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Editor's Page

It has been said that the APS is too medically oriented and should represent a broader spectrum of physiology than it seemingly does. The Society welcomes non-medically oriented physiologists in its membership but when one considers total numbers, the great majority of those who label themselves physiologists are medically oriented. Eighty-three per cent of the membership is associated with some sort of medical institution. There seem to be reasons for these proportions.

Most of the physiology departments are located in medical schools. There are 86 of these in the United States. This is undoubtedly because physiology is a required subject in the medical curriculum. Since it is in the medical curriculum, the subject material is naturally medically oriented. There are only 13 undergraduate schools, not associated with a university having a medical, dental, or veterinary school, that list departments titled physiology and some of these are combined with zoology, entomology, health, etc.

Many educators, including several in medical schools, would like to see those being trained in physiology have a broader background in all the other aspects of physiology besides mammalian physiology. There are not many places where such courses can be obtained in departments of physiology. Of the schools granting Ph. D. degrees in physiology between 1948 and 1958, 51 were medical schools and only 9 were schools not associated with medical schools. Of these 9 only 2 had departments officially titled physiology. It is obvious that biology, zoology, and natural science departments produce Ph. D's in physiology. It is excusable for schools not requiring physiology as a part of a curriculum not to have official departments of physiology but universities willing to recognize and grant a Ph. D. degree in physiology should have strong departments of physiology, at least in their graduate schools. Most of the non-medically oriented established persons who consider themselves physiologists are associated with zoology, biology, etc. and their primary loyalties often are to other biological disciplines at least in name.

One of the reasons why we are in the position of having few young people select physiology as a career is that they are not exposed to the subject as a career field in undergraduate school. Most obtain training in some areas of physiology in courses in cytology, zoology, botany, biology, entomology, hygiene, etc. but the emphasis on labeling dynamic biology as physiology is lacking, thus the student thinks of careers in other branches of biology but not specifically physiology. It appears that physiology, in its wide connotation, could be strengthened if the physiologists who are professors in departments of zoology, biology, etc. could urge the establishment of more official departments of physiology in non-medical institutions.

Now that several schools, with Federal aid available, are contemplating establishing programs for Ph. D. training in physiology could the APS lend guidance not only in types of recommended courses but also by stress-

ing the desirability of publicizing the word physiology more by the simple means of establishing official departments of physiology in non-medical schools? Would this materially aid recruitment?

This office receives many inquiries from high school students, teachers and parents for the names of colleges offering courses leading to graduate work in physiology. There are many excellent schools to recommend for training in dynamic biology (physiology) but few with official departments of physiology. It seems we have, through our career brochure and other means, at least instilled a desire among high school students. If we are to preserve this desire through the college years more emphasis must be placed on the word physiology through these years.

For those who think the Society is too medically oriented here is an excellent opportunity to work for a broader base, that is by encouraging more non-medical schools to officially recognize physiology not just as a sub-discipline of biology but as an important discipline in itself and important enough to warrant official recognition as a department.

Perhaps some members have additional or other ideas. We welcome letters to the editor.

CHANGE IN DUES AND METHOD OF PAYMENT

The November 1961 issue carried notification of the change in dues from $10 to $15 for regular members and the elimination of compulsory subscription to one of the APS journals. Associate membership dues remain at $5. Members will continue to be given reduced subscription rates to the journals if they choose to subscribe. The Federation Circulation office will handle all subscriptions. It is hoped that all subscriptions can be handled on a calendar year basis. The dues will be handled separately by the office of the society Executive Secretary-Treasurer. Dues will be on a July to July basis as before and are payable in advance. Dues notices are mailed to all members prior to July 1. Members are asked to submit separate payments for dues and journal subscriptions (if they subscribe) since they go to different accounts in different offices.

Correspondence relative to dues should be addressed to the Executive Secretary-Treasurer of APS and correspondence relative to subscriptions should be addressed to the Federation Circulation office.

SAMUEL JAMES MELTZER

The following material was taken from the History of the American Physiological Society and from an address given by William H. Howell at a meeting of the Society of Experimental Biology and Medicine on January 6, 1921, honoring Dr. Meltzer, founder of the Society.

Dr. Meltzer was the fifth person to serve as president of the American Physiological Society, serving in that capacity from 1911 to 1913.

Dr. Meltzer was born at Ponewjesh, northwestern Russia, on March 22, 1851. He died suddenly, while at work in his study, on November 7, 1920, New York City.

His preliminary education was received in a Realgymnasium in Königsberg, his training in medicine at the University of Berlin, 1882. While still a candidate for the medical degree he engaged in a research with Kronecker upon the physiology of swallowing. The final results were published in a joint paper announcing the Kronecker-Meltzer theory of deglutition. Shortly after graduation he came to New York and began the practice of medicine, but as soon as his financial condition made it possible he sought opportunities to continue his research work in Welch's laboratory at Bellevue and Curtis' laboratory at the College of Physicians and Surgeons. For a number of years he carried on simultaneously his medical practice and his laboratory investigations until, in 1904, he was offered and accepted a position in the Rockefeller Institute as head of a department of experimental physiology and pharmacology. His experience in the practice of medicine enabled him later to play a most successful role in bringing about cooperation and understanding between clinicians and laboratory workers. He was the chief founder of the Society of Experimental Biology and Medicine, affectionately known as the Meltzer Verein. He also was instrumental in founding the American Association of Clinical Research which was so revolutionary that it earned the title of "The Young Turks." A member of many scientific and medical societies, he was faithful in attendance upon all of them. His thoroughness in this respect was one of his marked characteristics. His fund of information and his excellent memory enabled him to contribute to advantage in the discussion of papers and there were few papers presented that he did not discuss. Unfortunately he never acquired a good English accent so that he was somewhat difficult to follow, but his contributions to the proceedings of any society to which he belonged were nonetheless important on this account, as may be inferred from the fact that at various times he was elected president of the American Physiological Society, the Society of Experimental Biology and Medicine, the Association of American Physicians, the American Association for Thoracic Surgery, the American Gastroenterological Society, and the Society of Clinical Investigation.

Dr. Meltzer's scientific contributions were so numerous and varied that it is difficult to summarize them in a brief statement. He had definite views in regard to the role of inhibition in the body processes

which found expression in a number of papers. In some of these papers he called attention to the reciprocal innervation of antagonistic muscles, called by him crossed or contrary innervation, before the publication of Sherrington's decisive experiments. He published a series of articles upon the action of adrenaline upon the blood vessels and the pupillary muscles, in the course of which he described the use of the excised frog's eye as a biological test for the presence of adrenaline. He discovered and described in a series of communications the inhibitory and anesthetic effects of magnesium salts. The older members will recall his dramatic demonstration in which a rabbit was rendered motionless and apparently dead by the injection of magnesium sulphate and then restored to a normal condition almost immediately by the use of a calcium solution. Later this action of magnesium salts found a useful clinical application as a means of obtaining specimens of bile from human cases. His later activities were largely centered round problems of artificial respiration in its application to resuscitation. It was in this series of experiments that he demonstrated the value and practicability of intratracheal and pharyngeal insufflation. As early as 1910 he had interpreted bronchial asthma as a phenomenon of anaphylaxis. As another indication of his originality reference may be made to his notable Harvey Lecture of 1906 in which he used so effectively the engineering term "factor of safety" as applied to the animal economy.

Something of the idealism and sincerity of his character is indicated by his noble although futile attempt, at the commencement of the great war, to establish a brotherhood of physicians, a Fraternitas Medicorum, for the furtherance of international understanding and good will and to point the way to a higher international morality. His idea met with general acceptance. Some 1600 names were enrolled in this country and interest was shown by leading physicians abroad, but the entrance of our country into the war suspended the movement and, after peace was declared, interest in the project could not be revived. After his death in 1920 memorial exercises were held by several of the societies to which he belonged. The Federation of American Societies for Experimental Biology held such a meeting at Chicago, and a large memorial meeting was arranged in New York by the Society for Experimental Biology and Medicine at which addresses were made by Drs. Calkins, Wallace, Levene, Lusk, Howell, and Welch.

Excerpt from Dr. Howell's Address

To do full justice to the influence exerted upon contemporary medical research by Meltzer's work would require a careful analysis of the entire medical literature of the period, for, as I have tried to indicate, his sympathies were very broad and his activity was great. In some measure, either as interpreter or contributor this influence was felt at many of the points of contact between medical science and medical practice. The borderland between these subjects was in fact his special field of work. He had the spirit and ideals of the scientists, and knew at first hand what research work really means. He had experienced the labor and care and devotion required of those who aspire to increase knowledge. On the other hand he had a personal realization of the difficulties and necessities of medical practice and so was especially fitted to act as a

sort of liaison officer between the two great wings of the medical army, the investigators who have the difficult task of discovering new truths, and the practitioners who must learn to apply these truths to the preservation of health and the protection from disease. No one in our generation, I venture to say, was more useful in this country in bringing about a helpful and sympathetic understanding between the laboratory worker and the physician. While his activities covered a large range he was interested primarily in physiology. "I belong," he said in a recent paper "to those who believe... that the knowledge of physiology is of special importance to clinical medicine." His work in this field entitles him certainly to be ranked among the foremost American physiologists. As a physiologist he enjoyed the best opportunities and training of his period. He was equipped with the methods and technique that the subject owes to the great masters of the latter half of the nineteenth century. The more modern methods of physics and chemistry which seem to be essential for the new generation of physiological workers he did not possess, but he did not let this deficiency discourage him nor diminish in any way his activity in research. He had the wisdom to understand that the armamentarium with which he was provided was adequate for the accomplishment of much important and necessary investigation. He was no faint-hearted seeker after truth. There never was a time, I fancy, in his active life when his mind was not full of problems that he wished to solve and which he intended to solve in part at least with the aid of his experimental methods.

Dr. Meltzer was elected to membership in the American Physiological Society at its first annual meeting held in Philadelphia in December 1888. From that time until his death he was perhaps its most faithful member in attendance, in the presentation of papers and in participation in the discussions and social intercourse. Other less heroic spirits might weary under the load of papers and seek respite and fresh air by frequent disappearance between acts, but this was never the case with Meltzer. He loved the meetings, he loved to listen to the papers and to take part in the discussions. He had something to say of value on almost every paper that was read. It is small wonder therefore that his position and influence in the society constantly increased in importance. He served as president from 1911 to 1913, but the older members know that before that time and since, his advice was paramount in matters of policy as well as in the selection of officers. He was sincerely and deeply interested in the welfare of the society and believed in its importance as one of the major agencies concerned in the advancement of the cause of physiological research. What he had to say in regard to its policies was always said in the opening meetings and in the plainest of terms, and if in his opinion it was necessary to be critical of either persons or things he never hesitated to express what was in his mind. His courage in stating his position in matters in which some personal criticism necessarily played a part in the discussion has often aroused admiration. He did not indulge in circumlocutions or euphemisms, but was entirely frank and direct. There could be no mistake as to what he thought and yet no matter how plainly and bluntly he might speak there was as a rule no offense taken, because it was evident to every one that what concerned him was not personalities but the principles involved. The American Physiological Society owes much to him for the sound policies and wholesome traditions which have characterized its history.

