Life Among Anesthetists: Recollections of Forty Years

Chauncey D. Leake

My earliest contact with great contributors to anesthesia was one which I did not appreciate at the time. I grew up in Elizabeth, New Jersey, and when I was about 10 years old I had difficulty in reading. Ophthalmology was then a new specialty in our country, and a number of smart young men were claiming to be specialists in this field. My mother took me to the local eye specialist and he told her that I was going blind. For ten dollars a week, he would take care of me. This was a bit too much for our family budget, so our family physician, Doctor Victor Marvalg, a Viennese who was Mayor of the city, was consulted. He told my mother to take me to a genuine ophthalmologist whose office then was on Madison Avenue in New York City.

I well recall the experience. There was the exciting trip, of only fifteen miles, but in those days, with slow trains and ferry, it was a time-consuming journey. I can still recall the hushed reception room, and then the short and rather frightening examination in the darkroom by the very awesome physician. His verdict was simply that I was astigmatic and nearsighted. A prescription was given to me signed by Carl Koller.

Twenty years later, in 1926, after I had learned who Carl Koller was, I had the pleasure of returning to his office in New York to have my prescription renewed. At that time, he told me much of his early associations with Sigmund Freud in Vienna. Freud had charge of a service in the Allgemeine Krankenhaus, on which Koller served as an intern. Freud had a patient who had become addicted to morphine as a result of seeking pain relief following the amputation of a thumb. Freud had the rather sensible idea to attempt to treat addiction to a central nervous system depressing drug, morphine, by means of a central stimulating drug, cocaine. Cocaine had recently been isolated in Wöhler's laboratory, but it was known to have central nervous system stimulating effects. Freud had studied cocaine and indeed wrote an enthusiastic account of its biological activity. Koller was asked to explore the actions of cocaine. Freud wisely did not use it until he had learned more about its activity.

Doctor Koller confided to me that he wasn't interested in this matter at all. He was looking forward to becoming an ophthalmologist. He said that he was searching for something which he could put in an eye so as to anesthetize it for operations for cataract, without having to go through the disadvantage of anesthetic cone or apparatus over a patient's face. Koller tasted cocaine, as many others had done, and noted that it numbed his tongue. He realized at once that the numbing effect was due to the blocking of sensation and that it might be what he was seeking. It took only a few experiments to convince him that he had what he wanted, and following his short report in 1884, cocaine was in extensive use as a local anesthetic agent throughout the world within a few weeks.

Carl Koller studied under Donders, and then came to New York City in 1889, and was a pioneer American ophthalmologist. It was gratifying to be able to arrange for his election as an honorary member of the American Society for Pharmacology and Experimental Therapeutics. At the time of the semi-centennial of the first use of cocaine as a local anesthetic, in 1934, further honors came to Doctor Koller, and continued until his death in 1944.

My interest in local anesthesia continued. In the pharmacology laboratory of Professor Arthur S. Loewenhart (1878–1939) at the University of Wisconsin, where I worked from 1918–1928, there was much interest in local
anesthesia. Loewenhart and his associates surveyed alkyl analogs of procaine. They found that the isopropyl derivative would probably be more satisfactory for local anesthetic purposes than procaine, since it is powerful enough to anesthetize intact mucus membranes, and is as relatively nontoxic as procaine. However, there were no patent rights involved, and as a result no commercial manufacturer was interested in developing the agent. It does seem rather peculiar that a chemical compound which can be clearly demonstrated pharmacologically to have worthwhile properties suggesting its probable value should not be available to anyone who might want to use it, because commercial factors block its manufacture. One of this series of drugs was actually patented, and widely exploited, although it was clearly apparent that it was relatively toxic.

Another interesting contribution from this famous laboratory resulted from the demonstration by Arthur Tatum (1884–1955) and Peter K. Knoefel that barbiturates antagonize the toxicity of local anesthetic agents. It was suggested that barbiturates are advantageous for preanesthetic medication before the administration of local anesthetic agents in order to reduce the possibility of unfavorable reactions from the local anesthetic.

