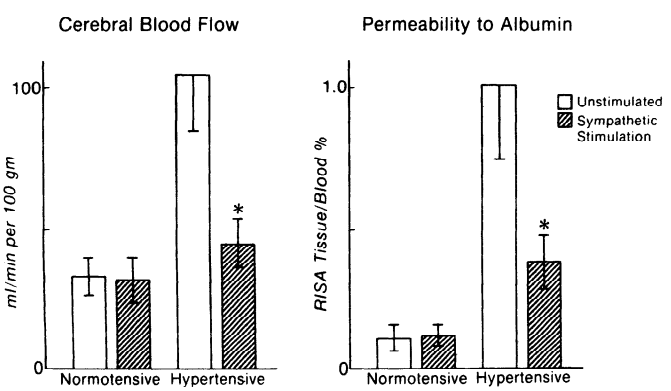

Fig. 6 CBF and permeability of cerebral vessels to albumin in cats during normotension and acute hypertension. Sympathetic nerves to one hemisphere were stimulated (cross-hatched bars) and, to the other hemisphere, not stimulated (clear bars). Values are mean ± SE, * = $p < 0.05$. From Heistad and Marcus, 1979.

Second, cerebral vessels appear to undergo hypertrophy during chronic hypertension (Hart et al., 1980). Vascular hypertrophy may attenuate increases in CBF during hypertension and protect the blood-brain barrier against disruption. R. Bevan (1979) has proposed that sympathetic nerves exert a "trophic" effect and contribute to the normal development of arteries. We have obtained evidence which suggests that sympathetic denervation attenuates the development of cerebral vascular hypertrophy (Hart et al., 1980). Thus, sympathetic nerves may exert a "trophic" effect on cerebral vessels during chronic hypertension.

In addition, neural stimuli have been reported to affect capillary filtration (Raichle et al., 1975), blood volume (Edvinsson et al., 1971), and production of cerebrospinal fluid by the choroid plexus (Lindvall et al., 1978). All of these studies suggest that neural stimuli may have important effects on cerebral vessels without corresponding changes in CBF.

Effects of Cholinergic and Peptidergic Nerves. Arteries on the surface of the brain are innervated by cholinergic nerves (Owman et al., 1974), but intraparenchymal cerebral arteries do not appear to have cholinergic innervation (Edvinsson, 1975). The greater superficial petrosal nerve, a branch of the seventh cranial nerve, is thought to provide part of the cholinergic innervation of cerebral vessels (Vasquez and Purves, 1979).

Acetylcholine produces cerebral vasodilation *in vitro* (Owman et al., 1974; Lee et al., 1978), when applied directly to pial arteries *in vivo* (Kuschinsky et al., 1974), and when infused into the carotid artery of rabbits (Heistad et al., 1980c) (Figure 7). In addition to its direct effect on cerebral vessels (which are muscarinic), acetylcholine also may modulate adrenergic responses (through nicotinic receptors) (Owman et al., 1974).

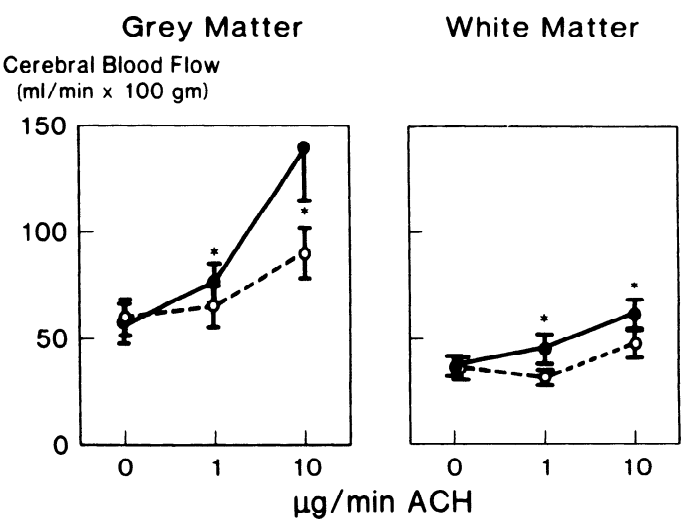

Fig. 7 Effect of intracarotid infusion of acetylcholine on CBF. Blood flow was measured on side ipsilateral to infusion of acetylcholine (●——●) and on the contralateral side (o----o). Values are mean ± SE in 8 rabbits; * = $p < 0.05$ (ipsilateral vs contralateral sides).

The role of cholinergic nerves in regulation of CBF is unclear. Studies by Ponte and Purves (1974) suggest that interruption of cholinergic pathways by transection of the seventh cranial nerve abolish cerebral vasodilator responses to hypoxia, but Hoff et al. (1977) suggest that responses are not attenuated. Pinard et al. (1979) found that stimulation of the greater superficial petrosal nerve increases CBF, but Busija and Heistad (1980b) found no increase in CBF. Thus, studies of effects of cholinergic nerves on CBF are at an early stage, and the functional importance of these

nerves is not yet clear. Important areas of future research will be demonstration of anatomical pathways of cholinergic innervation of cerebral vessels, examination of effects of the nerves on time-course or steady-state responses to vasodilator stimuli, and studies concerning the role of the nerves in modulation of adrenergic responses.

Vasoactive intestinal peptide (VIP) has been demonstrated in neurons on cerebral arteries (Larsson et al., 1976), but anatomical pathways of petidergic innervation have not been established. VIP produces cerebral vasodilatation *in vitro* (Larsson et al., 1976) and *in vivo* (Heistad et al., 1980 and McCulloch and Edvinsson, 1980). Initial studies have not yet demonstrated cerebral release of VIP during physiological stimuli (Wilson et al., 1979).

Provocative studies (Langfitt and Kassell, 1968; Raichle et al., 1975) suggest that central neural pathways, perhaps arising in the brainstem, have direct effects on cerebral vessels. This area of research has received limited attention.

Conclusions

The major message of this tutorial is that effects of sympathetic nerves on cerebral vessels do not appear to be important under most conditions, but they are very important during severe hypertension. Sympathetic stimulation attenuates the increase in CBF during steady-state severe hypertension, protects the blood-brain barrier against disruption, and buffers the transient increase in CBF during sudden increases in pressure. The role of cholinergic and peptidergic nerves in regulation of CBF is not clear.

We might consider neural control of CBF in light of what we have learned from other vascular beds. In general, neural control appears to be important in mediation of sudden changes in blood flow and in modulation of the time course of responses, and less important as a determinant of steady-state blood flow. Thus, although metabolic factors, blood gases, and perhaps autoregulation may be primary determinants of steady-state CBF, neural control may prove to be important in initiation or modulation of rapid changes in cerebral vascular resistance.

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LABORATORY ANIMAL DATA BANK

The Laboratory Animal Data Bank (LADB), a computerized online interactive data retrieval system, has been developed by the National Library of Medicine under the auspices of the Department of Health and Human Services. The LADB provides comparative baseline data on characteristics of control laboratory animals of various species and strains. Coverage includes information on animal environment and management, clinical chemistry and hematology, growth and development, and pathology. At present, the data bank contains approximately one million observations on more than 29,000 animals.