SECTION EDITORS FOR APS JOURNALS

PHILIP BARD

On January 1, 1962, the combined Editorial Board of the AMERICAN JOURNAL OF PHYSIOLOGY and the JOURNAL OF APPLIED PHYSIOLOGY was organized on the basis of eight Sections, each headed by a Section Editor, representing the following areas: Circulation -- M. B. Visscher; Respiration -- Hermann Rahn; Renal and Electrolyte Physiology -- W. D. Lotspeich; Gastrointestinal Physiology -- H. W. Davenport; Endocrinology and Metabolism -- Jane A. Russell; Environmental Physiology -- L. D. Carlson; Comparative and General Physiology -- Knut Schmidt-Nielsen; and Neurophysiology -- Elwood Henneman. This change, made by the Publications Committee with the approval of the Council, has been effected in order to distribute more widely the burden and responsibility of editorial decision on manuscripts, to provide broader competence in making decisions, and to obtain the services of more physiologists as referees and consultants in the editorial review of papers submitted for publication. It is fully appreciated that the eight Sections do not encompass all of the areas of physiology for which the two journals have provided--and will continue to provide--a means of publication. It may be that later a few more sections will be designated, but for the time being it seems wise not to attempt further editorial sectionalization.

All interested persons should understand that manuscripts dealing with subjects not specifically belonging in any one of the eight areas will be welcomed for consideration and that provisions have been made to place them in the hands of competent editorial referees.

A Section on neurophysiology has been set up despite the acquisition by the American Physiological Society of the JOURNAL OF NEUROPHYSIOLOGY. The Editorial Board of the JOURNAL OF NEUROPHYSIOLOGY and both the Council and the Publications Committee of the American Physiological Society are in agreement that authors of papers in this field should be free to submit their manuscripts to either the JOURNAL OF NEUROPHYSIOLOGY or the AMERICAN JOURNAL OF PHYSIOLOGY. Such authors should indicate their preference.

Under this new editorial organization all manuscripts will continue to be received and acknowledged by the Office of the Managing Editor where the decision will be made as to the appropriate Section for review. Each manuscript will then be forwarded promptly to a Section Editor who will assign it to referee editors (one of whom may be himself) and, as soon as possible, make the necessary decision or recommendation. If a Section Editor receives a paper which he regards as not belonging in his area, he may transfer it to another Section Editor or forward it to one or more individuals whom he regards as competent referees.

Papers deemed "acceptable as submitted" will be accepted forthwith and processed for the printer. Manuscripts that are "acceptable in substance" but require either minor or major revision will be returned to the author with the comments and recommendations of the referees and the Section Editor. In such cases the author will return the revised manu-

script to the Section Editor who will then decide whether or not it should go again to the referees and, finally, as to its acceptability in revised form. The same procedure will be used in the case of papers that are judged "unacceptable as submitted" but deemed worthy of revision for resubmission. Those found to be "unacceptable" and that provide no basis for encouragement of revision will be returned to the author with the reasons for rejection. Manuscripts originating from the institution at which a Section Editor is located will not be assigned to that Section Editor for review.

The AMERICAN JOURNAL OF PHYSIOLOGY and the JOURNAL OF APPLIED PHYSIOLOGY, in common with many other journals, now use an alpha-numerical rating system for a) the scientific quality of the content of a manuscript and b) the quality of the presentation. Thus a rating of 1 means that, in the opinion of the editors the paper is outstanding and definitive in advancing materially our knowledge of a fairly broad segment of physiology. A rating of 2 signifies that the paper is judged important in materially advancing conceptually and factually, with experimental data, a segment of a subfield of physiology or an application of physiological knowledge to a categorical problem. A rating of 3 means that the manuscript contains new experimental evidence and data in the topic area of the paper which are worthy of publication because they add to the factual knowledge of this particular narrow segment of physiology. Thus a paper that reports negative findings may be accepted because it may serve to sharpen and narrow the analysis of physiological actions and obviate the need for further exploration by other workers. A rating of 4 signifies those manuscripts which are unacceptable for one reason or another. Categories A, B and C relate to the quality of the presentation of the material in the paper. A means that, in the opinion of the editorial referees, the presentation is excellent in all respects; B, that it is acceptable ; and C, that either major or minor revisions should be made.

For some time the scope of the two journals has been broadened to permit the acceptance of papers that analyze and advance physiological concepts even though they contain little or no new experimental data. Obviously such papers are subjected to very careful editorial scrutiny and must receive a rating of 1 in scientific quality and of A in quality of presentation. They must show evidence of a high degree of scholarship both in regard to the concepts presented and the clarity and logic of the presentation.

The labor and the responsibility of each Section Editor will be great. The Publications Committee expresses its great appreciation of the willingness of these eight members to undertake this important service for the Society. In due time others will take their places and to them the Society will be equally grateful.

APS ACQUIRES JOURNAL OF NEUROPHYSIOLOGY

On January 1, 1962 the APS became the owner and published of the JOURNAL OF NEUROPHYSIOLOGY. The Society purchased the journal from the co-owners, Charles C Thomas, Publisher, and Yale University. The journal was founded in 1938 by the Charles C Thomas family and John F. Fulton and was operated by them jointly until Dr. Fulton's death in 1960. In his will, Dr. Fulton left his share of the journal to Yale University.

Dr. Vernon B. Mountcastle, Johns Hopkins University School of Medicine, has been appointed Chief Editor of the newly acquired journal. Manuscripts will be received and acknowledged by the APS Editorial Office in Washington and forwarded to the Chief Editor for assignment to review editors and for decision on acceptability. Manuscripts, when accepted, will be returned to the Editorial Office for copy editing for the printer. For the next year at least, the journal will be issued in its same format and printed by the Banta Company in Menasha, Wisconsin.

The journal will continue under the same name without break in continuity of issue or serial number of volume. Both the JOURNAL OF NEUROPHYSIOLOGY and the AMERICAN JOURNAL OF PHYSIOLOGY will accept articles in neurophysiology. The author must designate which journal he wished to consider his article. Articles in neurophysiology will not be automatically transferred from one journal to the other.

PAGE AND ARTICLE CHARGES FOR APS JOURNALS

Beginning in 1962 the AMERICAN JOURNAL OF PHYSIOLOGY and the JOURNAL OF APPLIED PHYSIOLOGY will impose a charge of $20 per page plus a charge of $20 per article. The page charge will be used to cover in part the cost of editorial work and type composition; the article charge will be for the support of abstracting and indexing media which serve the journals. It is intended that these charges are to be borne by the author's funds or the institution which supported the research and not by the author personally. Editorial appraisal of the scientific merits of a paper will be divorced from any question of these charges.

SIXTH BOWDITCH LECTURE

Surface Phenomena in Relation to Pulmonary Function

JOHN A. CLEMENTS

It has become traditional to honor Professor Bowditch by speaking about our own works. This rather presumptuous and strange custom may be one of the last rites of a dying society. The physiological chemists departed our ranks long since and became biochemists. The physiological physicists have fled to become biophysicists. The newest fledging science, bionics, has sprung away from physiology even before its domain and methods are clearly seen. But we, decadent physiologists, cling to the old ways, reluctantly accepting the benefits of progress, like rueful parents bemoaning the iconoclastic behavior of the younger generation.

Are these just and true statements? Are the voices of Bowditch lecturers merely feeble echoes in the mausoleum of a once-great science? Is this conclave assembled here amid the tropical splendor of Indiana only performing an ancient rite of scientific self-congratulation, thinking more of what has been done than of what lies ahead? I think not and I believe that most of you would agree.

We physiologists are as vigorously progressive as other scientists. We recognize that the subdivision of natural philosophy is a necessary phenomenon, required by the limitations of men's minds; that the founding of a new science facilitates the orderly and efficient increase of knowledge; and that the derivative science strengthens, rather than attenuates the parent. "You haven't lost a daughter, sir, you've gained a son." We are still members of the same family. So, the adherents of the apostate sciences and we, using their methods and disciplines, can dedicate ourselves to the elucidation of many subservient details of organization before we will be able to state biological administrative policies in all their ramifications.

Let us encourage the formation of splinter groups in our society and give them a hospitable place to conduct their affairs, since this policy is to the greatest advantage of scientific advancement in our field. This must be true, since understanding is not atomistic in quality. Any question when subjected to the white heat of intellectual curiosity, decomposes into component questions, and we have no assurance that an indivisible question ever will be asked. As an oracle of Hesiod states, "The part is greater than the whole."

Professor Bowditch maintained a militantly progressive attitude of this sort. He left the laboratory of Claude Bernard to study with Carl Ludwig. Bernard had all the answers; but better, Ludwig had questions. When he returned to America, Professor Bowditch formed his own splinter group in Bostonian medical science. Today, physiology is one of his beneficiaries. We would honor him best by emulating his vigorous devotion to the high ideal of scientific progress.

It is in this spirit of reaching for the future, of knowledge in flux, of imperfect understanding, that I should like to discuss one step in the development of pulmonary physiology. This step is the recognition that the lungs are "emulsions" of air in tissue and that the bulk properties of such a finely-dispersed system depend to a large extent on the properties of the interface between the two phases. Further, it is the recognition that the presence of materials in either phase that have special affinity for the interfacial region (surfactants), can modify the bulk properties of the system to a very great extent, far out of proportion to their bulk concentrations. Of the several properties that can be so-modified, let us confine our attention to those which can influence bulk elasticity and the distribution of forces in the lungs.

It may be of interest to examine briefly the history of the subject, as it relates to pulmonary function.

It is a remarkable fact that von Neergaard already set forth in 1929 (28) a significant part of what we know now. He stated that 2/3 to 3/4 of the elasticity of the lungs is derived from interfacial forces. He also stated in the summary of his classical paper: "It is possible that the surface tension of the alveoli is decreased below that of other physiological fluids by accumulation of surface-active material, in accordance with Gibbs-Thomsen law." Von Neergaard attempted to extract surfactant from lungs but had slight success, because of the limitations of his methods. It is surprising that his work attracted so little attention. There were sporadic references to it in the German literature of the next two decades. The earliest reference in English that I know of came 25 years later in a paper of Radford (20), although intensive studies of respiratory mechanics had been under way for more than a decade in several academic capitals. The importance of interfacial forces in the initial expansion of the lungs after birth was mentioned by Wilson and Farber (29) in 1933 and by Gruenwald (8) in 1947, but it remained for Mead, Whittenberger, and Radford (14) to clarify the matter in the early 1950's. They essentially repeated von Neergaard's experiments, came to much the same conclusions, and extended them. They showed the dependence of hysteresis in static pulmonary pressure-volume diagrams on surface forces; they emphasized the importance of surface tension in determining alveolar geometry and they made careful measurements of visible airspaces (22). They gave theoretical reasons why the alveolar population should be an unstable one (21). In 1953 Radford also showed how the internal surface area of the lungs could be calculated from pressure-volume diagrams, using an assumed surface tension (5, 20). These investigators apparently thought that pulmonary surface tension is comparatively high, approaching that of serum, although Radford (20) mentioned the possibility that it might be lowered by the presence of intrinsic surfactant.

