We have made a start. So far as his physical and his mental equipment are concerned, I see no evidence that man to-day is better than five thousand years ago. He does, however, have better tools—by tools I include the methods of science as well as the actual instruments, such as the microscope, which enable him to delve deeper into the unknown and learn the laws of nature. The development of science seems to act like a falling body in that, once started, its speed is enormously accelerated with time. There is an interrelation of science such that each new tool or method makes possible newer tools and further discoveries. In many branches, and perhaps in science as a whole, more progress has been made within the life span of a single man than in all time before.

Last week I had the privilege of taking part in the celebration of the bicentennial of the founding of the University of Pennsylvania by Benjamin Franklin. Two hundred years is not a long time so far as the recorded history of mankind is concerned. It is only a one-twenty-fifth part of the period of time we are discussing to-day. Two hundred years is a long time, however, in the history of my own field of biological research. In 1740 Benjamin Franklin and the other founding fathers of the University of Pennsylvania knew little about biology for the simple reason that biology at that time was an almost undeveloped subject. An adequate system of naming plants and animals was lacking, and it was only thirteen years later, in 1753, that Linnaeus published his "Species Plantarum" and introduced to the world the binomial system of classification which has been used ever since for the names of both plants and animals. Few of the titles of the biological papers which were given at last week's celebration in Philadelphia could have had any meaning to Franklin and his colleagues because such words as *germ plasm, chromosomes* and *genes* were not in use till more than a century after Franklin's time.

A couple of years ago at the Richmond meeting of the American Association for the Advancement of Science there was celebrated the one-hundredth anniversary of the cell theory. The newness of our knowledge of cells is evident when we realize that more than two thirds of the last century's study of cells is covered by the life span of one of the speakers on the program of the Pennsylvania Bicentennial. Chromosomes were discovered in 1873 when he was three years old and were given the name of chromosomes in 1888, when he was an eighteen-year-old freshman in Kansas University. An example from my own special field of genetics is the fact that knowledge of the mechanisms of heredity has been developed entirely within the last forty years. Progress was slow at first but has become increasingly rapid until now we feel justified in predicting the conscious control of the evolution of plants, animals and even of man himself. Thus in addition to having more and better tools, man, five thousand years hence, may be a better creature physically, mentally and morally.

Detailed prophecies, of course, are impossible. We can only guess at trends. The psalmist said, "Oh! had I wings like a dove, for then I would fly away and be at rest." Many doubtless have had the same desire to fly. Leonardo da Vinci less than five hundred years ago drew plans of a flying apparatus. It was only, however, after the invention of the internal combustion engine that flying became an accomplished fact. This was the outcome of centuries of yearning. We make progress in learning by yearning. If we study what the things are which mankind yearns for, we may be sure that these will be things in which progress will have been made five thousand years from now.

We have yearned not only for wings, which we have now acquired, but also that we may fly away and be at peace. I believe within five thousand years man will have made progress in satisfying this yearning; whether by changing his environment through improvements in social organization or through changing the nature of man, we can not foretell. I believe progress is due in knowledge of how man may live in harmony and at peace in large as well as in small groups. I believe that governments will depend increasingly on expert knowledge—that we shall seek information before legislation rather than the reverse. I believe that by the scientific method we shall more effectively seek the truth and that the truth shall make us free.

THE VALUE OF THE FUNDAMENTAL SCIENCES IN THE ESTABLISHMENT OF ANESTHESIOLOGY[1]

By Dr. JOHN S. LUNDY

SECTION ON ANESTHESIA, THE MAYO CLINIC, ROCHESTER, MINNESOTA

THIS seems to be a suitable occasion for an individual who has had an opportunity to participate in the development of anesthesiology,[2] a new specialty in medicine, to call your attention to the fact that the fundamental sciences are the outstanding factors in

[1] Read before the meeting of the North Dakota Academy of Science, Fargo, North Dakota, April 26, 1940.