By use of the LADB, scientists may 1) select and examine baseline data for various biologic and physiologic values; 2) determine the environmental and management conditions for each animal group selected; 3) determine the incidence of certain pathologic changes in animals; 4) statistically analyze the retrieved data; and 5) print out the data as distributions, such as data tables or histograms, and as complete reports. A long range goal of the LADB is to assist researchers in designing experimental protocols in which the number of control animals can be reduced.

Your cooperation in identifying sources of control animal data for possible acquisition by the LADB would be greatly appreciated. Potential contributors who have data and information that might be included in the LADB are invited to correspond with Dr. Orland A. Soave, Laboratory Animal Data Bank, Specialized Information Services, National Library of Medicine, 8600 Wisconsin Avenue, Bethesda, Maryland 20209; or call him at (301) 496-5022.

BELTSVILLE SYMPOSIUM IN AGRICULTURAL RESEARCH VI

The 6th annual Beltsville Symposium in Agricultural Research will be held at the U.S. Department of Agriculture, Beltsville Agricultural Research Center in Beltsville, Maryland on May 17-20, 1981. The subject will be "Strategies of Plant Reproduction."

Contact: Dr. Albert Piringer, BARC Symposium VI, U.S.D.A., Room 130, Bldg. 003, BARC-W, Beltsville, MD 20705, USA, for a copy of program and preregistration packet.

BIOTELEMETRY IN THE STUDY OF REGULATION OF VENTILATION*

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INTRODUCTION

Ventilatory control is accomplished by a highly complex control system that is composed of many neural, muscular and mechanical components (see Fig. 1). Clinical problems related to ventilatory control arise from disease-induced alterations in the function of these components. For example, prolonged hypoxia or hypercapnia could result in an insensitivity of central respiratory neurons to chemostimulation or an impairment of respiratory muscle function (37). Also, alterations in lung or chest wall mechanics could reduce aleveolar ventilation to critical levels (7,36). Consequently, investigators (61) have suggested that to better understand and treat ventilatory control abnormalities, studies should be designed to identify the function of these neural, muscular and mechanical entities in healthy humans and in patients with pulmonary disease. In man, the lack of techniques for proper study of these components has severely limited progress in our understanding of the ventilatory control process, particularly, in the presence of chronic pulmonary disease (35). In anesthetized animals, standardization of techniques for the measurement of neural activity in respiratory nerves and muscles has only recently been undertaken (12,13). Even so, data obtained from anesthetized preparations reflects only short term changes in physiological function, and data interpretation is always subject to the multiple effects of anesthesia. An alternative approach would be the development of unanesthetized animal models for the study of regulation of ventilation using modern radio-telemetry techniques.

A biotelemetric model would provide a good substrate for the study of ventilatory control mechanisms in unanesthetized, freely moving animals under normal physiological and psychological conditions. In addition, totally implantable sensors and transmitter systems would provide data from otherwise inaccessible regions and would allow characterization of changes in physiological function, not only to acute, but also chronic chemical and mechanical challenges similar to those observed in patients with pulmonary disease.

This report will primarily concern itself with a review of hardwire and radio-telemetry techniques for monitoring minute ventilation, intrapleural and intra-abdominal pressure, and the electrical activity of respiratory nerves and muscles in freely moving animals. No attempt will be made to fully review the literature dealing with either radio-telemetry systems development or telemetering of other physiological variables. For further information, the reader is referred to other recent reviews and symposia (6,15,21,27).

HISTORICAL DEVELOPMENT OF BIOTELEMETRY

Biotelemetry had its early beginning in "hardwire" form when Marey (39), in 1869, first transmitted chest wall movements and wingbeat frequency from flying pigeons. Biotelemetry today refers to the transmission of biological signals over a distance using radiowaves, and began in 1921 when Winters (68) was able to transmit heart sounds from ships at sea to hospitals on shore. Approx-

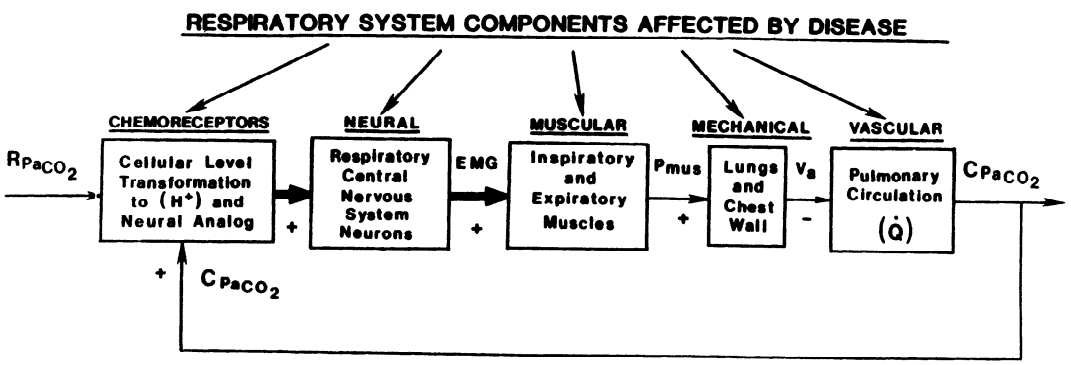

Fig.1. A simplified block diagram of the major components of the respiratory control system and variables used to quantify the output of these components. EMG=electrical activity; Pmus= respiratory muscle pressure; $\dot{V}_A$= alveolar ventilation. Broad arrows indicate multiple signals, thin arrows one signal.

*Tutorial Lecture presented at the 1979 Fall Meeting in New Orleans. Supported by NIH Grant HL-21743.

imately 50 years later, Holter (20) developed the first reliable radiotransmission system for the electrocardiogram (ECG) and electroencephalogram (EEG) that continues to be used clinically today. With the advent of solid state electronics, radiotelemetry systems became smaller, more reliable, and suitable for biological implantation (1,24,30). Using these techniques, MacKay and colleagues (38) telemetered heart rate, blood pressure, intraocular pressure, and gastrointestinal motility from freely moving subjects.

These early implantable telemetry systems were mostly restricted to transmission of one biological signal. This limitation led Fryer et al. (16), in 1969, to develop a multichannel telemetry system capable of simultaneously monitoring ECG, blood pressure and body temperature. Although improved over earlier designs, this system's power consumption was still excessive, limiting its useful battery life. Further developments in electronic technology and improved miniaturization and packaging techniques allowed Fryer et al. (17), in 1975, to report the development of a more advanced multichannel telemetry system. The relatively low power requirements of this system supported electromagnetic blood flow measurement. In addition, implanted batteries could be recharged through the skin by induction resulting in a prolongation of battery life. More recently, McCutcheon et al. (41) designed a multichannel telemetry system in which no active power source is implanted, but rather, the unit is inductively powered by coupling an external energizing coil to an internal receiving coil. The small size of this system allows implantation in animals as small as 5 to 10 kg. These telemetry systems continue to be improved (15,20). Thus, today's electronic technology allows for the design and construction of multichannel radio-telemetry systems. These units are custom designed to meet individual investigator needs and are expensive. Very few commercial manufacturers have shown significant interest in mass development of these telemetry systems.