I had further concern with local anesthesia. When I was in charge of the pharmacology laboratory of the University of California School of Medicine in San Francisco during the Great Depression (which we were too busy to notice), Gordon Alles (1901–1963) had been persuaded by Myron Prinzmetal to come up from Los Angeles to work with us. Peter Knoefel came to work with us also, and suggested that we study local anesthesia. We proposed making a new kind of chemical compound which would combine local anesthetic properties with the ability to constrict blood vessels, and thus to delay absorption on injection and both localize and prolong the effect. Epinephrine had long been added to local anesthetic solutions in order to accomplish these purposes. Gordon Alles was a brilliant chemist, and, having developed the amphetamines, knew plenty about handling the phenalkylamines. So he made some compounds combining procaine with epinephrine. They were found to have the desired biological properties. No one was interested in using them clinically. There is no need for new local anesthetics. We learned the hard way!

My direct association with anesthetists came about in rather an accidental way. When I was a student at Princeton, I was preparing to go to medical school. I sidetracked into philosophy and psychology, and wished to take graduate studies. Andrew Fleming West, Dean of the Graduate School, refused to accept me. This is probably one of the reasons why I subsequently took much interest in Woodrow Wilson, who also had been strongly antagonized by Dean West. I left Princeton in March 1917 when I was a senior, to go to war with the National Guard Unit to which I belonged. We were in the Twenty-ninth Division, and trained in Anniston, Alabama. About this time the Chemical Warfare Service was being organized, and I was transferred from the machine-gun battalion in which I was serving and was sent to a psychology unit at Camp Gordon in Atlanta. Presently, I was assigned to the Medical Defense Division of the Chemical Warfare Service at the University of Wisconsin.

One of my later teachers, and still one of my best friends, is Harold C. Bradley, who is Emeritus Professor of Physiological Chemistry at the University of Wisconsin. He was Personnel Officer of the Chemical Warfare Service, and somehow saw my personnel card, and assigned me to the Chemical Warfare Service. Later, I had much pleasure learning biochemistry from him, in company with Elmer Severinghaus and K. K. Chen. Following his retirement in 1948, he returned to his old home in Berkeley, California, where we still enjoy the opportunity of meeting together occasionally and discussing some of our common interests. Doctor Bradley, like so many great scientists, is an ardent conservationist, and in this I am happy to support him.

At the University of Wisconsin laboratories, I worked under the direction of that great teacher, Walter J. Meek, Professor of Physiology. We were studying the war gases. We used morphine to prevent pain in the animals we were using. Following the close of the war it seemed appropriate to study the effects of morphine as a control on the observations
we had been making. When I was mustered out of service, I was given the opportunity to continue with these studies.

I had been investigating the action of war gases on blood acid-base reaction, in connection with respiratory and other effects, and I continued these studies with regard to morphine. It seemed to me that many of the actions of morphine could be explained on the basis of interference with intracellular oxidative processes. It became a matter of interest to find out what general inhalation anesthetic agents might do to blood reaction in reference to respiration, circulation, and other effects. This I undertook.

A. E. Koehler, in the biochemistry laboratory of Harold Bradley, my wife and I studied the effects of inhalation anesthetic agents on blood acid-base equilibrium. This was quite a task, but we used very cooperative dogs, who learned to jump on the operating tables, to expose the areas in their legs from which we would draw arterial or venous blood. The animals actually were well cared for, and they seemed to enjoy being with us.

We found that the net effect of inhalation anesthetic agents on blood reaction is the development of a transitory diabetic episode. It seemed to us as though general anesthetic agents interfere with intracellular enzyme systems associated with oxidation, so that acid intermediate toxic products of cellular oxidation accumulate. We showed that there is a significant ketosis with ether anesthesia. This seemed to be quite independent of the respiratory factors that may have been involved in some of the effects of morphine on blood reaction. Our observations on the actions of morphine and ether on blood acid-base equilibrium were interpreted quite differently from the explanations offered by Yandell Henderson at Yale. Although we avoided a direct controversy, we had some snappy correspondence.