[2] J. S. Lundy, E. B. Tuohy, R. C. Adams, L. H. Mousel and T. H. Seldon, *Proc. Staff Meet., Mayo Clin.*, 15: 241–254, 1940.

the further development of this specialty. For a great many years anesthesia was largely an art, but now it is developing also into a science and into a major specialty of medicine. This progress has been recognized with the establishment of an Examining Board in Anesthesiology for the purpose of certifying those physicians who are considered to be competent to specialize in that type of medical practice. The American College of Surgeons and the American Medical Association both recognize this board and are advised by it in regard to certain surveys of anesthesia services that are made throughout the nation in the various hospitals. The rating of the hospitals in respect to anesthesia depends on how well they are supplied with anesthetic agents, what methods of anesthesia they are equipped to use, what library facilities in anesthesia they possess and what personnel trained in anesthesia they employ. Certain of the institutions do not attempt to teach, while others are considered to be satisfactory places for men to take training. At the New York World's Fair it was noted that more than 1,000,000 people interested themselves in the exhibit on anesthesia which was there.

There are societies of anesthetists and there are publications devoted to anesthesiology. I have had a hand in the development of one of them, *Anesthesia Abstracts*. The idea underlying this publication was obtained from *Chemical Abstracts, Botanical Abstracts, Physiological Reviews* and other magazines of a type which have been found very valuable to workers in the fundamental sciences. It seemed to me that a periodical of similar type should be equally valuable to those engaged in a specialty of clinical practice; happily for me the reception accorded this periodical justified my assumption.

In the effort to outline the development of the scientific side of anesthesiology, it is worth while to point out some of the incidents that illustrate the interrelation of the anesthetist and the scientist. The relationship of art and science in the development of a specialty was well stated by Jevons who said, "Science teaches us to know and an art to do."

The history of anesthesia dates back to the time of Herodotus, when concoctions of hemp and mandragora were used to stupefy the sensibilities of individuals who must undergo pain. It is said that even the ancient Chinese used opium to mitigate the horrors to which condemned criminals were subjected in order that the people, ignorant of the insensibility of the victims, might be impressed by the punishment, while those who enforced the law would not hesitate to carry out the sentences. In more recent years Henry Hickman, a young British physician who attempted to work in the field of relief of pain, carried out many experiments with various substances, among them carbon dioxide, but he died an early death filled with disappointment because of lack of sympathetic help and understanding from others. Another young British physician, John Snow, did pioneer work (1850) in the scientific study of ether, use of which for anesthesia had been made known by the dentist, William Morton of Boston. Both of these men died in disappointment, both when they were less than fifty years of age. Horace Wells, dentist of Hartford, Connecticut, introduced nitrous oxide as an anesthetic agent in 1844 and he ended his life shortly thereafter without having received the support of the dental or medical professions. Crawford Long of Georgia used ether in 1842, and for this he was harassed by the inhabitants of his community. Sir James Simpson of Scotland, who introduced chloroform, was persecuted by the people and only overcame their objections through royal favor. Very recently Howard Jones introduced a method of spinal anesthesia and, because of unfavorable criticism and non-support of his efforts, committed suicide. The lives of these men represent some of the unhappiness that has surrounded the development of the specialty of anesthesiology and serve as examples of the hindrances to the development of any specialty if support is withheld. Fortunately, there is a happier side to the story and it is that about which I would like to speak.

In the last twenty years opportunities have been made available to certain physicians throughout the United States and Canada, who are interested in the administration of anesthetic agents, to put into practice ideas that have come to them both in regard to clinical practice and to research. These individuals have become known and, as a result, drugs have been presented to them for investigation. When a new method of anesthesia has been devised these investigators usually have had a part in furthering its clinical application. Many a scientist has advised and cooperated with them in institutions of higher learning and they also have cooperated with scientists who are engaged in the development of new commercial products that are useful to the anesthetist. As a result, to-day training in anesthesiology is available in several places and more positions are available in this field than there are trained persons to fill them. This situation probably will continue to exist for at least the next fifteen or twenty years. It is, I believe, a pleasant thing to contemplate that opportunities do exist for young people in this field and that coexistent with those opportunities are many opportunities for contributions to the relief of human suffering. This situation will continue to exist, however, only if those engaged in work in the fundamental sciences will continue to cooperate in the future as they are doing at present. Therefore, if there are in this audience those who wish to investigate phases of anesthesiology which might well prove interesting to them, they will find the anesthetist eager to discuss the problems that face him and, in turn, to furnish his share of cooperation.