TELEMETRY OF RESPIRATORY SYSTEM VARIABLES

Minute Ventilation ($\dot{V}_E$) $\dot{V}_E$ (liters/min) cannot be directly measured in freely moving animals, but can be indirectly calculated as the product of respiratory rate (breaths/min) and tidal volume (liters/breath). The next two sections discuss the radio-telemetry of these two variables.

Respiratory Rate In 1967, Thompson and Ruhberg (60) designed a four channel, back-pack telemetry system capable of monitoring ECG and EEG, body temperature and respiratory rate. A special strain gauge sensor (59) was implanted between the fifth and sixth rib interspace such that the gauges electrical resistance changed with respect to expansion and contraction of the rib cage. The resultant electrical signal was used to determine respiratory rate of flying pigeons.

Another approach that has been used to measure respiratory rate in birds has been to record the changes in electrical impedance across the chest wall during ventilation (5,19,54). The resultant electrical signal has components related to both ECG and respiration. Since the harmonic content of these two components is significantly different, electronic filtering was used to isolate the low frequency component that is related to respiratory rate. An inherent advantage of this method is that both cardiovascular and respiratory information can be transmitted on a single data channel, thus reducing the cost, complexity and size of such telemetry systems. In 1975, Woakes and Butler (69) used a thermistor implanted in the trachea to study changes in respiratory rate in diving ducks. This technique was used to show anticipatory adjustments in ventilation prior to a dive. Thus, investigators have successfully used sensors that reflect changes in chest wall movement, electrical impedance and temperature to measure respiratory rate in freely moving animals.

Tidal Volume Tidal volume can be estimated by electronically integrating respiratory airflow signals. The technology for the determination of airflow in freely moving subjects is discussed in the following paragraphs.

In 1972, Kimmich et al. (25) developed an airflow rate transducer that was lightweight and compatible with a telemetry system to be used for monitoring ventilation in exercising human subjects. A small plate was inserted between two parallel coaxial tubes with the plate being attached to the outer tube by two strain gauges. When this plate is deflected by movement of air, one gauge is lengthened and the other is shortened, which results in opposite changes in their electrical resistance. These two gauges comprise opposing arms of a Wheatstone bridge circuit. In this arrangement the sensing elements are temperature compensated for inspiratory and expiratory flows, and are symmetrical in terms of voltage output. The system has good zero flow stability and is extremely accurate at high flow rates, but less accurate at low flow rates. Subsequently, Kimmich (26) developed a new magnetic type of flow meter which has good zero flow stability and linearity over a flow rate range of 0 to 8 liters/second. More recently, Kimmich and Spann (28) incorporated this flow sensor and an oxygen sensor for combined telemetering of flow and end-tidal PO_2 in horses.

Integrated circuit technology has led to the development of monolithic gas flow sensors (63). These sensors make use of the principle that a gas flowing across a heated surface will create a temperature difference measured between the two sensors that would be related to the velocity of flow. One advantage of this type of sensor is that it provides not only a measure of the magnitude of flow, but also, directionality. Although still in the developmental stage, this technology may lead to the production of lightweight, rapidly responding airflow rate measuring systems for use in large animals. The reader is referred to the following review articles for a more detailed discussion of silicon microtransducers (33,43,44).

More recently, Satomura and colleagues (52) reported the development of a flow rate monitor using tracheal sound analysis. Tracheal sounds produced by respiratory airflow were monitored using an accelerometer attached to the fossa sternothyroides of human subjects. After suitable electronic manipulation, the resulting electrical signal was used as an estimate of airflow and correlated with air flow rates measured with a hot-wire flowmeter. Sound levels in the 128-1280 Hz fre-

quency range showed the best relationships to flow. Thus, several techniques have been used to sense airflow rate, with varying degrees of success. Further development is required, particularly, with respect to their use in freely moving animals. Special attention should be given to (1) the rapid temperature compensation that is required for the sensors to accurately respond to inspiratory and expiratory flows; (2) the effects of foreign deposits (water and mucus) on the flow sensor output; (3) linearity; and (4) long-term stability.

Other techniques for estimation of tidal volume involve the placement of transducers directly on the chest and/or abdomen. Air-filled bellows or mercury in silastic strain gauges have been used to measure changes in chest wall circumference, but they only provide qualitative estimates of tidal volume (50). The effect of slippage of these devices with body movement limits the use of these techniques in freely moving animals.

Changes in electrical impedance measured across the chest wall have been used as a non-invasive means of tidal volume measurement (18,32,34). However, changes in body position (18) produce changes in chest wall impedance and thus, this technique is not suitable for quantitative measurement of tidal volume in moving subjects.

In 1967, Konno and Mead (31) used magnetometers to measure changes in the anterior-posterior diameter of both the rib cage and abdomen during breathing in conscious man. The magnetometers consist of a receiving and a transmitting coil that are placed on opposite sides of the thorax and abdomen. The strength of the magnetic field varies as a function of the distance between the two coils. This system can be appropriately linearized and calibrated to obtain changes in lung volume. To date, the magnetometer system has been used on conscious humans and anesthetized man and animals. However, since calibration of this device is highly dependent on changes in body position, it cannot be used on moving animals.

Recently, a respiratory inductive plethysmograph (RIP) (66) has been used to measure changes in the cross-sectional area of both the rib cage and abdomen. This system consists of coils imbedded in a cotton mesh garment that snugly fits around the body. Changes in mean cross-sectional area of the coil region, thoracic or abdominal, produce a proportional change in self-inductance of that coil, which is a function of lung volume. This measurement represents thoracic gas volume which, in normal subjects, reflects tidal volume at the mouth, because significant gas compression and decompression do not occur in the thorax (23). Cohn et al. (8) have shown that changes in body position do not significantly affect the calibration, nor the output of this device. The respiratory inductive plethysmograph has been used in humans to monitor ventilation at rest, during exercise and during sleep. This device has now been applied in studies using sheep and dogs in the awake state (Personal Communication, W. Gruen, Ambulatory Monitoring, Inc., Ardsley, New York). Finally, the respiratory inductive plethysmograph appears to be most promising for measurement of tidal volume in freely moving animals, particularly since the electronics portion of this system can be miniaturized and packaged for mating to an implantable telemetry system.

INTRAPLEURAL AND INTRA-ABDOMINAL PRESSURES

In recent years, catheter-balloon transducer systems have been used to measure intraesophageal (45) and intragastric pressures (2) in unanesthetized human subjects. These latter pressures have been used to indirectly assess intrapleural (P_{pl}) and intra-abdominal (P_{ab}) pressures respectively. However, these catheter systems suffer from several disadvantages, as discussed below, and also, require restraint if used on animals.

A more direct approach for measuring P_{pl} and P_{ab} would be the use of miniaturized, solid state pressure transducers that can be implanted directly in the thoracic and abdominal cavities. These transducers can be mated to implantable telemetry systems and are commercially available (Konigsberg Instruments, Inc., Pasadena, Calif.). Though these transducers have been used successfully to monitor arterial (62), left ventricular (64), and intracranial (48) pressures in awake, unrestrained animals, they have not been used to measure respiratory pressures. A brief discussion of the advantages and limitations of these devices is warranted in order to project necessary future developments.