The dramatic introduction of ethylene anesthesia by Arnold Luckhardt in Chicago and its careful study by V. E. Henderson in Toronto, stimulated us to study its effects on the acid-base balance in comparison with nitrous-oxide and other inhalation anesthetics. We obtained further evidence that the effects of inhalation anesthetic agents on blood pH may be correlated with the extent of interference with oxidation. We showed that ethylene anesthesia owes some of its superior properties as an inhalation anesthetic agent to its ability to be administered usually with enough oxygen to prevent a decrease in body oxidation processes, with a resulting minimum disturbance of blood pH. We were convinced that the greater the amount of oxygen that could be administered with an inhalation anesthetic agent, the better it would be for patients. This idea was confirmed later when cyclopropane was introduced.

The pharmacology laboratory at the University of Wisconsin in Madison was a busy place during the twenties. Our work in anesthesia had attracted the interest of practical anesthetists, and thanks to Frank McMeekin, who bravely with his wife was promoting the specialty of anesthesia, I was given an opportunity to discuss some of our ideas with the growing group of professional anesthetists. Wesley Bourne in Montreal confirmed and extended our ideas on ether acidosis, and we had many vigorous discussions in our Science Hall Laboratories on the influence of carbon dioxide and oxygen on the activity of the central nervous system. Arthur Loevenhart proposed to stimulate brain activity by blocking its oxidation mechanisms, by administering carbon-dioxide.

About this time, our work had attracted the interest of Ralph Waters. He was brought to the University of Wisconsin by Irvin Schmidt, then Professor of Surgery, to develop anesthesia in an appropriate university manner. Doctor Waters arrived to set up the first Department of Anesthesia in this country in the uncompleted new laboratory and hospital building. We started our work together on the anesthetic action of carbon-dioxide.

We had a great thrill when we found, in 1928, that carbon dioxide inhaled in a concentration of around 30%, with the balance oxygen, can anesthetize small animals and even dogs. We thus confirmed, after a century had passed, Henry Hill Hickman's pioneering observations on the anesthetic properties of carbon dioxide.

These studies on carbon dioxide led to its use by inhalation for stimulating central nervous system activity, in such conditions as schizophrenia. I had remarkable experiences...
along this line after we had moved in 1928 to San Francisco, where we studied the effect of carbon dioxide inhalations, with Doctor Mary Boitsoerd, in cases of catatonic dementia praecox. It was amazing to watch the negatively reacting schizophrenic take two or three deep whiffs of a mixture of 30% carbon dioxide and 70% oxygen, sit up, open his eyes, look around in a puzzled manner, ask, "Where am I?"; begin to converse reasonably, and then gradually, with glaze coming over his eyes, sink again into his catatonic "zombie" state.

Meanwhile, we had been greatly impressed with the demonstration by Ralph Waters of his developments of endotracheal anesthesia. With Arthur Guedel, he was developing the clinical application of Dennis Jackson’s demonstration in Cincinnati of the carbon dioxide absorption technique. We criticized the use of rectal "basal anesthesia" with tribromethanol in anylene hydrate (Avertin), when our patient almost passed out with circulatory depression as the demonstration was made by Hans Killian, who had come from Fritz Eichholtz’s laboratory in Heidelberg. Ralph Waters began his great residency training program in anesthesia at the University of Wisconsin in 1928, just as we were leaving. We also were studying blood cell fragility under anesthesia, with an enthusiastic group of students, at the same time. It was quite a wrench to pull away from Wisconsin to come to California.

At first, pharmacology was taught at the University of California in Berkeley. There, in an old laboratory in a wooden building, I continued the study of blood cell fragility under anesthesia. However, on returning to San Francisco in 1928, I had the problem of developing a new pharmacology laboratory, on the top floor of the old yellow-bricked, ivy-covered, medical school building, in the shadow of the eucalyptus forest on Mt. Sutro. This was to be a busy laboratory for many years thereafter.