I believe I can best illustrate some of the benefits of this cooperative effort by citing certain happenings of the past. Let us take at random a few of the sciences that are represented in this room and mention some of the contributions they have made to anesthesiology; we can not attempt to enumerate the contributions of all the sciences. The science of anatomy is of fundamental importance to all branches of medicine, including that which includes the anesthetist. Often he must deposit a local anesthetic agent near a given portion of a certain nerve trunk for purposes of producing anesthesia for operation or for diagnosis or for purposes of therapy. To know the location of blood vessels is important so that they may be avoided or entered accurately, as the occasion may require. Knowledge of the bony landmarks is essential in the localization of nerves and vessels. The anatomy of the respiratory passages is necessary knowledge to him who would administer anesthetic substances by inhalation. To know the anatomy of the colon is useful when anesthetic agents are to be administered by bowel. An anatomist's contribution that at first would seem to have to do only with his own science is the work of Clark, of Philadelphia, who devised a means of observing capillaries through an artificial window in a rabbit's ear. This device had been in use for thirty years when, about a year and a half ago, T. H. Seldon[3] began to utilize it for investigation of the effects of certain anesthetics on the capillaries. Much valuable information may be obtained from this application of Clark's investigation of capillaries, for it is not easy to find test objects that will give reliable information.

The work of Rosenow and Tovell,[4] in studying the cause of convulsions under general anesthesia has provided a possible solution of the problem through bacteriology. In the field of botany and horticulture, Knight, working with Crocker,[5] discovered that the ethylene portion of illuminating gas would put carnations to sleep. This information was related to Luckhardt,[6] the physiologist, who tried the gas on mice and then on himself and his other laboratory workers. Attention was called to it as an anesthetic agent for clinical use and it was administered by Dr. Isabella Herb in clinical practice at Presbyterian Hospital in Chicago. Recently when the supply of ephedrine was reduced because of the war in China, the plant Mahjung was cultivated in Brookings, South Dakota, thus showing how anesthetists may keep themselves supplied with this valuable stimulant to the cardiovascular system.

The contributions of chemistry have been of great value. Without them, much of the rapid development in the use of new anesthetic agents and certain other drugs would not have been accomplished. The isolation or manufacture of oxygen, nitrous oxide, carbon dioxide and cyclopropane, of ether and chloroform and ethyl chloride were gifts of chemistry. The synthesis of the barbiturates and of the local anesthetics, cocaine, procaine and others, also are contributions of chemistry, and it is to be hoped that further contributions will be made in the near future. The rapid development of the intravenous method of anesthesia parallels the rapid development of these barbiturates so that, between 1924 and 1934, we learned of the synthesis of barbiturates that would produce long-lasting anesthesia, then of other substances of the series that would bestow anesthesia for a somewhat shorter period and, finally, of still other barbiturates that would cause anesthesia of sufficiently brief duration so that the method is now firmly established in clinical practice and is becoming widely used throughout the world. The investigations of biochemists in the developing of new quantitative methods of analysis for the identification of drugs has made it possible to investigate many problems in anesthesia. As examples, I might cite the work of Dunlop,[7] in Osterberg's laboratory, where a method of identifying procaine in great dilution was employed. This permitted Dunlop to investigate the fate of procaine in the dog and he was able definitely to establish the role of the liver in the destruction of this drug (1935). Delmonico,[8] also working in Osterberg's laboratory, carried out a method of quantitatively estimating samples of barbiturates. This method permitted Delmonico to investigate the fate of certain barbiturates in the body. These are two of innumerable instances wherein methods developed through chemistry have permitted investigation of anesthetic agents used clinically and experimentally. Without the aid of chemists the work could not have been begun.

Physics has taught us to understand some of the actions of gases and liquids and also has contributed methods of measurement that have broad application in the field of anesthesiology. At present, a means of analyzing mixtures of gases by passing them through a fixed, small aperture under constant pressure, and timing the flow, is giving good results in the

[3] T. H. Seldon, unpublished data.

[4] E. C. Rosenow and R. M. Tovell, *Am. Jour. Surg.*, 34: 474–485, 1936.

[5] Crocker and Knight, quoted by A. B. Luckhardt and J. B. Carter.