In 1955 Pattle (15) reported that pulmonary edema foam is very resistant to anti-foam agents and that bubbles expressed from the lung into air-saturated water are stable for long periods. He deduced from these observations that the lungs contain a powerful surfactant, which reduces the surface tension of the alveoli nearly to zero. He concluded tentatively that the material is mucoprotein and lines the alveoli, as had been suggested by Macklin (12).

At Edgewood we had been much intrigued by Radford's method for estimating lung area and had examined his assumptions. Since the calculated area was inversely proportional to the surface tension and since his estimates appeared very low, we reasoned that the value he assumed for pulmonary surface tension might be too high. Brown, Johnson, and I (3) reversed the method of calculation and by assuming how the area of the lungs might change with their volume, worked out values for tension. These traced out a path from serum tension down to very low values, and when Pattle's estimates became available we felt we had nearly achieved a synthesis of Radford's and Pattle's concepts. In addition we felt that the change of surface tension as a function of lung volume was a necessary characteristic for stabilization of the alveolar structure.

How could the surface tension of the airspaces change so much? Was it a plausible physicochemical phenomenon? How might one put the hypothesis to direct test?

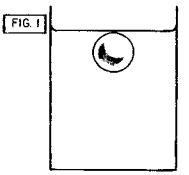
As we read the literature of surface physics and chemistry we became convinced that the notion was tenable. Numerous observations had been made on the behavior of monomolecular films of insoluble surface active materials floating on liquids. It had been clearly shown by many workers that such films were sometimes capable of changing the surface tension of aqueous solutions by more than 60 dynes per centimeter when the area of the liquid was changed. Furthermore, the substances that formed these films were ubiquitous biological materials, such as proteins and lipids. The concepts were older than we, and the methods to test their application to the lungs had been hallowed through decades of use by Langmuir, Adam, Harkins, Leathes, Rideal, Schulman, and Danielli. Thus, if our hypothesis was correct, we should be able to extract highly surface active material from the lungs and to measure its activity by standard methods. The result of this test was successful (7), and it launched us on a continuing program of theoretical and practical investigations of pulmonary surface phenomena.

In 1959 Avery and Mead confirmed our findings and applied the same test to the lungs of newborn infants that had died with hyaline membrane disease (1). These infants experienced severe respiratory distress, and at necropsy their lungs were extensively atelectatic and showed deposition of fibrin in the fine airspaces. Although such lungs expand normally with saline, very high pressors are required with air. Extracts of the lungs failed to show high surface activity. These results provided further indirect support of the hypothesis that stability of the alveolar structure requires the presence of surface active material.

In 1960 Bondurant developed a method for the large-scale extraction of surfactant from the lungs (2). This important step made possible unequivocal studies of the chemical composition of the material and greatly extended the vista for investigation of its functional role. It is evident now that the pulmonary surfactant is lipoprotein in nature and contains a large proportion of phospholipids (9, 17). Workers in several laboratories are actively pursuing the physical, chemical, and biological characteristics of the material.

With this hasty chronological review of the subject in mind let us examine the concepts and experimental evidence more closely.

What reasons had von Neergaard and other pioneers of pulmonary physiology to think that surface tension might affect the function of the lungs? The main reasons were the belief that the airspaces are covered with a thin layer of liquid, and the obvious fact that they are small in size. By virtue of its surface tension a liquid surface tends to contract, and if the surface is curved (in the mathematical sense) the pressure must be different on its two sides. The relationship between size, tension, and pressure difference is illustrated in figure 1, which shows a bubble of air in water. If the bubble is small enough, it is nearly



$$P = \frac{2\gamma}{r}$$

$$P = \frac{2 \times 72 \text{ DYNES/CM}}{40 \times 10^{-4} \text{ CM}}$$

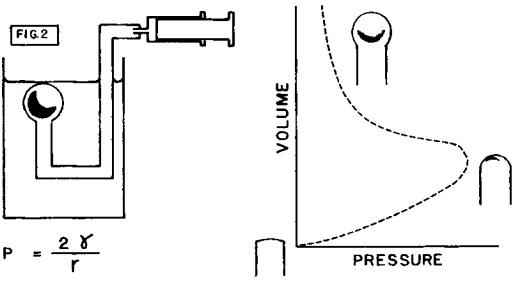
$$P = 36 \text{ CM } H_2O$$

$$\text{PRESSURE} = \frac{2 \text{ SURFACE TENSION}}{\text{RADIUS}}$$

spherical and the pressure of the air exceeds that of the water just outside by twice the surface tension divided by the radius of the bubble. If the bubble is of the average size of the alveoli in an adult dog lung, that is about 40 microns in radius and the surface tension of the water is 72 dynes per centimeter, the air pressure exceeds the water pressure by 36 centimeters of water. Consider a bubble very close to the surface of the water, so that the water pressure is very nearly atmospheric, and the water is saturated with air at atmospheric pressure when the bubble is introduced. Then the air pressure in the bubble is 36 cm H_2O greater than in the atmosphere and the water, and under this gradient air rapidly diffuses out. The bubble contracts and disappears in a few minutes. If the surface tension of the water surrounding the bubble were reduced to zero or nearly zero, the air pressure in it would essentially be atmospheric and the bubble would be stable or would contract very slowly. This is the final behavior of bubbles squeezed from normal lungs into air-saturated water and is the observation that caused Pattle to deduce that their surface tension is nearly zero. We shall return to this phenomenon presently.

If we introduce a tube into the water and deliver air into a bubble at the end of the tube from a microsyringe (figure 2), we find that the same formula governs the relationship between surface tension, curvature, and pressure difference at the air-liquid interface. In addition we can see, as depicted in the graph, that the bubble has a peculiar pressure-volume relationship. As the bubble forms the pressure rises, and reaches a peak when the bubble is hemispherical; as it grows further in volume the pressure declines. For the purpose of our analysis we may call the

tube and "airway", the bubble an "alveolus", and the water the wet pulmonary parenchyma. It was this kind of model that von Neergaard (28) and the Harvard group (14) used to explain the effect of surface tension on the lungs.



In both instances they put the model to the same test. The surface tension exists because of the contact of the dissimilar materials, gas and watery liquid. They reasoned that if the bubbles were filled with aqueous solution, the surface tension would not exist. Therefore, if surface tension contributed to the elasticity of the lungs the effect would be eliminated by filling them with aqueous liquid.

In figure 3 we see the results of such an experiment (19). The totally collapsed lungs were first filled with saline and emptied and then inflated with air. The loop on the left shows the recoil of the lungs when filled with liquid; that to the right their recoil when filled with air. The

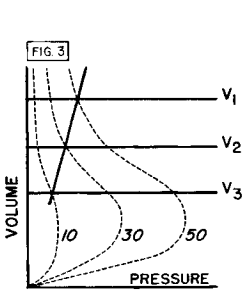


Fig. 3. Effect of changing surface tension on compliance. (Mead: Am. Rev. Resp. Dis. 81:739, 1960).

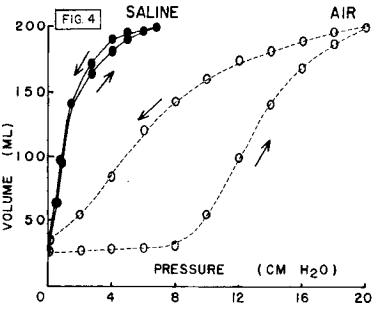


Fig. 4. Pressure-volume relationship, cat lungs. (Radford: Tissue Elasticity, 1957, p. 185).

same result is obtained if the air is presented first and the saline second. Clearly the force of recoil, measured as pressure on the abscissa, is less with liquid than with gas-filling. The saline pressure-volume loop shows little hystersis and is taken to indicate the true elastic behavior of the pulmonary tissue. The added pressure required for air-filling is attributed to the action of surface tension, and represents about 2/3 of the total.

Let us see if this idea has reasonable consequences. Since we have estimates of the average size of the airspaces and of the pressure due to surface tension at various lung volumes, we can calculate surface tension by the bubble formula. At full volume we get 47 dynes/cm; at mid-volume 9 dynes/cm; and at lower volumes still lower values. We cannot rely on the estimates at small lung volumes because bronchiolar collapse intervenes and the transpulmonary pressure is not a proper measure of the pressure difference across the alveolar "bubbles." However, even at mid-volume, when the airways are manifestly open, the estimate of surface tension is significantly less than that of serum. Thus, one consequence of the idea is that surface tension in the lungs must be much less that that of serum, and as a corrollary to this, that surface active material must be present in the lungs. Another consequence is that the surface tension must change as lung volume changes, and as a corrollary to this, that the surface active material must act as an insoluble film, rather than as the reversibly adsorbed Gibbs film postulated by von Neergaard. A further consequence is that if the surface tension changes so much with volume, the negative slope of the pressure-volume diagram of the "alveolar bubble" is made positive. On this basis we can understand the stability of millions of wet airspaces inflated in parallel.

Figure 4 shows how change in surface tension converts negative to positive compliance (13). Each curve in the family gives the pressure-volume relationship of the bubble at a given, constant, surface tension. If as the volume decreases from V_1 to V_2 to V_3, the tension decreases from 50 to 30 to 10, then the pressure declines rather than rises. An assemblage of bubbles having this positive characteristic is stable, and could be ventilated in parallel. Not so a group of bubbles with negative compliance; in such a system the smaller ones empty into the larger ones, much as an emulsion breaks down by the addition of smaller droplets to larger ones. In the lungs we would call it atelectasis.

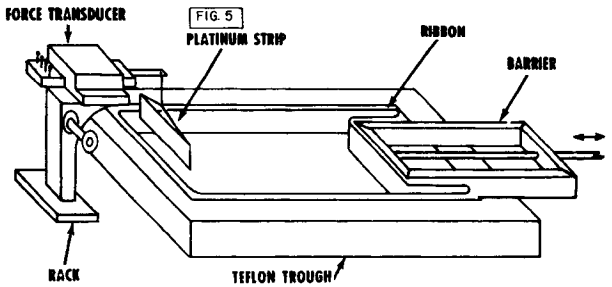
At this moment I think you would be quite justified in pointing out that the lungs are obviously more than aggregations of bubbles on tubes: the tissue must at least determine the size and shape of the lungs and the order of airspace size. I admit to having slighted the role of tissue elements. Since it leaves more time for describing the studies of surface tension, I shall continue to neglect the "too, too solid flesh."

We may summarize the consequences of applying the "alveolar bubble" model to pressure-volume data in one statement: the observations can best be accounted for by assuming that the lungs have a moist interior covered with an elastic film of surfactant. This assumption is reasonable only if material exists in the lungs which can form such a film. If one could extract such material, it would be logical to think that it might

have been located at the surfaces of the airspaces, especially if it could be washed out the airway without traumatizing the tissue. Several workers have extracted pulmonary surfactant, and I should like to discuss their results now.