A main reason for using an implantable pressure transducer is to obtain information by telemetry that would be otherwise inaccessible from freely moving animals. Another reason for using solid state sensors is that they do not encounter problems with a transmission line as do air or fluid filled catheters, such as patency due to clotting or compression, and they are less susceptible to movement induced artifacts (4).

Several practical problems are associated with the use of implantable sensors. First, they must be small, lightweight and interfere as little as possible with physiological function. Secondly, they must be constructed or coated with materials that are compatible with biological tissues to minimize inflammatory reactions, fibrosis and blood clotting (42). Finally, the placement of the transducers must be such that accurate measurements are obtained and not artifacts due to mechanical impact (53).

At this time, an implantable differential pressure transducer does not exist. A significant effort should be made toward its development (58) because of the increasing need to measure differential pressures in either the respiratory or cardiovascular systems (51). The available solid state transducers are absolute pressure measuring devices and are sealed at ambient pressure and temperature, and hence, lack a true zero pressure reference. Thus, daily fluctuations in barometric pressure will influence the output level of the transducer and must be considered if changes in baseline pressures are to be studied. A temperature coefficient may be used to correct for any differences in calibration temperature (approximate body temperature) and recorded body temperature.

Two other major problems with solid state implantable pressure transducers are the changes in baseline output levels and calibration sensitivity that occur as a function of implant duration. These alterations must be evaluated using cross-

calibration techniques (4). Briefly, a known pressure change is produced in the system under study and simultaneously measured in vivo with both the implanted transducer and either a catheter-tip pressure transducer (46), or a fluid filled catheter transducer system (3). The period between cross-calibration is determined by individual experimental situations.

Thus, many of the problems that are associated with implantable pressure transducers have either been overcome or have been taken into account by appropriate calibration procedures. With respect to the specific measurement of intrapleural and intra-abdominal pressure, the development of a differential pressure transducer would be extremely valuable. Whether either differential or absolute pressure sensing devices are used for the measurement of respiratory pressures, their zero stability and calibration sensitivity must be improved to provide the required accuracy of these low pressure measurements. Finally, the unique nature and location of these potential spaces demands improvement in biocompatibility and placement techniques.

ELECTRICAL ACTIVITY OF RESPIRATORY NERVES AND MUSCLES

To better understand how the respiratory controller regulates ventilation, investigators have recorded the electrical activity from the respiratory nerves of anesthetized animals. However, respiratory nerve electrical activity has not been telemetered in awake, unrestrained animals, but should be attempted, since chronic recordings of sympathetic (29,47) and mammalian (9,50) nerve activity have been obtained. In these studies, reliable recordings have varied over the range of one day to 10 months,indicating that the technical difficulties associated with chronic monitoring of nerve electrical activity have not been completely overcome. Most of the problems are associated with the electrode's design to minimize injury to the nerve and to maintain a stable nerve electrode interface in the presence of tissue and fluid infiltration. The most common design of electrodes has consisted of bipolar wires encased in pre-formed silastic rubber chambers (55). Several attempts have been made to insulate the nerve electrode interface with fast-curing silastic rubber applied directly to the phrenic nerve, but this approach results in nerve destruction during the curing process when heat and by-products are released (Personal Communication, F. Eldridge). Another problem with chronic neural recording is the reproducibility of the measurements, which must be clearly defined. For this purpose, the relatively simple method of electrode impedance determinations (57) provides a sensitive method for evaluating the effects of implant duration on recording electrode properties. Autocorrelation (65) and cross-correlation (11) functions have also been used to estimate reproducibility of EMG measurements.

A hardwire telemetry approach has been used to telemeter the electrical activity of the diaphragm, external and internal intercostals and neck muscles in unrestrained sleeping cats (10,22,49). In 1979, Evanich et al. (14) also used hardwire telemetry to characterize changes in the electrical activity of the diaphragm and external oblique muscles in awake goats during CO_2 rebreathing. The electrical activities were quantified as peak moving time average (12) and found to vary linearly with increasing levels of end-tidal P_{CO_2} and these responses were reproducible over a 3 to 6 month time span.

Though muscle action potentials (EMG) have been telemetered (radio) from other skeletal (67) and smooth (40) musculature, using EMG amplifiers-transmitter systems, no published reports of radio-telemetered respiratory muscle EMG have been located. Our laboratory is currently developing a totally implantable 10 channel radio-telemetry system that is capable of monitoring the electrical activity of several respiratory muscles, including intrapleural and intra-abdominal pressures, using the aforementioned solid state pressure transducers. Electromyographic activity has now been reproducibly recorded from the diaphragm, external oblique and external intercostal muscles in one goat for 2 months (unpublished observations). This neural information, along with the simultaneously recorded respiratory pressures, will allow us to better characterize both the neural and muscular components of the respiratory control system in intact animals.

CONCLUSION

Current electronic technology allows for the development of miniaturized radio-telemetry systems for use in freely moving animals. The design and development of suitable sensors appears to be the main limiting factor in the use of radio-telemetry for the study of regulation of ventilation. More cooperative efforts between respiratory physiologists and engineers should prove fruitful for the development of biotelemetric techniques for the long term study of respiratory control mechanisms in unrestrained animals.

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Interactive Computer Graphics in Science Teaching. J. McKenzie, L. Elton, and R. Lewis, Eds. Horwood, Chichester, 1978. 248 pp. illus. index, $19.95.

This compact volume represents the collaborative efforts of 22 contributors most of whom are affiliated with three educational institutions in the United Kingdom, namely: Chelsea College at the University of London, University College London, and the University of Surrey. It represents primarily the experience of a large computer-assisted learning project sponsored by the National Development Programme and entitled Computers in the Undergraduate Science Curriculum (CUSC) which started officially in January 1974. In addition to being multi-institutional CUSC was also conceived on a multi-disciplinary basis with concentration in the subject areas of physics, chemistry and biological sciences. The book can be thought of as divided into four parts. In the first of these an introductory chapter is followed by those which deal with Product Design and Development, Graphical Displays, Software for Graphics, and Computers for Computer Assisted Learning. In the second portion of the volume there is a chapter devoted to Computer Assisted Learning in each of the three primary subject areas of the project. The third part deals with Evolution and Evaluation, there are two chapters on View of Teachers, and the final three chapters which discuss Transfer and Transferability, Counting the Cost and Trends in Computer Assisted Learning. The final portion of the book consists of four appendices and a 13 page index. The former include a Glossary of Terms and a Classified Listing of the 38 CUSC Teaching Packages.

Prior to making any evaluative comments on this volume, it may be worthwhile to acknowledge that the reviewer is: a) an American, b) a physiologist, and c) an enthusiast of computer-based education who has devoted the last ten years to nurturing that fledgling in the indifferent environment of a traditional medical school.