[6] A. B. Luckhardt and J. B. Carter, *Jour. Am. Med. Asn.*, 80: 765–770, 1923.

[7] J. G. Dunlop, *Jour. Pharmacol. and Exper. Therapy*, 55: 464–481, 1935.

[8] E. J. Delmonico, *Proc. Staff Meet., Mayo Clin.*, 14: 109–112, 1939.

hands of H. O. Brown[9] working in Boothby's laboratory. The physical principles concerned in the use of a light gas, such as helium, in the treatment of asthma is an illustration of the practical clinical application of physical principles. The clinical problem is that the patient is unable adequately to ventilate himself with air because air can not be easily drawn through the air passages, the caliber of which has been diminished by the disease, without extreme physical effort. However, by using a mixture of oxygen and helium rather than the mixture of nitrogen and oxygen that exists in air, the patient is able to breathe with not more than the physical effort exerted by a well person. Another application of physical principles has caused a therapeutic procedure to be developed, the use of which is becoming well recognized and will be widely applied. It concerns the difficulty of a patient after operation to ventilate himself with air or oxygen when there is present in his air passages any solid or fluid material which tends to obstruct his respirations. It has been found that by inserting a lighted, tubular instrument into the air passages, the obstructing material can be aspirated. This permits the patient to breathe in more normal fashion and often to avoid the development of pneumonia which carries with it a considerable mortality or subsequent morbidity.

In the field of electrical physics many contributions have been, and will be, made. An example is the use of the photo-electric cell in determining the coagulation time of blood. The use of the electrocardiograph has permitted study of the effect of various anesthetic substances on the heart. Betlach[10] used the string galvanometric electrocardiograph. Others have used more modern apparatus and the problem remains one of those which will be of interest in the future. I am greatly interested to see whether or not devices may be made that will permit us to follow functions of the cardiovascular system in many operating rooms and bedrooms throughout several hospitals and correlate information for the benefit of patients who are unable to help themselves. Both anesthetist and physicist are greatly interested in air conditioning of operating rooms and hospital rooms; the physicist must provide means of testing the air and the physician must observe any untoward effects on the patient. The loss of body heat by the patient also concerns both physicist and physician, and this problem must yet be investigated. Control of static electricity has become of great importance to the anesthetist recently because he employs various inflammable and explosive mixtures in connection with inhalation anesthesia. Here again the anesthetist must turn to the physicist for information. An excellent example of cooperation in this problem has been the combined efforts of Tovell and Woodbridge, respectively of Connecticut and Massachusetts, together with Horton of the Massachusetts Institute of Technology. From their study has come the intercoupler, a device which connects the anesthetist, the gas machine, the patient and any fourth object or person that must be brought in contact with them. The principle is that the static electricity must pass through a given amount of resistance so that it can not suddenly reach its objective and cause a spark that is hot enough to ignite the vapor or gases. So far as I know there have been no explosions where this intercoupler has been used.

In resuscitation, a type of work which naturally falls to the anesthetist, the physicist has a real interest. Mechanical means of producing artificial respiration have been investigated and some of them have proved effective, although much remains to be done in this field. The so-called iron lung has proved of value, and in surgical cases mechanical devices for pulmonary ventilation have been useful. However, because of the expense of the equipment and the consequent small demand for it, the field has not been thoroughly investigated. In the administration of anesthetic agents by inhalation it has been necessary for so-called gas machines to be devised. Again, physical principles govern the construction of these devices but the construction is not always carried on under the direction of a physicist; this no doubt has retarded the development of an entirely satisfactory machine. For example, when it was decided that ether should be administered with gases an attachment for administration of ether was added to the gas machine. The flow of the gases through the ether bottle resulted in an undetermined concentration of ether in the breathing bag. As yet, no one has devised a means of indicating when concentration of this ether vapor is too strong and consequently the use of the gas machine is often unsatisfactory.

The preservation of blood by chilling has been a great boon to the physician, who frequently finds use for the transfusion of blood. It is to be hoped that some physical means other than centrifuging may be developed for the purpose of separating the cellular elements of the blood from the fluid portion. There are many uses for blood and many uses for each of the elements of blood. The existence of war increases the urgency for solution of this problem.