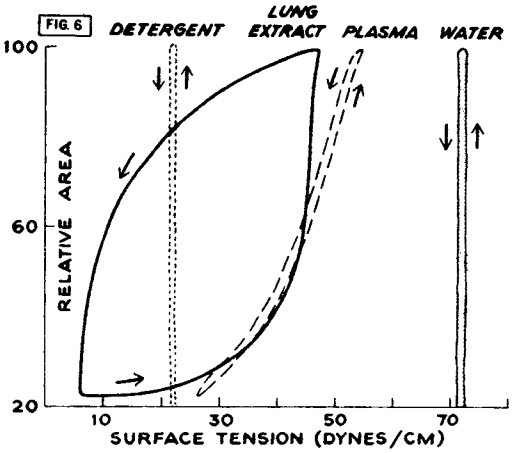
Pattle (15) squeezed microscopic bubbles that contained surfactant from cut alveolar tissue. Brown, Johnson, and I (3, 7) made saline extracts in three ways: by touching cut alveolar tissue to saline, by mincing the lung with saline, and by rinsing via the airway with saline. Bondurant (2) prepared artificial pulmonary edema foam that contained large amounts of surfactant.

Pattle's method requires microscopic observation of bubbles in air-saturated water. The other methods require the use of the surface balance, an instrument not so familiar to physiologists as the microscope. Figure 5 shows the essential parts of a surface balance. It consists of a tray filled with liquid; a barrier pushed along the tray to reduce the area of the liquid and compress a surface film if it is present; and a thin, frosted, platinum plate, hanging vertically in the liquid to measure the pull or surface tension of the liquid. The operation can be made automatic,



so that area and tension are plotted against each other on an X-Y recorder. When the tray is filled with very clean water, the platinum plate experiences a pull of about 72 dynes per centimeter of its perimeter, and this pull does not change when the barrier is moved. If a tiny amount of a protein or a lipid containing hydrophilic functional groups is dropped on the surface, it spreads out as film and the pull on the platinum plate decreases. If the barrier is now moved, the surface tension falls when the area of the liquid is reduced, and rises when area is increased. When protein is dissolved in the water, it forms a similar surface film by spontaneous adsorption. If a detergent is dissolved in the water, the surface tension falls to about 30 dynes/cm and does not change when the barrier is moved. These relationships between area and surface tension are given diagramatically in figure 6. The thin loop to the right represents clean water with a tension of~72 dynes/cm; the next curve, blood plasma; the thin loop to the left, 1% Tween 20. The large loop is the type of tension-area diagram found with saline extracts of normal lungs. Similar results have also been obtained with the other methods of extraction. Clear-

ly such lungs contain substances that can bring down surface tension of aqueous solutions to very low values. In addition, the tension varies with the size of the surface. Thus, both assumptions which we made earlier would be borne out if such material came from the alveolar surfaces.



For purposes of comparison figure 7 shows tension-area diagrams recorded on saline extracts of infant lungs. The loop (B) represents a normal lung; the loop (A), one showing congestive atelectasis. Gruenwald, Johnson, Hustead and I have made this determination on 37 neonatal specimens. At autopsy Dr. Gruenwald made pressure-volume measurements on the specimens and calculated an index which expressed numerically how well they remained expanded at physiological pressures, after being fully inflated. Without knowledge of his results we measured the surface tension of saline extracts of the specimens and calculated an index of surface activity for each. The two indices were well correlated (figure 8). Whatever post mortem changes occurred in this material were insufficient to obliterate the correlation.

You recall that Pattle squeezed microscopic bubbles from cut alveolar tissue into air-saturated water and concluded from their stability that their surface tension was nearly zero. We have repeated and confirmed his observations, and are also forced to the conclusion that highly surface active material is present in the alveolar tissue. Since the stable bubbles can be obtained either directly from cut alveolar tissue or indirectly via the airways of undamaged lungs, the surfactant is almost certainly present in a film at the alveolar surfaces. This conclusion is supported by two lines of evidence. First, when a solution of it is placed in the surface balance, the surfactant spontaneously concentrates in the surface. Secondly the electron microscopic studies of Chase (4) show a distinct extracellular film of molecular thickness at the air surfaces of mammalian alveolar membranes.

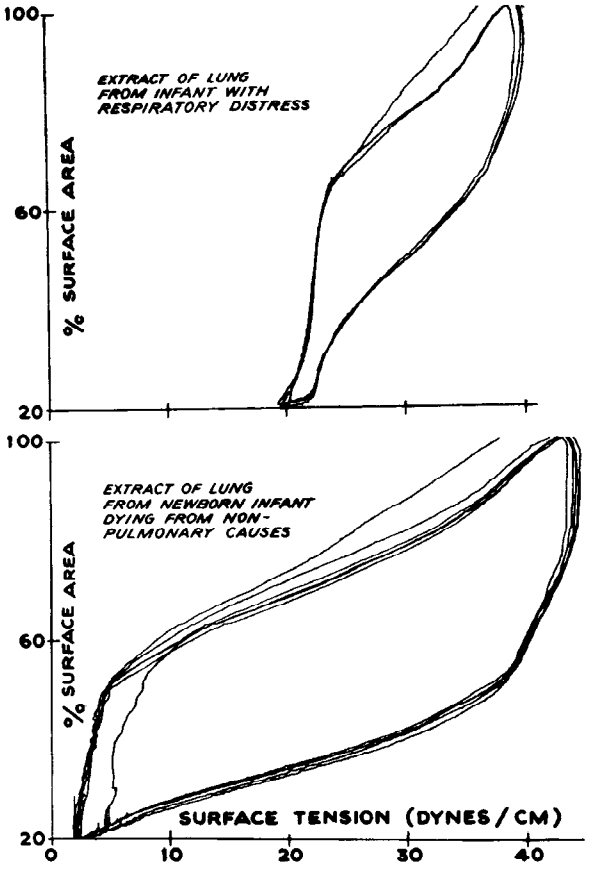
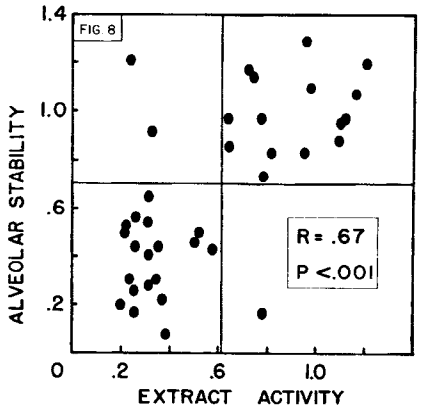


Fig. 7. Respiratory distress in newborn infants.

Let us examine some of Pattle's intriguing data (16). Figure 9 shows a plot of bubble diameter against time. The steep curve to the left indicates how a bubble of air in air-saturated clean water rapidly contracts and disappears from view. The flat curve to the right shows the persistence of an "alveolar bubble" under the same conditions. Using the laws of LaPlace and Fick we have derived an approximate formula (similar to one of Pattle's) which relates the rate of bubble contraction to its surface tension. As the formula in figure 10 indicates, the surface tension is directly proportional to the bubble area and the rate of change of radius, and inversely proportional to the diffusion coefficient and solu-



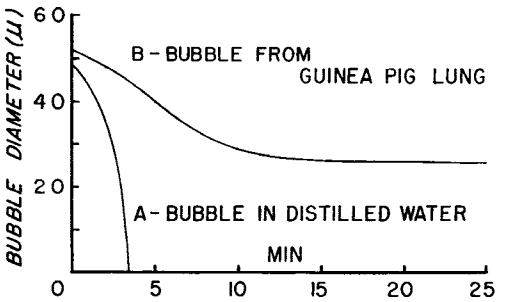


Fig. 9. Contraction of microscopic bubbles in air-saturated water. (Pattle: Proc. Roy. Soc. (London) B 148:223, 1958).

bility of air in water. From Pattle's data (16) we have calculated the relationship between surface area and tension of two "alveolar bubbles". The two curves to the left show that the tension fell from 19 or from 10 dynes/cm to practically zero. The slopes of the curves vary from 0.060 to 0.025 cm/dyne. The third curve is surface balance data on a lung extract; slope varies from 0.025 to 0.099. The curve to the right was cal-

culated from pressure-volume data on a dog lung (3); the slope lies between 0.028 and 0.16. The time interval between points on the curves is about one minute in all cases. When one considers that area-tension slopes for surface films of various biological substances differ by a factor of a million, the six-fold variation shown here does not seem large.

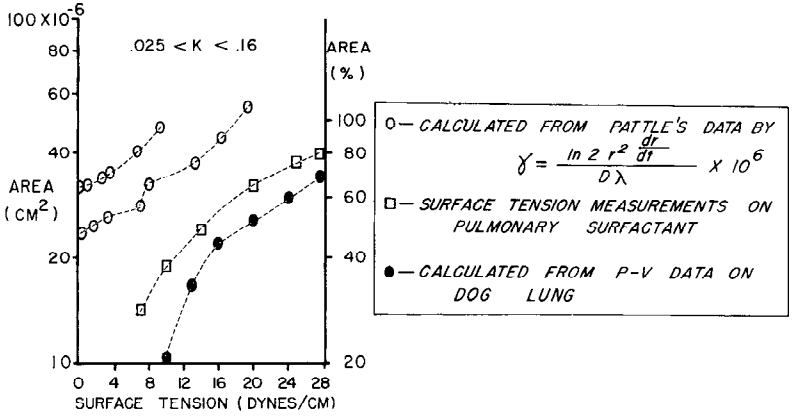


Fig. 10. Tension-area relationship.

Although it has been implied in our previous remarks, we might now make explicit the differential relationship between surface film pressure and surface tension. The effective surface tension of film-covered liquid is the resultant of the contractile strength of the liquid and the force with which the film tends to expand in the surface. Thus, if the water tension is 72 dynes/cm and the film pressure is 60 dynes/cm, the surface tension is 12 dynes/cm. In terms of molecular mechanism there is little difference in this situation between a surface tension of 0.1 and 4 dynes/cm. Although there is a factor of 40 between the tensions, the corresponding film pressures on water are about 68 and 71.9 dynes/cm, a variation of less than 1 part in 20. These considerations make it evident that the change of surface tension that occurs with change of area is really dependent on the elasticity of the surface film; and further that the minimum surface tension that can be achieved in a given system is partly determined by the pressure at which the film collapses. When we say that a material is "highly surface active," we mean that it reduces surface tension to very low values and hence that the surface film it forms is comparatively stable at high pressures. Since the maintenance of moderately low surface tension appears to be important in the lungs, we must therefore be interested in the critical pressure for collapse of films of pulmonary surfactant and the rate at which collapse occurs once initiated. We know from the fundamental studies of Langmuir and Schaefer (10) and others on films of pure substances and on mixtures that these properties depend on molecular

size, on the nature, number and arrangement of functional groups in the film molecules, and on the pH and ionic composition of the subjacent liquid. We know that a mixture of two substances can give a film that is more stable than the better component, or less stable, depending upon the nature of the substances. It has also been shown (24) that secondary adsorption of materials from the subphase can unstabilize a surface film, causing it to collapse or desorb from the surface, with a consequent rise in tension; or on the other hand can complex with it, raising the film pressure and lowering surface tension (23). These interactions depend again on the nature of the substances. Studies of this type of phenomena carried out with pulmonary surfactant have been initiated by Tierney and Johnson (26) and have already been helpful in understanding pulmonary responses.