The viewpoint of the volume is quite narrow. This is to be expected when a relatively small number of persons who are geographically isolated attempt to describe a short-term experience. But these unavoidable elements are exacerbated by two unfortunate tendecies: 1) to deride earlier work in the field as inferior to their own, and 2) to suggest that they were the persons who discovered interactive graphics. The chapter on Product Design and Development is parochial at best. Your reviewer who has been exposed to a number of different philosophies for the development of computer-based educational materials cannot confirm the adivce provided and therefore denies the implications that this is the preferred development style. In the chapter on Graphical Displays for Computer Assisted Learning it is suggested that "at least 30 (and preferably 50) terminals" are necessary to support a class of 100 students. Such a large number of terminals is rarely necessary when terminal access is scheduled for small groups or made available outside the customary class schedule. Similarly, much is said about the superiority of small, free-standing microcomputers over large, time-sharing computers without addressing the fact that a variety of hardware approaches for different kinds of teaching packages will supply a better set of tradeoffs between cost and performance.

The book attempts a number of interesting presentation techniques to cope with the inevitable computer jargon which accompanies such a subject. The first time a word is used in the text, it is printed in bold faced type. This means that it is listed in the Glossary. In the Index the bold faced type has the same significance. Italic type is used to reference in the Index the actual teaching packages which are both described in the text and summarized in the appendix. Although the Glossary defintions were uniformly well-done and usually informative even to those with minimal exposure to computer jargon, there were some gaps. Neither the defintion for "core" nor the one for "store" make it clear that the same item which we in America call "memory" is being defined. Similarly, there are differences between American and British usage in certain abbreviations. The use of CAL which stands for Computer Assisted Learning implies a difference and even by the authors of this work, a superiority, to CAI, Computer Aided Instruction, the more conventional American term. Attempting to make such distinctions ignores the fact that CAI is usually used in a broad sense which encompasses all the stated benefits of the CAL approach.

Now for a few more comments about specific chapters. The chapter entitled, "Computers for CAL" is superficial and does not provide a genuine framework for understanding this complex subject. The chapter on, "Transfer and Transferability" does not mention networking, a process whereby courseware is shared by interfacing the host computer to regional or even international computer networks which greatly increases access. Similarly, there is no mention of the "clearing house" approach to sharing courseware as has been developed by CONDUIT here in the U.S.A. By contrast the chapter called, "Counting the Cost" is excellent. This is not so much because it will be of direct application either to physiology as a discipline or to American institutions, but because it discusses the issues on such a broad scale. This contrasts with the narrower scope of so much of this work and explains why the book as a whole is less valuable to the general reader.

The last chapter entitled, "Trends in CAL" also has a useful broad perspective. It makes the excellent point that those teachers who have become involved in computer-based education have developed a more general interest in problems of teaching than their colleagues who have avoided computer interaction. Because of its commentary on institutional support this chapter will be of value to educational administrators particularly those whose responsibilities include allocation of resources within a given institution.

One should recognize the descriptions of the educational packages: 10 in Physics, 3 in Statistics, 14 in Chemistry, and 11 in Biology and the Biomedical area. The classified listing in the back of the volume provides a brief sketch of the package, but each package has been presented in greater detail in the text which has also included excellent illustrations.

It is also legitimate to acknowledge an emphasis on interactive graphics which has not always accompanied prior work in this field. The CUSC project did create a systematic graphics package which was implemented in two computer languages: FORTRAN and BASIC, to improve the transferability of their packages from one type of computer to another. The graphics package contains

such routines as those used for scaling displays, presenting text interspersed with figures or displaying figures from different vantage points. Many routines of this sort are available from the manufacturer of graphic display terminals; other routines represent standard utilities which are available in most large computer centers. Nevertheless, a service has been performed if a set of instructional modules has utilized the same graphics package and that instrument, as seems to be the case, is capable of being adapted to more than one graphics display terminal.

To sum up, a well-indexed presentation of short term experience among a close-knit group who were not always aware of what else was going on in the world. This monograph and excellent Glossary will be of value as a reference work, but it is *not* the definitive treatment of how to bring the computer into the classroom or laboratory.

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Comparative Physiology of Osmoregulation in Animals. G.M.O. Maloiy, Ed. Academic press, London, 1979. 677 pp., illus., index, $100.50.

In the 16 years following the publication of a comprehensive volume on salt and water balance in different kinds of animals, the advances have been so numerous that the coverage in general texts, however recent, is often dated. Somewhat surprisingly, the editor apparently regards the use of enzymology and the measurement of bioelectrical potential differences as less significant than earlier technical advances, which may explain the selection of topics. While the predecessor (1) of this volume was notable for the consistency of a work written by two collaborators, the present anthology is uneven in both scope and in quality. Nonetheless, several of the chapters are excellent.

The book begins with an exceptionally clear and succinct but thorough account of ion transport across the tubular epithelium of the mammalian kidney, presumably chosen to serve as a model system which is reasonably well understood. Fortunately, the author (Giebisch) conveys uncertainties as well as paradigms, without sacrificing simplicty of presentation. A rather eccentric chapter on 'Marine and Euryhaline Invertebrates' (= estuarine invertebrates) is disappointing, more so because of the important subjects given slight notice than for the focus on the author's (Spaargaren's) own controversial theses. A chapter on freshwater invertebrates (Greenaway) is useful, though the emphasis remains on papers published many years ago. Mantel, who was assigned the formidable task of producing a coherent chapter on a group so disparate as 'Terrestrial Invertebrates other than Insects,' has delved deeply into an obscure literature generally remote from her own interests, and the result is a very useful chapter of considerable scholarship.

The chapters insects (Wall and Oschman) and amphibians (Alvorado) provide timely interpretations of very recent works, without ignoring the classic contributions of several decades ago. Evans' chapter on fish, an area of heavy investigative activity, is his usual critical summary of present knowledge, with the controversial aspects of present opinion (including his own) often made explict. The book ends with an encyclopedic (40% of the total volume!) chapter on reptiles (Minnich) which must contain many of the numerical data on these animals. Here the traditional ecological, endocrinological and developmental aspects are emphasized.

While the book may not be within the price range of the non-expert, it should be given high priority for acqusition by the institutional library. A second volume covers birds and, mainly, mammals.

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1. Potts, W.T.W. and G. Parry (1963). *Osmotic and Ionic Regulation in Animals.* Pergamon Press, Oxford. 423pp.

Female Sex Steroids: Receptors and Function; Monographs on Endocrinology, Vol. 14. J. H. Clark and E.J. Peck, Jr. Springer-Verlag, New York, 1979. 245 pp., illus., index, $44.80.

This is the fourteenth volume of the series "Monographs in Endocrinology," all which are intended to present the experiments and interpretations of a given laboratory. Toward this end, the authors have succeeded very well. The volume concerns primarily the relationship of estrogen and progesterone interactions to biological events in reproductive target organs. Dr. Clark and Dr. Peck have accumulated an impressive array of key experiments which relate receptor levels, occupancy, nuclear localization, and replenishment to a variety of changing biological situations. These include studies on early development of the reproductive tract and changes throughout the estrous cycle, in neoplasia, and during treatment with hormone agonists or antagonists.