Before leaving the University of Wisconsin, I had become interested in the problem of the relation between chemical constitution and biological action. This had been aroused by conversations with Arthur Loewenhart and the great toxicologist Clarence Muelhberger. The Wisconsin laboratory had made many advances in this matter in connection with arsenical compounds such as tryparsamide in the chemotherapy of neurosyphilis. The studies which we had made on ether and ethylene suggested that it would be interesting to determine whether or not the characteristic unsaturated carbon atoms of ethylene could be incorporated in the ether molecule, and thus improve the anesthetic properties of ether.

Such a compound did not exist. It had been vaguely described as having been isolated from a species of allium by Semmler in 1885, but it had never been synthesized, nor was it certain that it had ever been isolated. The compound in which I was specifically interested was divinyl ether. I was unable to interest my colleagues in the Department of Chemistry of the University of California in this matter, so I wrote to Lauder Jones, Professor of Organic Chemistry at Princeton, suggesting the problem. He asked his graduate student, Randolph Major, to undertake the synthesis of the new compound. The problem was difficult, but eventually pure samples had been obtained, and we began working with them. Meanwhile, Sigmund Fraenkel of Vienna, who had been working with Herbert Evans in Berkeley, attempted the synthesis of other unsaturated ethers. Fraenkel was unable to synthesize divinyl ether, but he did make us several other unsaturated ethers which were useful for comparison with divinyl ether.

By applying principles outlined by Benjamin Ward Richardson (1828–1896), in studies on alcohol series, we could confidently predict that divinyl ether would be the most satisfactory of the unsaturated ethers for inhalation anesthesia. Experimental studies on the compounds submitted to us verified this prediction. These studies were carried out in cooperation with some brilliant young workers in our new laboratory.

When the new pharmacology laboratory was operating, Peter K. Knoefel came as a National Research Council Fellow, having completed his medical studies at Harvard. He had been a fellow worker with me at the University of Wisconsin. When I attended the International Physiology Congress in Boston in 1929, I met a brilliant young Chinese girl who had been born in San Francisco, and who wanted to return there to work before going back to China. She was the daughter of the Minister
of Education in the Chinese government, and had studied in London. Mei-yu Chen, Knoefel and myself began the systematic survey of the unsaturated ethers.

Meanwhile Randolph Major and his associate, R. L. Ruigh, had left Princeton to organize research work for Merck & Company at Rahway, New Jersey. They improved on the method of preparing divinyl ether, and worked out a procedure for stabilizing it by adding an anti-oxidant. This product was called "Vinethene," and a patent was obtained for it. This annoyed me a bit, but I suppose it was justified.

Our first reports excited a number of scientists. Samuel Gelfan in Canada asked for the privilege of studying the effect of divinyl ether on human beings. I arranged for samples to be sent to him, and expected that his publication would appear with the extended pharmacological report which we made. In this, we attempted to cover as carefully as we could all factors of significance in the pharmacological appraisal of a new anesthetic agent.

We had previously established ideal standards for the introduction of new drugs, and we were trying to live up to our own pronouncements. My colleagues at the University of California School of Medicine were not particularly impressed with our studies. We made demonstrations in the laboratory, and there was courteous interest, but this was tempered by proper professional caution. Although the first surgical anesthesia with divinyl ether was carried out in the University of California Hospital under the direction of Dorothy Wood, the agent was not further used, since Howard Naefziger, Professor of Surgery, was not interested.

The clinical use of divinyl ether was thus thoroughly studied at the request of the Merck Laboratories by J. S. Bavin, Professor of Surgery at the University of Pennsylvania. These studies established the clinical value of divinyl ether. It amused me that Ralph Waters at the University of Wisconsin was unable to use divinyl ether satisfactorily as an anesthetic agent. He didn't seem able to anesthetize dogs with it. Nevertheless, its anesthetic power was dramatically demonstrated personally when Waters inhaled it himself at a meeting in Milwaukee.