When venipuncture is difficult because of smallness of veins, it has been shown that by application of heat to an extremity, small veins may be better filled and venipuncture made easy.

The fields of pharmacology and physiology are of

9 H. O. Brown, unpublished data.

10 C. J. Betlach, *Jour. Pharmacol. and Exper. Therapy*, 61: 329–337, 1937.

such direct application to the work of the anesthetist that the point need not be especially illustrated. It may be said, however, that many agents and methods contributed by chemists and physicists are first applied by the physiologist and pharmacologist to determine the use to which the new agents or methods can be put before they are applied clinically. While the first agents to be introduced may have come into use without such preliminary investigation, those that are introduced to-day are subjected to thorough tests. The interest of the physician anesthetist in the effects produced by anesthetic substances and other drugs which he uses is evident in the work of Searles,[11] who studied the effect of ether and sodium amytal anesthesia on the blood. Such investigation emphasizes the importance of collaboration of clinician and scientist for, if possible, the separate effect of the anesthetic and of any other drug that may be used must always be determined. It is in this field that the study of psychology becomes important, for it must never be forgotten that the psychologic processes of the animal differ from those of the human being. Therefore, it is not always possible to apply the information obtained from animal experimentation to clinical application of the agent.

The study of languages requires the attention of the anesthetist. Obviously, in scientific writing, many of the same words are adopted by users of different languages, but it is of great importance to the reader of scientific articles that the author should have had at his command a sufficient choice of words that his meaning may be exactly expressed and that, if his article is translated into another tongue, it will not suffer thereby.

By mathematicians many fundamental contributions had been made, usually through physics; however, the mathematician is indispensable in the correlation of data that are gathered not only in the course of experimentation but also in clinical application of anesthetic preparations. It is not easy for those of us who are not mathematicians to assemble statistics derived from our work and properly to interpret their value.

I hope that these illustrations of the indispensable value of the fundamental sciences in the establishment of anesthesiology, a new specialty in medicine, will interest you sufficiently so that your continued assistance may be anticipated. Unfortunately, those of us who are interested in the development of this new specialty and those who will follow us in the field of endeavor are not sufficiently well equipped from your point of view. In the absence of an individual genius, then, development of the new medical specialty will, in all probability, take place in institutions where scientists and clinicians can work together and where facilities exist whereby investigation can be carried on, new facts established and new agents and methods developed; these factors, together, will permit further reduction of pain among human beings. In the future, I hope that animal experimentation, made painless by anesthesia, will be accepted by those who have condemned it in the past when their attention is called to the fact that needless pain caused by disease will be spared both animals and man.

[11] P. W. Searles, *Am. Jour. Surg.*, 41: 399–404, 1938.

OBITUARY

PHOEBUS AARON THEODOR LEVENE
1869–1940

Phoebus Aaron Theodor Levene, member emeritus of the Rockefeller Institute for Medical Research, died at his home in New York City on September 6, 1940. He had returned from a vacation in Montana but a short time before, and was about to resume his insistent quest for the knowledge of life processes.

Dr. Levene was born in Sagor, Russia, on February 25, 1869. When he was about two years old, the family moved to St. Petersburg.

The young Levene entered the Classical Gymnasium, and from this school he enrolled in the Imperial Military Medical Academy in St. Petersburg. He was one of the five Jewish students allowed to enter his class. At that time Borodin was the professor of chemistry. It was Borodin's son-in-law, Professor Dianin, who allowed Levene to carry on work at will in the chemical laboratory.

During the year 1891, because of the growing anti-Semitism in Russia, and the resulting need for education of the younger members of the family, the Levenes migrated to the United States, arriving July 4, 1891. After a few months, Levene returned to St. Petersburg to finish his examinations for his medical degree. He was graduated in the autumn of 1891. He returned to New York in March, 1892, and soon took his examinations for the practice of medicine and practiced on the lower East Side until 1896.

Because of his conviction of the importance of chemistry to the advancement of medical science, he enrolled at Columbia as a special student in the Department of Chemistry in the School of Mines. At the same time Professor J. J. Curtis kindly gave him a place to work in his laboratory at the College of Physicians and Surgeons. In later years he supplemented this training by periods spent in Berne under Professor Drechsel, in Marburg under Professor Kos-