The authors attempt to cover most recent aspects of the receptor field. Following a brief introduction, there are three chapters on basic considerations: receptor characterization and measurement, cellular compartmentalization, and cytoplasmic and nuclear receptor forms. The next five chapters are more biologically oriented and cover: nuclear binding and biological responses, steroid antagonism, neoplasia, physiological relationships and steroid binding, and steroids and brain function. The final chapter on speculations and conclusions is well done and rather thought provoking. Throughout the book, the authors have provided a good balance of hard results and interesting speculation. The volume has a stronger emphasis on physiological relationships than on the basic physicochemical characterization of receptors, which is consistent with the authors' approach to the subject.

Overall, this volume is very readable. It contains few errors and the reader is aided by a large number of figures and diagrams (116 in all). Since the chapters are fairly self-contained, portions of this book would be of value to those with only a general interest in the subject and also to those with interest in only a particular aspect. However, this monograph is probably of greatest value as a reference text particularly for young students and investigators in this and related fields.

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Octopus, Physiology and Behaviour of an Advanced Invertebrate. Martin J. Wells. John Wiley & Sons, New York, 1978. 368 pp., illus., index, $42.50.

OCTOPUS, Physiology and Behaviour of an Advanced Invertebrate, by M.J. Wells, came out in 1978, and has been widely and favorably reviewed. The editor and the reviewer agree that the appearance of a complete physiology of one species of invertebrate animal is so noteworthy an event that the book should be reviewed in *The Physiologist*.

The information gathered in this book cannot be found in any other single work. There is Bauer's little introduction to cephalopod physiology of the Naples series in 1909, far too out of date to be useful. There are two popular works on cephalopods (Lane's Kingdom of the Octopus (1957); and Cousteau's, Octopuses and Squids 1973) but there is little physiology in either. The Festschrift for J. Z. Young, Biology of Cephalopods, was misnamed since, while the chapters are excellent and intensive they deal only with bits and pieces of physiology. So this is *the* book.

In a sense there was a preliminary edition of this book. Stanford University Press published Wells' Brain and Behaviour in Cephalopods in 1962. There can be little doubt that the writing of that work conditioned him for the current book. While the early work did not pretend to cover the other systems of the body, the present work is still quite uneven in its coverage. Biochemistry is almost unacknowledged and the book, while detailed in reporting the histology of some sensory and nervous system structures, omits the histology of many systems.

Nevertheless the book has a rationale. Wells believes that the molluscan heritage in several aspects of physiology is crippling. For instance he considers the circulatory system to be barely adequate for so active an animal, forgetting the power of many squids. He thinks the digestive system also to be limiting. So, he asks, what has enabled this animal to compete and his answer is The Nervous System. His treatment of the maintainance systems is therefore somewhat grudging. In fact he excuses himself most elegantly, confessing that his interests lie elsewhere. In a way he reminds the reviewer of a distinguished neurophysiologist who could dismiss all of these grubby aspects of physiology with the words: "The rumbling of the guts."

In fairness to Wells it must be said that he has taken the trouble thoroughly to digest the fundamentals of these systems. He presents clearly and well the basic physiology so that, for example, a budding neurobiologist will quickly appreciate the organization of each system. What is missing is the probing interest of the generalist. As an example let us take the interaction of respiratory and circulatory systems. Johansen and colleagues, working with *Octopus dofleini,* have put out a series of solid reports from which Wells might not only have reported the standard physiology but derived such parameters as minute and stroke volume, so interesting in comparison with other animal species and so revealing of the ultimate capacity. In fact Johansen has himself made the computations in a paper hardly likely to have escaped Wells' eye, but not appealing to his view of what detail might be included. Or take the matter of an animal with a closed circulatory system (it is not certain that Wells believes this) and a high protein content, but without a lymphatic system. How does it cope with the problems Starling so cleverly resolved for the vertebrates?

By confining himself to reasonably well understood physiological processes Wells is able to deal with respiration, circulation and excretion in a single chapter. Metabolism, in the sense of oxygen consumption y mentioned, but feeding and digestion warrant an interesting chapter together since a good deal of behaviour is involved. Reproduction and growth are well done, and the endocrinology of the animal, as far as it is understood, is the subject of another chapter. The author has now, in about a third of the book, prepared the physiological substrate for the topics that most interest him.

In his introduction the author showed that the brain of an octopus, in proportion to its body weight, is as large as that of fishes and reptiles, and this even omitting the vast number of neurones that make up the nerve cords of the arms and that might properly be included as equivalents in part to a spinal cord. Now he presents an inventory of the sense organs, and of the sorts of sensory information with which the animal has to work. This is followed by a review of the theories of shape recognition by the eyes. In speaking of the inverted projection of the visual field from retina to optic lobes which, of course, re-erects it, he reminds us that Young suggested this to be necessary if a topological relation between visual receptors and the projection from gravity receptors was to be preserved. Wells finds this suggestion unconvincing; and he does not mention Cajal's brilliant insight of a possible role of image inversion by the lens as necessitating the complicated crossing of fiber tracts in the vertebrate brain. Of course it may not be necessary to make a more complete chiasma since the octopus appears to prefer to scan with each eye separately. Part of the solution, too, may be that visual memory is already present in the optic lobe of the ipsilateral side. Information is transferred to the opposite side by the optic commissures, but imperfectly and with some delay, and the vertical lobe is necessary for any long term transfer. Cuttlefishes and squids should be of great interest in this respect because they use binocular vision and there might be some arrangement in the nervous system for fusion of the two images, lost, so far, in the enormous size of their optic lobes in comparison to the rest of the brain.

We are now more than half-way through the book and the author is entering the area of his greatest expertise. Octopuses are nearly as much creatures of touch as they are of vision, and this subject is well handled, especially touch learning. Proprioception is, of course, essential to coordinated movement, but does not seem to contribute substantially to judgment and learning. Wells accounts for this as due to the lack of any fixed position of the body parts to serve as a reference base for movement, a base which is provided in other phyla by either an internal or an external skeleton, and he points out that this is a substantial limitation.

Motor control is the next topic discussed, and warrants considerable space. The eight arms are full of local reflexes, with several levels of control provided which may fail in some instances. The animal must let go of a surface to be free to move away; sometimes animals brought to the laboratory after capture on a rocky bottom are found to have held small stones on some suckers for many hours. This cannot be due to confusion with retaining small crabs, which also is often seen, because the suckers have sufficient chemical sense to recognize food objects. Perhaps it is merely lack of attention because when orientation is critical it can be very exact. For example a relatively small octopus can immobilize a large crab simply by arraying a different arm along each leg of the crab. The events following removal or denervation of an arm are discussed, but this area is not thought to be fully understood. Motor control is also usefully discussed after split-brain and lobe-deletion experiments.

Learning and brain lesions make up the final topics, and this portion of the book is slighted in this review because of the complexity of the area. Competitive theories are assessed, and clever experiments analyzed, so that reading this part of the book demands complete attention that goes beyond the average interest, so this part is clearly for the dedicated neurobiologist.

We come out then, as the quatrain goes, by the same door where in we went. This book is the only complete physiology of an octopus and, when properly supplemented, conveys a sense of understanding of much of this special physiology.