The differential relationship between film pressure and surface tension results in an interesting feedback characteristic in "alveolar bubbles." Let the surface tension be 0.01 dyne/cm, as indicated by Pattle's measurements of the eccentricity of a typical bubble. Then the film pressure is about 71.99 dynes/cm. Let sufficient collapse or desorption of film material occur to lower the film pressure by 0.09 dynes/cm. The surface tension is now 0.1 dyne/cm. The film pressure has diminished about 1 part in 1000 but the surface tension has increased 10-fold. The rate of contraction of the bubble also increases 10-fold, the surface area of the bubble decreases comparatively rapidly, and the remaining film is re-compressed. This occurs because the diffusion of gas from the bubble is increased proportionately 10,000 times as much as film pressure is changed.

Microscopic observation shows this phenomenon to occur periodically, as the surface tension oscillates. If we neglect the oscillation and consider it a slow, steady state of contraction, we can solve the formula shown in figure 10 simultaneously with a general formula relating film pressure, area, and molecular density. The result, given in figure 11, shows that the "steady state" tension is proportional to the size of the bubble and to the rate of loss of film material.

In this situation film pressure, and hence surface tension, are self-determining, and surface area is a dependent variable. We may call it very-low tension state, or the "constant-tension, variable-area," limiting state.

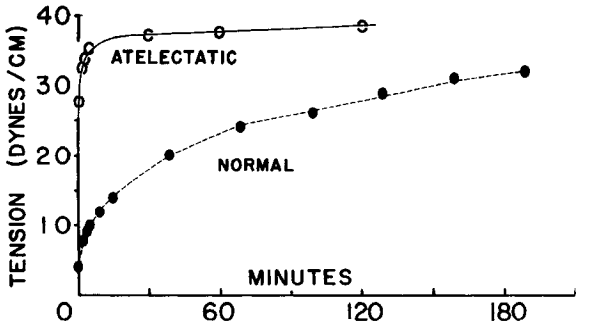
Another limiting state is "constant-area, variable-tension." The lower curve in figure 12 shows the result of compressing an extract of a normal lung in the surface balance to a tension of 4 dynes/cm and holding it at constant area. The tension rises slowly to a higher value, about 36 dynes/cm, as film collapse or desorption occurs. The upper curve gives the result of the same experiment done with an atelectatic newborn lung. The tension rises comparatively rapidly from 28 to about 38 dynes/cm. The rate of change of tension is proportional to the difference between the tension at any time and the final tension. The time constants are about one hour and one minute, respectively. The final tensions are determined by the critical collapse pressures of the films and we shall call them the "critical tensions."

Both the "constant-area" and the "constant-tension" limiting states

$$\gamma_{STEADY} = \frac{\ln 2 \quad k\,T\,r \left(\frac{dn}{dt}\right)_{steady}}{8\,\pi\,D\,\lambda\,\gamma_w} \times 10^6$$

k = *BOLTZMANN CONSTANT*
T = *ABSOLUTE TEMPERATURE*
r = *RADIUS*
D = *DIFFUSION COEFFICIENT OF GAS IN WATER*
λ = *SOLUBILITY OF GAS IN WATER*
γ_w = *SURFACE TENSION OF WATER*
$\left(\frac{dn}{dt}\right)_{steady}$ = *RATE OF FILM COLLAPSE*

Fig. 11. Steady tension radius x rate of film collapse.



RATE OF TENSION RISE $\propto$ DIFFERENCE BETWEEN FINAL TENSION AND OBSERVED TENSION

$$\frac{d\gamma}{dt} = K(\gamma_f - \gamma)$$

γ_f = FINAL SURFACE TENSION
K = RATE OF FILM COLLAPSE

Fig. 12

reflect the same property of the surfactant, namely its metastability in the film when compressed above the critical collapse pressure. In the constant-tension state ("alveolar bubbles" in water) the steady tension is nearly zero; in the constant-area state (on the surface balance) about 36 dynes/cm.

Is either of these states apposite to the living lungs? Unfortunately, we cannot come to an irrefutable conclusion by observing the intact organ. It is unlikely that the "very-low-tension state" occurs in normal lungs, because the magnitude of the transpulmonary pressure requires, in addition to tissue recoil, the contribution of significant surface tension. On the other hand, in pathological conditions where transpulmonary pressure is not maintained, the alveolar surfaces might approach the zero-tension state. Indeed, there could be a causal relationship (6).

If the reflexes which regulate lung volume tended to maintain substantially constant alveolar area, the tension might approach 36 dynes/cm. This would be consistent with a transpulmonary pressure of about 10 cm H_2O. However, the maintenance of constant total area would not insure that individual airspaces remained constant, especially in view of their well-known independence of action (21, 22). Since there are very many airspaces, a reasonably small fraction of them could be contracting without significantly changing the average transpulmonary pressure. In terms of a single airspace, this behavior is intermediate between the two limiting states we have been discussing and corresponds to the contraction of a bubble at constant pressure, with rising tension. The relationships between size, tension, and time are complicated but can be approximated by solving simultaneous formulae for alveolar elasticity (including tissue forces), for surface tension versus surface area, and for the rate of film collapse. The resulting expression is given in figure 13 with reasonable values substituted for the variables. At a pressure of 5 cm H_2O the half-life of an average "alveolus" is about equal to the time constant for film collapse, according to the simplified expression at the bottom of the figure. With the time constants from the previous figure, this expression

$$4 \ln \frac{r_i}{r_f} + \frac{2P}{\left(\frac{8E\gamma_{crit}}{r_0} - P^2\right)^{\frac{1}{2}}} \left(\tan^{-1} \frac{\frac{2E}{r_0} r_i - P}{\left(\frac{8E\gamma_{crit}}{r_0} - P^2\right)^{\frac{1}{2}}} - \tan^{-1} \frac{\frac{2E}{r_0} r_f - P}{\left(\frac{8E\gamma_{crit}}{r_0} - P^2\right)^{\frac{1}{2}}} \right) = Kt$$

IF $P = 5$ CM H_2O , $E = 5$ CM H_2O

$r_0 = 100\ \mu$, $\gamma_{crit} = 36$

$$t_{50} = \frac{1.06}{K}$$

Fig. 13. Contraction of "alveolus" at constant pressure.

indicates that the alveoli of the normal lung should have half-lives about 60 times as long as those of the lung with hyaline membranes. Needless to say, if the transpulmonary pressure were temporarily raised to expand the airspaces and brought again to low pressure, the individual airspaces would have a new lease on life as their tensions began to rise again from lower values. The frequency of sighs or deep-breaths in the living animal with intact reflexes would be expected to reflect the rate of surface film collapse.

Thus, the time-dependent properties of surface films can endow the lungs with a memory for their volume history. This kind of memory should be limited to about one hour for normal lungs and must be very short for those with hyaline membranes. On this basis we can understand at least qualitatively, the reversible atelectasis and loss of compliance that occur with prolonged shallow breathing at low transpulmonary pressure, and their predilection for dependent regions of the lungs. These calculations of half-life neglect the effect of volume instability on the alveolus. Many airspaces, particularly in lungs with hyaline membranes, collapse or fall to small volumes immediately when transpulmonary pressure is reduced to resting, physiological levels. This action intensifies atelectasis in two ways - by completely removing some units from function, and by shortening the useful lifetime of others.

From quite a different point of view we may expect the tendency for surface tension to rise to have beneficial effects, provided that transpulmonary pressure is maintained at moderate values. The increased pressure gradient required to maintain alveolar volume biases the collapsible portions of the bronchial tree open, and thus acts to homogenize alveolar ventilation. We might speculate that if alveolar surface tension were zero, the tendency to bronchiolar collapse would increase the atelectasis that occurs in the absence of inert gases, especially under circumstances of acceleration and low ambient pressure. Pulmonary function in a space vehicle might be seriously compromised by lack of alveolar surface tension.

I have made a rather long digression to describe microscopic observation of alveolar bubbles and studies of lung extracts with the surface balance, and to develop theoretical notions that might aid the understanding of pulmonary interfacial reactions. If I have dwelt too long on matters of theory it is because some of these concepts also have application to other interfaces in heterogeneous, cellular living things. I do not apologize for the heuristic nature of the argument. I believe, as Henri Poincaré, the great French mathematician and physicist stated, discussing the relations of facts and hypotheses in his "Foundations of Science", that "It is better to foresee even without certainty, than not to foresee at all"(18).

I should like to devote the remaining paragraphs to a discussion of recent advances in the characterization of pulmonary surfactant and related studies of biological reactions of the lungs.

Recently Pattle and Thomas reported (17) that the infrared absorption spectrum of dried pulmonary edema foam is like that of a mixture of 95% lecithin and 5% gelatin. They suggested that the pulmonary surfactant has

a similar composition.

In the meantime Klaus, Havel and I had been analyzing the components of dried foam (9) prepared by Bondurant's method (2) from beef lungs. This material is about 70% soluble in 50:50 alcohol-acetone, the remaining material presumptively containing protein. Although the crude powder is highly surface active, neither of these major fractions produces low surface tension in the surface balance. Separation of the lipid fraction on silicic acid columns yields about 74% phospholipids, 8% cholesterol, 10% triglycerides, 8% fatty acids, and essentially no cholesterol esters. At Edgewood, Siakotos (25) separated the lipid fraction by paper chromatography and estimated that the phospholipid fraction is about 40% lecithin and contains several other phosphatides in smaller amounts.

In an elegant experiment Klaus showed that only the phospholipid fraction was capable of giving very low surface tension in the surface balance. This activity disappeared in several hours while the material was in the balance in air. If, however, the measurement was made under nitrogen, the activity remained.

This most important clue may give added insight into the nature of oxygen toxicity not only in the lungs but also in other tissues, where phospholipid-filled membranes are exposed to high partial pressures of oxygen.

The high activity of the crude powder is maintained for several days in air, and it is reasonable to think that it contains substances whose anti-oxidant potential protects the phospholipid fraction. Their presence may be required for preservation of the surfactant film in its normal situation in about 15% oxygen. It is likely that they are the unsaturated lipids of the non-phosphated fractions. Since the combined lipid fraction does not give low surface tensions, the complex most probably is physically stabilized by the presence of protein. Furthermore, the complex surfactant is known to be attacked by trypsin.

The current state of our knowledge indicates that pulmonary surfactant is a complex of at least eight components in fairly definite proportions. These fall into three major categories and a function can be tentatively assigned to each: unsaturated phospholipid to give low tensions; non-phosphated lipid to protect the phospholipids against oxidation; and protein as the skeleton which holds the lipid body together.