Merck & Company established a fellowship in the Pharmacology Laboratory at the University of California in San Francisco for a systematic study of various types of hydrocarbons as possible anesthetic agents. We held many long and interesting debates over details of techniques. S. Anderson Peoples even attempted mathematical treatment of time-concentration relations. David Marsh (1919-1958) reported in a systematic way on an extensive series of hydrocarbons, many of which he synthesized for the first time. The results showed that it was not likely that more practical inhalation anesthetics could be obtained than those already well known. We extended the series to include halogenated hydrocarbons in order to try to get an agent which would be useful clinically, but would not be inflammable or explosive. We could find nothing that would be very satisfactory. It was only much later that John C. Krantz and his colleagues at the University of Maryland were able to obtain fluorinated hydrocarbons, and thus to introduce the studies which led to the development of halothane.

Much to our chagrin, clinicians discovered that divinyl ether is potent, and in fact dangerous if its administration is pushed too vigorously or too long. Evidence of liver injury occurred, and we were deeply concerned. It was finally agreed that divinyl ether has an important place in the induction of anesthesia, in the management of short anesthetic states, and that it is especially useful in children and older people.

We held many vigorous discussions on anesthesia and on problems associated with central nervous system depression. Arthur E. Guelde of Los Angeles, a long-time friend of Ralph Waters, joined us during the summer in cool San Francisco. Often our seminar discussions would be held on Sundays at "Pharmacles," a sheltered little redwood grove in the Santa Cruz Mountains along the San Lorenzo River, about sixty miles south of San Francisco. Some half-dozen cars would take twenty or thirty of us from the laboratory down the winding Skyline Highway to our retreat. There we would take a little recreation, swimming in the cold water of the stream, and after lunch devote ourselves to a couple of hours of detailed discussion on various aspects of
central nervous system depression with chemical agents.

At these meetings, Arthur Cuedel would elaborate on a blackboard nailed to a redwood tree his ideas regarding the stages of anesthesia. We came to a good understanding of many of the physiological problems involved in satisfactory anesthesia. Even these discussions went to a study of various chemical adjuncts to anesthesia. We investigated the metabolic depressant action of morphine in comparison with barbiturates. Hamilton Anderson participated in much of this work.

George Emerson was interested in various aspects of the relations of anesthesia to oxidation. After he had gone to the West Virginia University School of Medicine, he continued some of his work, even using fireflies, and getting his daughter to catch them for him. In searching for a nonaddictive pain-relieving agent, he, with Benedict Abreu and Nilkanth Phatak, developed dinitrophenyl morphine. This appeared to us to be a useful pain-relieving drug, and we had some evidence that it might not be as addictive as morphine. In spite of the careful studies we reported, we could not convince the well-entrenched Committee of the National Research Council which had charge of work of this sort that we had anything worthwhile to say on addiction.

Our studies on morphine were well developed by Elton McCawley, Ross Hart, David March (1919–1958), and E. Leong Way. In our work on the unsaturated ethers, we had noticed the respiratory irritating and stimulating effects of allyl compounds. In order to try to get a pain-relieving morphine free from respiratory depression, Elton McCawley, Ross Hart and Dave Marsh tried to substitute the N-methyl group in morphine by N-allyl. Their results justified the idea, and again Merck took it up, developing nalmorphine (“Nalline”) which was found to be a powerful morphine antagonist. Later, Henry Elliott and Eddie Way noted its effect in dilating the eye-pupils of morphine addicts. Now it is widely used to aid in the detection or diagnosis of addicts to morphine or heroin.

Our opinion was that drug addiction is largely a psychiatric reaction to an unbearable environment. Addiction seemed to us to be a form of “escapism.” John Schuman, the sharp clinician of Los Angeles, supported Arthur Cuedel in this approach. Although we were deeply concerned in the general problem of the relationship between chemical constitution of chemical agents and their biological activity, we could not get ourselves to believe that the addictive properties of morphine could be effectively divorced from its pain-relieving powers.