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Dimensional Analysis in the Biomedical Sciences. Bernard Schepartz. Charles C. Thomas, Springfield, 1980. 172 pp., illus., index $19.75.

This book is intended for students and research workers in biology and medicine. It reviews a branch of engineering physics which biomedical engineers have used with considerable profit during the post World War II era. The style is clear and forthright, the book is well manufactured and there are two useful appendices. One appendix is a list of symbols and the other is a collection of dimensional formulas. In the bibliography, the author seems to have made a sincere effort to mention the relevant English-Language publications. One notes the absence of titles in any other language. The index is entirely satisfactory.

The book is built around a set of fifty problems ranging from studies of the swimming of spermatozoa to the physics of coughing. There is even a discussion of the running of dinosaurs! The first chapter introduces the concept of dimensional analysis by reviewing Warburg's analysis of oxygen diffusion in tissue slices. Given the external 0_2 concentration and internal consumption rate how thin must a slice be, so that all parts get 0_2? Rather than solving the differential equation, one examines how the primary physical units of mass, length and time enter into the problem. It is first shown dimensionally that the limiting tissue thickness depends not only on concentration and consumption-rate but on a measure of the ability of the gas to traverse the tissue - the diffusion coefficient. By inspection one immediately sees that it is the *square* of the limiting thickness which is proportional to the concentration times D and inversely proportional to the consumption rate.

One may recognize that a well-trained physicist has developed his physical intuition by working many hundreds or perhaps thousands of physics problems and that dimensional analysis applied to simple models plays a vaulable role in this process. Physical intuition can often be useful in biomedical science. Nevertheless, there are times when a pragmatic engineer can simplify a problem to death. Careful reading of the author's discussion following the solution of each problem will help the reader to avoid this trap.

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Insect Neurophysiological Techniques. Thomas A. Miller, Ed. Springer-Verlag, New York, 1979. 303 pp., illus., index, $25.80.

This book is the first volume of the new Springer Series in Experimental Entomology. The goals of the series are to " 1) report new developments in methodology, 2) to reveal sources of groups who have dealt with and solved particular entomological problems, and 3) to describe experiments which might be applicable for use in biology laboratory courses."

The first topic in this volume is the basic equipment needed for neurophysiology experiments including electrodes, instruments, tools and materials. The next section deals with many of the materials and methods used to observe and measure activity of unrestrained insects. Part three is concerned with devices for recording nerve and neuromuscular activity simultaneously with the study of behaviors such as walking or flying in free-moving and tethered preparations. The concluding section deals with special techniques for the study of many different dissected preparations such as nerve, nerve-muscle, heart and digestive tract.

Throughout the book, an abundance of useful information is presented on the selection of materials and their sources. Experimental procedures are outlined clearly. Many of the experimetal pardigms are diagrammed schematically. In addition there are many helpful illustrations and relevant circuit diagrams which apparently have not been published before. Too often, texts discussing techniques are written so the reader must have experience with a procedure in order to understand the description of it. The author avoids this problem by writing clearly and by paying attention to common technical problems one is likely to encounter in an experiment. Some of the described procedures clearly are not for the student laboratory or for the novice. Usually, forewarning is provided. For example, on page 92, the author cautions about the technical difficulties involved in the use of capacitance shifts in a tuned resonant circuit for monitoring activity. Although published in 1979, most of the references date prior to 1976. This may produce an occasional problem. For example, the RCA 5734 mechanical transducer is cited in a few places, but is no longer manufactured. Inevitable difficulties such as this should pose no serious problem since most suppliers will provide help in securing substitutes.

The book is weak in the treatment of the practical consideration of cost. Although quality and utility of different techniques and associated equipment are compared, the question of relative expense of alternate choices is slighted. Hidden costs such as exotic types of chart paper, instrument maintenance and repair are important and sometimes neglected considerations when equipping a new laboratory.

This volume will prove useful for people already established in the field wishing to broaden their range of techniques, as well as for the novice setting up an insect laboratory for the first time. Many of the described procedures and techniques should prove useful to the teacher wishing to demonstrate neurophysiological and behavioral concepts. Hopefully, teachers of physiology will find in this book relatively simple and inexpensive preparations for demonstrating fundamental principles of modern neurophysiology.

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Dear Doctor Reynolds:

The explanations of mechanisms of changes in pulse pressure given by Heusner and Tracy (*The Physiologist,* June 1980) are incomplete in that they do not include effects related to changes in diastolic arterial volume (V). The influence of V is paramount even when compliance remains constant, and no explanation that neglects this factor can be complete.

Increases in heart rate or in peripheral resistance lead to a decrease in pulse pressure only as they lead to increased V. If a change in V is prevented, as by lowering the total volume in the system, no change in pulse pressure occurs since the fractional increase in volume in the arterial tree per stroke (v/V) is unchanged.

The above is the way Wiggers explained pulse pressure in Circulatory Dynamics, and it is inescapable because it is based on a formula which presents the relation between pressure and volume in a system in which compliance is constant. My explanations, as presented in the enclosed, are derived from his and have been approved by Dr. George Washa, Professor of Engineering Mechanics at the University of Wisconsin.

Sincerely,

W.B. Youmans
Emeritus Professor of Physiology
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PHYSICAL FACTORS DETERMINING ARTERIAL PRESSURES

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Wiggers used a model to illustrate physical factors determining arterial pressures and described its characteristics in his textbook and in Circulatory Dynamics (1952). D.W. Rennie and I built a closed-system model in 1952 that was used regularly in demonstrations until 1975. I described it in my textbook (1957).

The circulation schema demonstration proved to be useful if careful attention were given first to emphasizing that what was to be learned was the effect of a single change imposed on the system and second, to explaining why the changes in pulse pressures observed in the schema were not those seen from imposing the same initial change on the circulation in the intact mammal. A few examples will serve to point out the problem.

A progressive increase in peripheral resistance in the circulation schema, in which compliance does not change, leads to a rise in mean pressure and reduction in pulse pressure. In the intact circulation as peripheral resistance is progressively increased the pulse pressure shows at first little change or decreases; and then, as peripheral resistance is increased further, the arterial tree becomes less compliant so that pulse pressure greatly increases. Of course this is instructive in itself in that it shows that both increased peripheral resistance and relative non-compliance of the arterial tree must be present to produce the arterial pressure pattern typically seen in essential hypertension.

In the closed system schema containing enough fluid to establish a positive mean circulatory filling pressure an increase in pump output causes a rise in mean arterial pressure and a lesser fall of pressure in the more compliant venous side (as occurs in the actual circulation). Thus the pump produces an arteriovenous pressure gradient not only by raising the mean arterial pressure but also by decreasing the mean venous pressure. Anyone who contemplates this fact does not fall into the trap of referring to a rise in venous pressure produced by decreased cardiac output as "back-pressure." If one bleeds this closed system from the venous side (lowers MCFP) the mean arterial pressure falls and the pulse pressure increases; whereas in the actual circulation bleeding causes a decrease in pulse pressure. The increase in pulse pressure in the schema produced by decreased MCFP is fully predictable. Pulse pressure is directly proportional (in a system having constant compliance) to the fractional increase in volume (v/V); i.e. *pulse pressure varies directly with the ratio of stroke volume to diastolic arterial volume.* In this case V has been reduced and v is unchanged; v/V is increased. In the actual circulation hemorrhage leads to a decrease in stroke volume both because of a lowered head of pressure to produce cardiac filling and because of less time for filling as the heart rate reflexly increases. Although V is lowered during hemorrhage there is a greater per cent decrease of v; v/V is decreased.