The experiments of Tierney and Johnson (26) are of great interest in connection with the properties of the surfactant. They have shown that addition of petroleum ether-soluble lipid from blood, tissue, or even from the strongly active surfactant powder itself can inhibit its activity. The chemically characterized materials thus far known to inhibit the pulmonary surfactant are lipoidal, oxidative, or proteolytic. Tierney and Johnson also found it possible to extract highly surface active material by Bondurant's method from experimentally atelectatic lungs that gave inactive saline extracts. If the surfactant had been destroyed by oxidation or proteolysis, it could not have been extracted by any method. It is possible, therefore, that atelectasis was caused by accumulation of excess free lipid in the alveolar membranes and that the interfering mate-

rial was rejected in the foam extraction but not in the saline extraction. This concept would fit with the astounding results reported by Tooley, Finley, and Gardner (27). They were studying the mechanism of the respiratory distress that sometimes follows the use of pump-oxygenators on patients undergoing cardiac surgery. By conducting the bypass procedure in experimental animals, they were able to cause the syndrome at will. Both patients and animals died in respiratory failure and at necropsy their lungs were grossly congested and atelectatic. Saline extracts of the lungs were deficient in surface activity.

As the next step in their study Tooley, Finley, and Gardner recirculated donor blood in an extracorporeal circuit and exchange-transfused recipient dogs. If the blood had been pumped 6 hours or longer, the recipients developed congestive atelectasis and died. Saline extracts of their lungs lacked the normal surface activity. In addition these workers found that adding a small quantity of the pumped blood to an active lung extract inhibited it. Normal whole blood had no effect; nor did washed, pumped red cells, hemoglobin, or heparin. Plasma from pumped blood, however, did inhibit an active extract.

These results prove that material is added to the plasma during extracorporeal circulation, which can unstabilize the pulmonary surfactant in extracts and which can produce congestive atelectasis in the living animal. It is tempting to speculate that both effects result from the same interfacial reaction between pulmonary surfactant and free lipid in the plasma. Heparin may play an essential part in the process. Whatever the explanations of these effects may finally prove to be, it is already clear that Tooley, Finley, and Gardner have made an important and exciting contribution to the understanding of pulmonary disease by their demonstration that the lungs can be lethally disturbed by substances liberated in the circulation.

I have restricted this resume of surface phenomena in relation to pulmonary function to mechanical effects and to some chemical and physical properties of interfacial films that may help in explaining such effects. In so doing I have neglected studies of the influence of films on diffusion and electric charge at interfaces. I have said almost nothing about chemical reactions in films and have entirely omitted the interactions of drugs and mediator substances with films, even though these are pertinent to my subject. Studies of such processes are coming into vogue again. It behooves the present-day student to learn the fundamentals of interfacial physics and chemistry well. He will be able to apply them to many fields of biology, as we have already done in a modest and unsophisticated way to pulmonary function. The concepts and methods of surface chemistry and physics which blossomed with such great promise in the '20's and '30's, and which suffered unwonted neglect by biologists in the '40's and '50's may in the '60's and thereafter yield a rich harvest of understanding for physiology.

We follow in the Bowditch tradition. Nathaniel, Henry's father, helped men find their way in the great interface between ocean and sky. Henry performed epochal experiments on excitation and impulse conduction in cells - prime examples of interfacial reactions. Alexander Leathes,

professor of physiology at Sheffield, was I believe the first physiologist to use the surface balance and to investigate phospholipid films. He said in his Croonian Lectures (11) before the Royal College of Physicians of London in 1923 that the study of surface films concerns "the very foundations of physiology, though not of physiology alone." And speaking further of surface effects, he said "The role of fats in vital phenomena is a subject on which... much may turn that is important to physiologists and to physicians." Scientists have verified his prediction in part, but his challenge remains.

Acknowledgment

It is a pleasure to acknowledge the stimulation and help of many collaborators and colleagues whose work is the main basis of this lecture.

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PRESIDENT'S MESSAGE

H. W. DAVENPORT

Somebody is Doing Something!

Members who attended the Society's business meeting at Bloomington will remember that most of the discussion was devoted to the problem of the Federation meetings. The trouble with the meetings is that there are too many ten-minute papers which in turn require too many simultaneous sessions, and all signs point to a worsening of the situation. Although our members' opinions ranged from fatuous complacency to a demand that a radical and permanent solution be found for all our ills, the members were, in general, willing to accept some limitation of ten-minute papers. They were agreed on this, because they believe the positive values of the Federation meetings must be preserved. Of three methods of limiting numbers of ten-minute papers, that of eliminating the right of sponsoring papers by non-menbers was most popular. Members would also accept restriction of the right to present a paper to once every other year. Limitation by some method of selection was entirely unacceptable. All members recognized that such measures would probably be only temporarily efficacious, but they thought evolutionary changes wiser than more violent ones.

Prepared by this discussion with members, I attended part of the meeting of the Council of the American Society of Biological Chemists on September 23, 1961. I was cordially welcomed, and I found that the Biological Chemists have many problems identical with ours. They too are much concerned about the future of the Federation meetings. Most of their Council want to retain the opportunity for crossing over with all other societies, yet they do not want the meetings lengthened beyond five days. This means that long meetings in which two societies (say Physiology and Pharmacology) meet early in the period and two others (say Biological Chemistry and Nutrition) meet late in the period is not an acceptable solution. Personally, I agree with this conclusion, for I believe there are cross linkages among all societies which should not be broken. The Council of the Biological Chemists voted as described in the following excerpt from their minutes:

> "Dr. Horace Davenport, President of the American Physiological Society, joined the Council to discuss with it the consensus which came out of the recent fall meetings of his Society about steps which might be taken to control the growth of the annual Federation meetings. There is general concern about the large number of ten-minute papers and the increasing attendance which could easily strangle these meetings. Following the extended discussion of a variety of alternatives it was moved, seconded, and carried that, effective with the 1963 Federation meetings, the programs of the scientific sessions of the Society,

> other than those devoted to symposia, will be made up of volunteer papers, submitted in accordance with prevailing rules, on which members are authors or co-authors and will be filled out to predetermined limits by selection by the Program Committee from among papers sponsored by members. The Society will not accept sponsored papers from other societies or to intersociety sessions. However, all abstracts submitted to it in accordance with the prevailing rules will be published in the annual abstract issue from Federation Proceedings."

There are three points which I commend to your attention:

1. The only ten-minute papers which will be on the program automatically by right of membership are those which have a member of the American Society of Biological Chemists among the authors. Although a non-member may present the paper orally by virtue of being listed as senior author, a paper not having a member among the authors will not automatically be placed on the program if it is sponsored by a member. A member may be responsible for only one paper, but two or more members can, as now, be responsible for two or more papers if they are joint authors of them. I recommend that the American Physiological Society adopt a similar rule.

2. When the Federation program is being made up there is a lively interchange of papers among societies. One society takes the responsibility of programing a particular subject to make an intersociety session, and in addition papers are transferred from one society to another where it finds a more appropriate place on the program. The physiologists, biological chemists, and pharmacologists have a one member-one paper rule; the other societies do not, and a member may be responsible for several papers on his society's program. If we are not to give unfair advantage to members of societies with laxer rules, we must limit exchange of papers to societies having equivalent rules. Until all societies have rules as strict as those of the biological chemists, restriction of interchange is essential. This will cause difficulty in making up the program, and the societies' secretaries will be even more harrassed than they are now. Nevertheless, I recommend that we enact a similar restriction and hope that the remaining societies will make it unnecessary by limitation of papers.

3. The biological chemists voted to allow papers by non-members to be sponsored by a member of their society who is not an author of the paper. This introduction will use up the member's right to have a paper on the program. Abstracts of such papers will be printed. Out of these non-member papers the Program Committee of their society will select those it wants for oral presentation. The thought behind this is that the non-member with a red hot paper should not be denied his chance to give it. The biological chemists do not have a Fall meeting open to non-members as we do, and they have a long-standing and strong-minded Program Committee which is willing to undertake the task of screening non-member papers. On all counts I think this should not be done by our society, and

the rest of our Council agrees with me.

At the next business meeting in the Spring you will be asked to vote on a motion changing section 4 of Article VII of our standing rules to read:

ARTICLE VII Standing Rules

(Change requires majority vote of those present at a Spring Business Meeting)

4. Presentation of Papers. At a Spring meeting of the Society, held in conjunction with the Federation meetings, a member, retired member, or honorary member may present orally or be co-author of not more than one scientific paper, except upon invitation of the Council. An associate member or a non-member may present orally one scientific paper only if a full member is a co-author.

At a Fall meeting of the Society a member, retired member, honorary member, or associate member may present orally, be co-author of, and/or introduce non-members to present scientific papers. Any one person cannot orally present more than one scientific paper, except upon invitation of the Council.

Upon invitation of the Council, a member may contribute papers to specifically designated sessions of the Society without forfeit of his privilege of presenting a regular scientific communication.

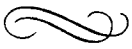
PROGRAM ADVISORY COMMITTEE

The Society's Council has appointed a Program Advisory Committee composed of L. L. Langley (Chairman), Parker Anslow, and Robert Berne. The Committee is charged with organizing symposia for the Spring meetings, suggesting topics and speakers for the 30-minute introductory talks at scientific sessions, appraising the quality of the scientific sessions and receiving and forwarding to the Council any suggestions from members regarding programs. Programs are beset with problems and are in a period of rapid evolution. It is hoped that the Program Advisory Committee, by giving more time and thought to the subject than is available to Council members, will be able to help the Society maintain satisfactory programs. Any member who wants to contribute ideas about the program should communicate with one of the members of the Committee.

WORKSHOP ON THE TEACHING OF UNDERGRADUATE PHYSIOLOGY

The Education Committee will sponsor a Workshop on the Teaching of Undergraduate Physiology at Purdue University, Lafayette, Indiana, June 4 through 15, 1962. Dr. Richard Sanborn of Purdue will be the Director of the Workshop. Discussion leaders of national prominence in teaching and research will be in attendance. Discussions will concern approaches to subject matter, recent advances and projections and especially laboratory experiments in physiology. General educational problems will be discussed and sessions will be informal. Those chosen for participation will be reimbursed for transportation to and from Lafayette and will be provided with board and lodging while in attendance. This is made possible by a grant from the National Science Foundation.

To a great extent the details and success of a Workshop on Undergraduate Physiology depend on the interests and creativity of the participants. Many of the participants in past Workshops have been motivated by desires to have their physiological knowledge brought up-to-date, to see and do good classroom experiments arranged with equipment of moderate or low costs, and to share backgrounds of experience with teachers on neighboring campuses. Since the first Worksnop (1955) a favored pattern of organization has included in each day's program; 1) lecture-discussions on modern subject matter, 2) demonstrations and informal work sessions to develop and extend experiments for teaching laboratories and 3) discussions of topics of broader educational interest. Subject-matter presentations stress general physiology, often applied to plant as well as animal material. The informal work sessions have sometimes involved the participants' working in smaller groups to develop or construct new equipment or to make ideas workable; reports are made later in plenary session. Information on sources of supply is shared and there is a collection of current physiological monographs on display throughout the conference. The discussion sessions on topics of common interest in the educational field have proven very popular. The same educational problems occur on several campuses. Solutions to problems are often found by discussion and some participants have later enjoyed the satisfaction of seeing their suggestions put into practice on a national scale as new phases of the educational program of the American Physiological Society.