Peter Knoefel, who had come as a National Research Council Fellow, began the preparation and pharmacological study of a large series of paraldehyde substitutes. Norman David worked with George Emerson on morphine derivatives, and Nilkanth Phatak studied local anesthetics. Milton Silverman, who became one of our country’s great science reporters, studied halogenated hydrocarbons with Benedict Abreu. Later he contributed greatly to the study of the pharmacology of alcohol.

As early as 1934, we had demonstrated effective intravenous anesthesia with sodium thiopental. We were not convinced, however, that this form of anesthesia had any great advantages over more conventional anesthetics. We could not foresee that the terrible World War II would make intravenous anesthesia very effective indeed.

Some of the exciting work in our San Francisco laboratory was captured by Bernard Zakheim in brilliant water colors and frescoes. He would paint us in the Redwood circle in the Santa Cruz Mountains, as well as in the laboratory. One of his paintings, dated 1936, was a demonstration of intravenous thiopental anesthesia.

When I left the University of California in 1942, to take charge of the Medical Branch of the University of Texas in Galveston, including its hospitals, I had little time for further laboratory work. Nevertheless, I tried to retain an active interest in anesthetic affairs. An interesting recent development in our scientific knowledge of morphine came as a result of some of my efforts to improve the scientific attitude in Texas. I persuaded Charles M. Pomerat, the distinguished biologist, to join our staff in Galveston and promote a tissue-culture laboratory. With the support of Jack Ewalt, then Professor of Psychiatry, he did this superbly. Among the many who came to
study there was Cuner Corssen, a brilliant German anesthetist. In studying the effects of depressant drugs on tissue-culture preparations of nerve cells, he noted adaptive signs. Later, at the University of Michigan, he found that nervous tissues become dependent on morphine, if continually exposed, so that withdrawal of morphine from the culture results in gradual deterioration and death of the cells. Here then is direct evidence for physical dependence of nerve cells in morphine addiction.

At Galveston, we were able to develop an excellent Department of Anesthesia under the direction of Harvey Slocum. This continued with the skilled guidance of Charles Robert Allen. Both had been trained by Ralph Waters and by my former teacher, Walter J. Meek, at the University of Wisconsin. They taught our son, Wilson, who is now an anesthetist in Seattle.

Apart from those with whom I have directly worked, my contacts with anesthetists have been few. I felt a bit of annoyance over the strenuous efforts to obtain status for anesthesia by organizational methods. Frank and Lurette McMechan gave solid impetus to the scientific development of anesthesia, but they were pushed aside as the certification program got under way. In spite of the “grandfather clause” there were injustices, I thought, for some individuals as certification became increasingly important. I had talked about these matters with John Lundy at the Mayo Clinic, and Paul Wood (1894-1963), who so well led the organized effort. We were astonished at the amazingly rapid growth of anesthesia as a specialty. Perhaps for the same reasons that led Ralph Waters to retire prematurely to the peace of the orange groves of Florida, I found it wise for me to withdraw from active work in anesthesia. The young and vigorous, with the current conventional jargon, became too much for me. So, as old-timers often do, I took refuge in historical studies in anesthesia. These remain good fun.

Always in my work with inhalation anesthetics, I had been impressed by the skill of our manufacturing technologists in developing highly efficient equipment for administering gaseous and volatile anesthetic agents. The McKessons, the Baxter Laboratories, the Ohio Chemical, and S. S. White were among those who pioneered with flowmeters, soda-lime absorbers and mechanized monitoring. Now a host of keen competitors fill the advertising pages of Anesthesiology with devices scarcely dreamed of a few decades ago.

I remember how glad I was, three decades ago, when the service of anesthetists was extended to resuscitation, and Alvin Barach’s pioneering reports on oxygen therapy seemed to fit into our scheme of rational applications of basic biochemical, physiological and pharmacological knowledge to practical clinical affairs. This calls for a lot of wise judgment. To this call, anesthetists have gloweringly responded, as indicated in every issue of Anesthesiology and the many other anesthesia journals which have been established in all great countries. I well recall how pleased I was in 1924 when the young British Journal of Anaesthesia accepted my long and detailed survey of the scientific aspects of the effects of anesthetic agents on the acid-base equilibrium of blood: it augured well for the future, I thought, that practical clinicians would feature such a discussion. My thoughts were fully justified.