An increase in stroke volume will give rise to an increase in pulse pressure, along with the rise in mean pressure, in a circulation schema only if the distensibility characteristics of the "arterial tree" are such that the pulse pressure-reducing effect of the rise in diastolic arterial volume (incident to increased cardiac output) is not sufficient to override the direct pulse pressure-increasing effect of the rise in stroke volume. In other words, when v is increased as the initial change V also becomes increased. The values for peripheral resistance, V, and compliance could be a combination such that the increase in V is the same as the increase in v; and, if so, pulse pressure would remain unchanged. To simulate correctly even the direction of the effect on pulse pressure which increased v produces in the actual circulation one needs to simulate properly the peripheral resistance and the compliance of the arterial tree at each pressure level. Since the actual values are not available by trial and error one obtains a combination that gives pulse pressure changes at least in the right direction. At relatively high peripheral resistances in the actual circulation increasing stroke volume produces a predictable increase in pulse pressure not necessarily because v/V is increased but because the compliance of the arterial tree is greatly decreased. To show the full direct pulse pressure-increasing effect of an increase in stroke volume one first increases v and then, when equilibrium is established at the higher V, bleeds the system from the venous side until control diastolic pressure (and V) is restored; then, invariably a rise in pulse pressure is demonstrated.

In our model we used a piston type pump hence increased pulse pressure from increased v was due not only to increased v but also in small part to increased rate of ejection since the greater amount of fluid was ejected in the same time interval.

In the paper by Heusner and Tracy (1) the typical effect of increased heart rate on pulse pressure is shown. At the new equilibrium reached after increasing the heart rate the reason for the decreased pulse pressure is that V has been increased while v has not changed; v/V is reduced. The decrease in pulse pressure is progressive as diastolic arterial volume rises. If one wishes to see the effect of the increased heart rate per se on pulse pressure (i.e. without the effect from elevated V) he may bleed the system sufficiently to restore the diastolic pressure that existed before the increase in heart rate. When this is done it is demonstrated that pulse pressure is not changed.

Some of our colleagues do not believe that circulation schemas are useful in teaching hemodynamics. However, I am convinced that to study the physical effects of changes in pump rate, stroke

volume, peripheral resistance, compliance, and fluid volume in a simple schema that shows only physical changes as a consequence of the imposed change is a necessary step toward understanding circulatory patterns in man in health and disease. Such information must be acquired because the physical changes incident to the initial change imposed on the system in turn elicit the physiological responses.

Summary

The physical factors which determine pulse pressure are: 1) Stroke volume. 2) Velocity of systolic ejection. 3) Compliance of the arterial tree. 4) Diastolic arterial volume. Pulse pressure varies directly with 1 and 2 and inversely with 3 and 4. Changes in heart rate, peripheral resistance, and blood volume lead to changes in pulse pressure by altering one or more of these.

REFERENCE

1. Heusner, A.A. and M.L. Tracy. Arterial pressure analog. *The Physiologist* 23: 47-56, June 1980.

Dear Dr. Reynolds:

Thank you for your letter of September 9 concerning Dr. Youman's comment on our article published in the June, 1980 issue of *The Physiologist*. We would like the following to be published in response to Dr. Youman's comment that our explanation for the mechanisms of changes in pulse pressure is incomplete (Re: Dr. Youman's letter to you dated September 1, 1980):

We fully agree with Dr. Youman's point that the arterial volume V is "paramount" in determining arterial pressure. Indeed, it is the instantaneous volume of arterial blood in conjunction with the prevailing arterial compliance which determines the instantaneous arterial pressure. Our aim is to enable the students to directly relate changes in arterial pressure to changes in peripheral resistance, compliance, stroke volume and in heart rate by means of a simple concept. Even though the relative change in blood volume in the arteries is the main physical cause of the change in pressure, it is of little practical use since it cannot be measured readily under dynamic conditions, even in a simple physical model.

Since the time relationship between rate of inflow and rate of run-off govern the instantaneous volume of blood in the arteries, the time constant of the arterial tree in relation to the duration of the cardiac cycle is a reliable and readily determined factor for predicting changes in arterial pressure. This is why we have chosen to use the concept of time constant (RC) rather than the relative volume change (v/V) in the arterial tree. This does not imply, however, that we neglect the significance of volume changes in the arterial tree. As a matter of fact we illustrate the importance of the arterial blood volume in Exercise No. 2 in establishing the pressure-volume relationship in the Arterial Analog. In particular, Figure 6 (Exercise No. 2) shows clearly that at constant compliance any change in pressure in the arterial system of the analog is associated with a change in the volume of fluid contained in it. This conclusion, of course, also holds in the arterial system of a living animal.

In the subsequent exercises on the effect of changes in peripheral resistance (Exercise No. 5) and those of changes in heart rate (Exercise No. 7) we did not emphasize the change in volume because we cannot measure this change under dynamic conditions. Instead, we illustrate the use of the concept of time constant to explain the changes in pressure, since this is a variable which is readily determined in our Analog. Implicit in the following statement is the fact that the actual volume of fluid in the arterial system is greater at the end of the cardiac cycle than before, because runoff is decreased due to the increase in peripheral resistance (or time constant): "with an increase in peripheral resistance, the time constant of runoff increases, the rate of decline in diastolic pressure is slower and consequently the diastolic pressure reached at the end of the cardiac cycle is higher."

We deliberately have chosen to use the concept of time constant rather than the changes in arterial volume because we think it more useful in predicting the changes in arterial pressure.

Sincerely yours,
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Univ. of California, Davis

FIRST INTERNATIONAL CONFERENCE ON HUMAN COMFORT

The first international Conference on Human Comfort will take place in August 1981 in Portugal. All aspects of the subject will be included in the programme, which will consist of a mixture of lectures, given by internationally-recognised experts, and discussion periods. Topics to be covered in lectures include psychological aspects (such as privacy, social distance, spiritual comfort), physiological aspects (such as thermoregulatory and sensory mechanisms, thermal and noise stress) and physical aspects (such as the contributions of textile, clothing, design or transportation factors). In addition, up to twenty specific areas of interest (depending on the interests of the delegates) will be examined in depth.

A major purpose of the Conference is to bring together specialists in a relatively narrow area of interest related to comfort so that they can share their expertise and, in return, learn more about other aspects of human comfort outside their normal professional field. For this reason, it is hoped that all delegates will be willing to contribute a brief presentation to one or more of the discussion sessions.

Further details of the subject matter, information concerning registration, and application forms are available on request from Professor K. Slater, Textile Science Division, University of Guelph, Guelph, Ontario, Canada, NIG 2WI. Accommodation facilities are limited, so attendance is restricted and early application is advised. The deadline for registration is Ist February 1981, and requests will be handled in strict order of receipt.

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