SPECIAL APS PROGRAMS AT THE SPRING MEETING

Thirty-minute Introductory Talks

Comparative Physiology of Urinary Excretion - Bodil Schmidt-Nielsen

Troublesome Features of Respiratory Mechanics - Jere Mead

Venous Blood Flow - Gerhard Brecher

Chemical Environment of the Central Nervous System - John Pappenheimer

Regulation of the Pulmonary Circulation - Alfred Fishman

The Control of Aldosterone Secretion - James O. Davis

Temperature Regulation and Cold Acclimation - Loren Carlson

Motivation, Learning and Behavior - R. W. Doty

Neurohormones - Ernst Florey

Symposia

"Mechanical Aspects of Cardiac Muscle" - J. W. Remington, Chairman

"Adaptation for Temperature Regulation in Homeotherms" - cosponsored by the Comparative Physiology Division of the American Society of Zoologists - P. R. Morrison, Chairman

"Borderline Probe Around the Field of Active Transport" - W. F. H. M. Mommaerts, Chairman

Teaching Session

"The Use of Television and Programmed Instruction in Physiology" - R. D. Tschirgi and B. M. Wenzel, Chairmen

TRAVEL GRANTS TO LEIDEN CONGRESS

The XXII International Congress of Physiological Sciences will be held in Leiden, The Netherlands, 11 to 17 September 1962, under the sponsorship of the International Union of Physiological Sciences. The United States adheres to the International Union through the National Academy of Sciences which has established a National Committee for this purpose. Societies represented on the U.S. National Committee are: American Physiological Society; American Society for Pharmacology and Experimental Therapeutics; and the Society of General Physiologists.

The National Committee is seeking funds to provide a limited number of allotments in support of travel to the Congress for scientists residing in the United States who do not have sufficient funds from research grants or other sources. The Committee plans to offer a grant sufficient to cover the difference between other funds available to the applicant and the costs of domestic travel (jet tourist), charter flight overseas ($260), registration, and subsistence during the Congress. If funds permit, awards may be increased for persons unable to use charter flights.

Application forms should be requested from and returned to:

USA National Committee for the IUPS
Division of Medical Sciences
National Academy of Sciences -
National Research Council
2101 Constitution Ave., N.W.
Washington 25, D.C.

The deadline for receipt of applications is 15 March 1962.

All applicants will be responsible for their own passports, visas, registration, travel arrangements, and hotel reservations.

Applications for assistance toward travel expenses are entirely separate from applications for registration for the Congress and for the submission of papers.

THE MATURATION OF PHYSIOLOGY IN AMERICA AFTER 1830

C. I. Reed

The events recounted briefly in the first two installments* of this series brought physiology, as an educational discipline, to a poorly-appreciated status in the intellectual community of young America from which it did not emerge completely for a century. New textbooks were imported from abroad and more were being written at home, starting with Dunglison's masterpiece. Of equal importance was the brilliant pioneer group that emerged from his sphere of influence to play important parts in later happenings. Among them was Daniel Brainard (1812-1866), founder of Rush Medical College; William Travis Howard (1821-1907); Jonathan Letterman (1824-1872); Edward Hazen Parker (1823-1896); George R. Morehouse (1825-1905) who collaborated extensively with Weir Mitchell in his work on immunity; James Aitkin Meigs (1829-1879) who succeeded his master; Levi Cooper Lane (1830-1902), one of the most prominent promoters of scientific education on the west coast; Austin Flint, Jr., (1836-1915) (M.D. Jefferson 1857) and Weir Mitchell, himself. Besides our own comments, Dunglison's career has been extensively treated in THE PHYSIOLOGIST previously. Some of his important contemporary associates were Oliver Wendell Holmes, Sr., Samuel David Gross, Reuben D. Mussey, Edward R. Peaslee, Nathan S. Davis I, John C. Dalton, Charles Edward Isaacs, John W. Draper, and Weir Mitchell's father, John Kiersley Mitchell.

The establishment of the Smithsonian Institution gave an impetus to scientific research that had been lacking before. While there was little direct influence on the teaching of physiology, several members of the staff, from time to time, collaborated with physiologists and in general encouraged them and occasionally issued monographs too extensive to be published elsewhere. Later, both the American Medical Association and the American Association for the Advancement of Science established journals with liberal policies. A still more important influence of these two organizations was the fruition of scientific and intellectual trends begun two centuries earlier. Not only did they furnish means of publication but both became important influences in thinking.

Geneva Medical College (1834-1872) was the scene of an unpredicted mutation in medical education when Elizabeth Blackwell was granted a medical degree (1849). The event touched off such a storm of criticism that the college was obliged to refuse admission to her sister. As usual, such opposition only strengthened the determination of other feminists of that day, with the result that female medical colleges began to appear like mushrooms after a rain. The first of these, now known as Womens Medical College was formed in Philadelphia and is the only one of 15 to survive to the present. The counter reaction was the liberalization of policies by other schools so that women were admitted quite freely in a few years. Unfortunately, where opposition was too inflexible on the part

* The Physiologist, May 1961, p. 34, and November 1961, p. 44.

of the "regular" or allopathic physicians, the women embraced some one of the numerous cults. Homeopathic colleges exclusively for women were apparently thrifty for a time but soon died out. Physiology fared badly in most of these as in the rank and file of proprietary schools, or even in some of the university schools. Most of the female medical colleges had to depend largely on male faculties. There were no female physiologists of note until near the end of the century. The female seminaries suffered the same deficiency for the first 50 years of inclusion of human physiology in the curriculum.

On the other hand, several men of ability taught physiology in the large city high schools: Henry McMurtrie (1793-1865) (M.D., Penn. 1814) lectured on anatomy, physiology and natural history in the Philadelphia Central High School (1839-1859) and was followed by Henry Hartshorne (1823-1897) (M.D., Penn. 1845). Mitchell stated later that, while neither of these men contributed to research, many of the more able graduates of Pennsylvania who were noted for physiological thinking had received an initial indoctrination under these two.

Early in the decade of the "thirties", an American Physiological Society was formed which attracted great interest for about five years, but died a natural death 50 years before the current society was formed. Both lay and professional people were admitted to membership and the group seems to have enjoyed considerable social prestige for a time. It appears to have sprung from the group of intellectuals which embraced the Alcotts. The ultimate demise was due, it may be said, to a surfeit of Graham bread(!) as the originator of that delicacy, a member, advocated its universal adoption so vigorously that others less fanatical were repelled. Probably the most able professional member was E. R. Peaslee.

Another radical innovation came about in Baltimore, when Horace H. Hayden (1768-1844) organized the first dental school in the world after a vain effort to induce the Maryland faculty to include dental instruction in the medical curriculum. With no special preparation, Hayden taught physiology and geology! (Mineralogy or metallurgy?). Physiology made little impression in dental schools until early in the present century.

For many years, the homeopathic doctrines of Hahnemann had been adopted progressively among physicians to the disgust of some of the more conservative practitioners. When the American Medical Association was formed, Nathan S. Davis I, though usually a progressive advocate, spearheaded an attack on all of those adhering to homeopathy and succeeded in having them excluded from membership in the new association, despite the fact that the virtue of smaller doses of drugs had been widely accepted. The result, as in most other restrictive movements, was immediate formation of homeopathic medical colleges everywhere - ten years later they were almost as numerous as the accepted schools; the stubbornness of the Davis group fastened on the medical world a problem that was not solved until 75 years had elapsed. At least two state universities, Michigan and Ohio State, established homeopathic schools alongside "regular" or "scientific" schools ("allopathic" had been discarded as a designation for the latter group). Many graduates of these schools attained to successful careers and it must be admitted that a patient could not distinguish

between the best homeopaths and the best regulars. The old Hahnemannian precis, "like cures like", was considered to have been vindicated by the evolution of immunotherapy and the concept of low dosage had been vindicated already by the scientific group. Otherwise, even the most obtuse layman could see the fallacy of the division.

When Ohio State University admitted the Starling-Ohio Medical College to the status of the college of medicine of the university, the homeopathic group insisted that their specialty be given equal representation, with its own faculty. A nearly defunct homeopathic school was transplanted bodily, incidentally bringing in a few very able physicians. They did not demand separate departments of anatomy, chemistry, or bacteriology; pharmacology was not yet developed to a degree that caused them much concern. But they did want a separate course in physiology. The lay Board of Trustees refused. "If you do not need separate treatment of anatomy, chemistry, and bacteriology, why do you need to have physiology in a separate category?" They had trapped themselves. This author was an instructor in physiology at that time. There were 15 students in the regular class and 12 homeopaths. Dean W. J. Means had long held the view that if he could build a new medical faculty according to his own ideas, he would bring in the best representatives of the numerous healing cults he could find, including Christian Science, and give each a chance to exploit his own beliefs and then, after a decade or so take the best of each. Consequently the board's decision was fully in accord with Mean's ideas. Furthermore, he insisted that the two groups work together in the laboratory as well as attend the same physiology lectures. We made every effort to treat all students alike, even crossing the division to assign desk partners. Both groups had been rigidly selected. Except for three homeopaths no one could identify either group when graded anonymously. I frankly told them that no expression of enmity would be tolerated, that each group must prove its merits. It required another decade for the leaven to exert its most dynamic effect. It cannot be demonstrated that anyone suffered in any degree by this tolerant approach.

John Kiersley Mitchell (1793-1858) (M.D., Penn. 1819) early came under the influence of Nathaniel Chapman who had succeeded Rush, after a brief hiatus, as professor of the institutes (physiology) and who was the first president of the American Medical Association; the younger man, throughout life exemplified an order of scientific analysis unsurpassed for physiological orientation. He taught both physiology and chemistry in the Philadelphia Medical Institute and in Franklin Institute, later becoming professor of theory and practice of medicine in Jefferson Medical College. Probably his most striking paper was "On the Cryptogamous Origin of Malarial and Epidemical Fevers"(1849), believed to be the first scientific dissertation on that subject. He also published experimental reports on mesmerism, animal magnetism, osmosis in living tissue, and on liquefaction of carbon dioxide. His most important original work was a series of reports on the function of the sturgeon heart which anticipated work done a half century later but which overshadowed his because of inadequate communication media.

Popular agitation for a medical college in Georgia began in 1785 but

did not materialize into a definite project until 1826 when a group of physicians in Augusta, under the leadership of Milton Anthony (1789-1839), began private postgraduate instruction in a number of fields. He had no medical degree but when the Medical Academy of Georgia was chartered, he undertook a large part of the instruction under an omnibus title. Alexander Dugas (1806-1884), who became professor of anatomy and physiology (1832-1855) was the only other person of initiative in this group. He visited Europe several times to study with Gay-Lussac, Cuvier, Magendie, Lisfranc, and Pouillet. It is doubtful whether any other American of this period enjoyed as extensive association with continental colleagues. He brought back large complements of books and equipment, some retained in use until fairly recently. His main field was the investigation of hypnosis for anesthesia; he had made substantial progress when the use of ether was introduced, a whim of fate which pushed aside his findings. This was not an unusual outcome of research efforts in those early periods. Alexander Means (1799-1883) who became professor of chemistry in Emory College in Georgia (1838-1869) published a monograph comprising a collection of essays under the title "Electricity as a Therapeutic Agent" in which he advanced remarkably modern comprehension of biophysics. Verily the men of old suffered more from want of equipment and facilities than from the lack of ideas.