In 1946, for the centennial of the ether demonstration by W. T. C. Morton in Boston, I thought it would be appropriate to undertake some sort of historical account of the development of anesthesia. My enthusiasm ran away with me. I put my account in cadenced form. This means that it was an attempt at a long poetical narrative set up in rhythmical lines, and giving me a great deal of trouble with trying to get names into the rhythm. The volume was finally published by the University of Texas Press in 1947. This made it appropriate for the centennial of the discovery of chloroform anesthesia by James Young Simpson. The most significant part of my effort was the appendix of chronological notes, with the bibliographical detail.

I tried this effort on a number of surgical groups. It was a flop. It really disturbed me to see how pained were the expressions on the faces of most of those who tried to listen to me. Actually, the effort was highly praised by some discerning critics, such as George Sarton, but otherwise it was not successful at all. The University of Texas Press refused, in spite of many requests, to issue it
in the second edition. I think I might have improved it!

My interest in the history of anesthesia arose in connection with the seminar on medical history conducted by William Snow Miller, the distinguished histologist at the University of Wisconsin. In 1925, I wrote an illustrated account of the development of anesthesia which was published in the Scientific Monthly. This effort stimulated me to form a considerable anesthesia library. Some four hundred historical items were left at the University of California Health Center Library to form the nucleus of a special collection in the history of anesthesia, to give some distinction to the library I had tried to guide for so long. When I returned, I found to my dismay that many of the fine items, such as the autographed Davy and the Simpson volume had been put in the general shelving, and the anesthesia collection as such neglected. Libraries grow too rapidly these days. Even in the field of anesthesia, we may be getting so much published information that we can't take it all in.

In Prospect

Sal! It's very inspiring for me to be back in the busy School on Parnassus in San Francisco, where the old comfortable laboratories have given way to shiny new and already overcrowded work rooms, and where so many keen young biomedical scientists and clinicians so eagerly seek ever more precise information on anesthetic action. Under Robert Featherstone's guidance, many study basic intracellular and molecular reactions to anesthetics; Edward Way, Henry Elliott and Terrine Adler study morphine derivatives, and under Stuart Callen's direction, clinical search and research flourish, with R. H. de Jong on local anesthesia, and John Severinghaus on oxygenation.

The practical importance of the scientific background for anesthesia is well indicated by the many editions of John Adriani's skillful summaries of the basic facts. To do justice now to the physiology of anesthesia, on which Henry Beecher once wrote so well, would take a many-volumed treatise. Nevertheless, it is worth doing.

It aids every generation to take stock of itself, to discard the useless, to amplify the promising. Ever there is more factual information to digest, appraise, and bring together, in order to search out the underlying principles which continue to operate. In this effort even the historical approach can help.

I began my story with an account of how Carl Koller influenced my career. It is interesting that I may return to him in closing. His daughter Hortense, Mrs. James Becker of Chicago, recently reported on her father's work with cocaine in 1884, after going over his notes, and especially his correspondence with Sigmund Freud (Psychoanal. Quart. 32: 300, 1963). When she kindly sent me a copy, I was amazed to discover that she thought she was writing to one who must be my son, my correspondence with her father having been so long ago. Her account is a delight to read, and it does bring me a glow to realize now what I had never suspected, that Carl Koller did think of me as his friend. Well, I had tried to be, for he had well cared for my eyes.

It is thrilling to have had a little part in the past forty years of the glorious growth of anesthesia. My memories of it are vivid and still exciting. May the next forty bring as much success and satisfaction in the age-long struggle to relieve physical pain—and may we also, meanwhile, find ways to ease our burden, conscious or unconscious, of mental pain.