Henry Fraser Campbell (1824-1886) (M.D., Georgia 1842), in 1850, published "The Influence of Sanitation in Producing Disease", and three years later began the remarkable project that places him in the ranks of true scientific pioneers, first announced under the title "The Sympathetic Nerve in Reflex Phenomena". Then in 1857 appeared "The Excito-secretory System of Nerves". The American Medical Association awarded a prize for this work. This man clearly deserves priority because Claude Bernard did not publish his observations on the same subject for some years. So far as I can learn, Bernard never acknowledged this point; Marshall Hall did not publish his work on this subject until 1857, when he read a paper before the Royal Society. He evidently did not know of Campbell's accomplishment until the latter wrote him calling attention to it. Hall promptly and graciously replied (May 2, 1857) "I arrive at this conclusion: the idea and the designation of the excito-secretory action belong to Dr. Campbell, but his details are limited to pathology and observation. The elaborate action is the result of the labors of M. Claude Bernard.... My own claim is of a very different character, and I renounce all other. It consists of the vast generalization of the excito-secretory action throughout the system." Hall sent copies of his letter to Bernard and to the London Lancet. President Doubouvitsky of the Imperial Academy of Medicine of St. Petersburg sent through the American minister to Russia a gracious expression of the judgment of the Academy that Dr. Campbell's claims to priority were amply justified. (Have any of my colleagues ever noted mention of this incident in any textbook or in any general review of the subject? I have heard the claim made that Kuntz mentioned it but I have not been able to verify this).

Another forgotten man, except for Raymond Bieter's biography, was Charles Edward Isaacs (1811-1860) (M.D., Maryland 1832). He resigned from the Army in 1846 because of ill health, taking post as professor of anatomy in New York University, and launching at once into a career as

a functional anatomist, or physiological anatomist. After several original anatomical publications, he centered attention on kidney function, probably completely unaware of the heavy handicap of the Bowman-Ludwig-Heidenhain triumvirate already dominating the field. Bieter has insisted, with much justice, that Isaacs should supplant Heidenhain in this trio because he began to use vital dyes 17 years before Heidenhain and carried his studies far beyond anything ever reported by the latter. And he was more successful in duplicating Bowman's findings than most modern workers because he improved the methods so that constant results were assured. His experimental subjects included frog, turtle, snake, alligator, fish, bird, mouse, rat, squirrel, cat, dog, raccoon, rabbit, hog, sheep, deer, elk, moose, ox, horse, black bear, rhinoceros, monkey, and man! Has any other American worker ever used such a wide range of subject material?

Isaac's results were mentioned briefly in Schmitt's Jahrbücher but otherwise completely ignored at home and abroad, except for Bieter's paper and mention by Walter Meek in a paper published a third of a century ago.

John Call Dalton (1825-1889) (M.D., Harvard 1847) was the first native American to devote full time to physiology throughout life, and he was probably the first to study with Bernard. The immediate result of the association was a paper on "The Corpus Luteum of Pregnancy" which was published in the Transactions of the American Medical Association in 1851 and was awarded a prize for scientific excellence. This brought appointment as professor of physiology in the University of Buffalo. His adoption of the microscope as a physiological tool and as pedagogical equipment has been mentioned; also, he was probably the first American physiologist to use the spectroscope. His association with the Flints began in Buffalo but Austin, Jr., was his assistant for a time in Vermont Medical College. He also taught in Long Island Hospital Medical College but terminated his teaching career in Columbia where he served the last four years as president of the university. His name is memorialized there in the Dalton professorship. He joined the new American Physiological Society and lent his prestige to its early progress but never attended a meeting as his death occurred only two years later. John Green Curtis, his successor, invited the organization meeting to the department. Dalton served during the four years of the war as a surgeon but was assigned to the New York area. His military career apparently had little influence on his further progress.

Dalton's text on Human Physiology is a model of literary style which other physiologists of today might adopt with profit. He also instituted a private research laboratory wherein he invited his collaborators and friends to join him. He was a strong advocate of the teaching laboratory but it was not until 14 years after his death that such an installation was made in that department. From his earliest teaching days he did use some very simple experiments, more in the nature of demonstrations by students under his guidance. His lecture demonstrations were richly informative and eagerly anticipated by students, many of whom have commented on the teaching instinct which he possessed. Unlike Dunglison, he could call on his own experience as an investigator for confirming

evidence. In 1885, he published "Topographical Anatomy of the Brain", one of the most accurately illustrated works of its kind ever published in this country. He was present at the first demonstration of the use of ether and very early made use of it in his demonstrations.

Paradoxically, it was his use of animals in demonstrations that sparked the first antivivisectionist agitation in this country. His valiant defense finally culminated in a book, "The Experimental Method in Medicine"(1882) which has sounded the keynote for all of his successors, even though most of them are unacquainted with its text. Bowditch and Mitchell later took over leadership in the perennial fight but it is to Dalton the modern experimentalist is indebted for defining the issues and sounding the keynote of defense against the tide of hysterical zoophily that threatened for several decades to curtail all such activity, as actually occurred in England in 1876.

Other research publications by Dalton are "Decomposition of Iodide of Starch in Animal Fluids", "Digestion of Starch", The Constitution and Physiology of the Bile", and "Movements of the Glottis in Respiration". In his studies on bile, he prepared, for the first time in history, a duodenal fistula: a remarkable accomplishment for that age and environment. Another important accomplishment was of an entirely unique nature. We are so accustomed today to regarding Bernard as a sort of physiological demigod, that it comes as a shock to know that his status once depended on Dalton. Following the publication of the Frenchman's theory of glycogenic function of the liver, Dalton began a long and meticulous investigation, some of the results of which anticipated those of Bernard. When Pavy, an English physiologist, attacked Bernard's thesis so vigorously, he cast doubt on the validity of the findings; there is no doubt that Pavy was sincere and honest and that fact alone convinced many colleagues of the correctness of his views. Dalton now came to his friend's defense with a volume of data that could not be controverted and Pavy conceded his error. In 1871 Dalton read a paper on "Sugar Formation in the Liver" before the New York Academy of Medicine which was widely acclaimed but now forgotten while the thesis he defended is standard information in every text. Again the publication medium proved decisive in establishing the comparative reputations of two able researchers.

William Sweetser (1797-1875) (M.D., Harvard 1818) corresponded with Beaumont and apparently examined St. Martin intensively, later publishing a monograph on "Digestion and its Disorders" which must have been based largely on his direct investigations. He also published original work on capillary function which, at a later date, might have been announced by Sir Thomas Lewis. Joseph Carson (1808-1876) (M.D., Penn. 1830) published a monographic review on "Animal Temperature" which embodied many original observations. Samuel David Gross (1805-1884) (M.D., Jefferson 1827) in 1830 published "Anatomy, Physiology, and Diseases of the Bones and Joints", the first compilation on that subject; some of his findings have been rediscovered in recent years. Charles Cogswell (1813-1892) (M.D., Edinburgh 1836) while practicing in Halifax was awarded the Harvey prize for a dissertation on "The Physiological Action and Medicinal Properties of Iodine and its Compounds". And in 1851 he read a paper before the Medical Society of London on "The

Endosmotic Action of Medicines". The comparative anatomist, Joseph Leidy (1823-1891) (M.D., Penn. 1844) lectured on physiology in the Philadelphia Medical Institute for a time and always encouraged and supported progressive trends in that field and was associated with physiologists throughout most of his career. Another comparative anatomist who greatly influenced the trend of physiological affairs was Jeffries Wyman (1814-1874) (M.D., Harvard 1837). When Holmes returned from Dartmouth as professor of anatomy and physiology in Harvard Medical School, Wyman was assigned to the college. He had come under the influence of J. C. Warren who had taught both surgery and anatomy. After a brief tenure in the medical department of Hampden-Sidney College, he returned to Harvard. There he met Charles Edouard Brown-Sequard when the latter, under Holmes' aegis, was teaching neurophysiology in the medical school. This combined influence turned Henry Pickering Bowditch toward a physiological career. Wyman, himself, published much scientific work strongly oriented physiologically, especially that on reproductive phenomena. Space will not permit listing all of those individualists who made contributions comparable to those of Liebig, Du Bois-Reymond, Helmholtz, Bernard, and others of the classical school of continental workers, only to have them ignored by their own associates.

However, John W. Draper (1811-1889) (M.D., Penn. 1836) cannot be ignored. His graduation thesis "Absorption" was published by the faculty in recognition of its high quality. He was promptly appointed professor of chemistry, natural philosophy, and physiology in New York University. When the medical faculty was organized in 1841, he was the logical candidate for appointment there, also. Early publications were on glandular function, auditory and ocular physics, capillary mechanics and bronchial musculature. Papers on light and thermoelectric phenomena were translated and republished in German and French. A treatise on the forces which produce organization in plants was similarly recognized. A textbook on chemistry (1846) was followed by one on natural philosophy (1847), and "History of the Intellectual Development of Europe". The last was republished several times in German, Italian, Polish, and Russian. "Memoirs on Radiant Energy" was awarded the Rumford medal. Other publications on history, politics, science,and religion were less distinctive but still widely circulated. When Daguerre first succeeded in photographic reproduction, Draper fitted a lens from some old spectacles into the side of a wooden box and made what is believed to be the first photograph in America. On the local scene, his most influential work was his text on physiology which replaced all others then in use and presented new concepts to professional students.

The stage was now set for a new mutation in physiology in this country. Again a sharp demarkation between periods is impossible. Another installment will present developments.

COURSE FOR PHYSICIANS

Another course for physicians is being organized by the American Physiological Society and the American College of Physicians.

The course is entitled CURRENT CONCEPTS OF THE PHYSIOLOGY OF THE ENDOCRINES, ELECTROLYTES, AND THE KIDNEY. The course will be given April 5-7 in Philadelphia. It will be a three-day session which will immediately precede the annual meeting of the American College of Physicians in Philadelphia.

The course will be devoted to summarizing the current status of knowledge of physiological processes in the fields of the kidney, electrolytes, acid-base regulation, and the endocrine system. The discussants will be widely recognized authorities in each of the areas they cover. There will be an attempt to correlate the physiological material with techniques currently used in diagnosis and treatment of diseases of the systems being considered.

The course is under the joint direction of Drs. Daniel H. Simmons and Charles R. Kleeman of the UCLA School of Medicine and Mount Sinai Hospital in Los Angeles. For further information write Dr. Simmons.

INTERNATIONAL ORGANIZATION FOR PURE AND APPLIED BIOPHYSICS

This new international organization was formed in Stockholm on August 2, 1961, by representatives of 26 nations.

The objects of the new organization are to organize international cooperation in biophysics and to promote communication between the various branches of biophysics and allied subjects. It also is to encourage within each country cooperation between the societies that represent the interests of biophysics and to contribute to the advancement of biophysics in all its aspects.

The officers of the new organization are as follows:

President - Prof. A. Engstrom of Stockholm, Sweden
Vice President - Prof. A. Katchalsky of Rehovot, Israel
Sec'y General - Prof. A. K. Solomon of Boston, USA