

THE FRONTIERS OF ANESTHESIA *

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PRESENTING a paper on anesthesia in historic Boston in the year 1945 would call for unusual forbearance to avoid reference to this being the traditional centenary of the discovery of general anesthesia, and Boston the focal point from which this magnificent advance emanated. It was during the years 1844 to 1846 that the battle to popularize general anesthesia was joined here in this part of the world. From here it was successfully propagated to every center of medical practice until, in an amazingly short period of time, all surgeons had adopted anesthesia as an indispensable part of their armamentarium.

We ordinarily think of such a development as being the result of a stroke of genius, whereby an intense beam of light is thrown into a previously dark or poorly illuminated area. However, I would like to point out that progress in medicine does not always occur by such an abrupt means; rather there are two ways in which medical developments come into practical acceptance. The first nonspectacular but perhaps quantitatively most important method is the continuous slow accumulation of bits of knowledge which insensibly modify the current practices day by day, until the accepted technic of today becomes markedly different from that of a generation ago. In this process there is no clear break with past tradition, but only a gradual improvement of methods, a sharpening of diagnostic criteria, a division of some previously grouped phenomena into two discrete entities, or other nondramatic advances comparable only to the slow flowing of a broad river toward the sea.

The other type of progress is discontinuous; it is accompanied by no steady flow of ideas. It is much more like the breaking of a dam, which releases a tremendous flood of pent-up knowledge into areas previously barren. In this second type of medical advance there is a slow accumulation of facts, an increased familiarity with disconnected phenomena which, taken separately, do not lead to any startling innovations. A great volume of knowledge piles up behind a dam of indifference, behind the closed wall of the human mind, the wall of inability to correlate and integrate the significance of things new and strange. Suddenly there is a dramatic incident, men's imaginations are fired, and overnight there is a rush of eager workers to translate

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this dammed-up store of knowledge into an entirely new concept of practice.

So it was with anesthesia in the year 1844. Anesthesia was not new, but old. The idea of being able to produce surgical anesthesia was as ancient as the history of medicine itself. In the first pages of the Bible there is a description of a general anesthetic procedure during which Adam was subjected to the earliest recorded thoracotomy (1). The writings of Hippocrates, Pliny, Dioscorides, and others of the ancient world contain many references to producing insensibility to pain through the use of alcohol, cold, pressure on nerves, or, perhaps in the not quite so distant past, through drinking alcoholic extracts of opium, or administration of mandragora or other stupefying drugs.

Nitrous oxide was well known as a chemical material long before the time we ordinarily consider as the period of the discovery of anesthesia. In 1800, for example, as famous and competent a man as Sir Humphry Davy published an entire book on nitrous oxide in which he states, "As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place" (2). Davy was not an obscure man working in some small isolated community, but was in the important Medical Pneumatic Institution in Bristol, a research center for medical problems. Certainly the powers of nitrous oxide and ether to destroy consciousness and overcome pain were widely known at that time. Hickman, for example, worked on the production of surgical anesthesia about 1820. He went so far as to memorialize Charles X in 1828 on this subject, however, apparently without arousing any interest. Probably there were numerous other experiences in the production of anesthesia, possibly even some as clear-cut as those of William E. Clark (3) and Crawford W. Long (4). These went entirely unnoticed because the proponents of the idea of anesthesia either lacked faith themselves in its essential value or failed to generate a heat of enthusiasm sufficient to kindle a self-perpetuating flame.

In Boston, however, when Horace Wells and Wm. T. Morton made their famous and well known demonstrations of the value of anesthesia in surgical procedures, they made them in a medical center in the presence of what had apparently been lacking before, that is, prepared minds. They not only demonstrated that such a thing as surgery without pain was possible, but they did it in such a way as to convince an influential group of physicians that this was a procedure worthy of being vigorously advocated and adopted generally for the benefit of all. That demonstration of Morton's was the crack in the dike that allowed the accumulated backwater of interest in painless surgery to burst through and to spread over the entire face of the surgical world at a rate limited only by the speed of communications. This demonstration was not instantly accepted at face value by all. There were many who

looked at the new procedure through spectacles tinted with skepticism, conservatism, or even open hostility. As an example, when Professor Velveau reported his first series of ether anesthetics in Paris in 1847 (5) the discussion was acrimonious and apparently quite heated. May I quote selections from Professor Magendie's discussion of the paper on that occasion to illustrate the viewpoint of this famous physiologist and many others like him?

Magendie: "It seems very certain to me that the surgeons are experimenting on human beings without knowing what they are producing nor what are the results they obtain. This conduct perhaps is not morally desirable. You plunge patients into a state of drunkenness; for this is nothing else than a drunken state; whether the substance be inspired or taken as a drink is of no significance.—But there is something still more serious. In proceeding thus on a patient, you deprive him of the consciousness of his condition; you deliver him entirely over to those surrounding him. Plunging a woman into a drunken state, making her insensible, making her lose consciousness, is this a moral deed? Have you reflected on all which might result? In my eyes this new method is subject to grave inconveniences and I cannot too actively protest against the general use of such a procedure.—There is more than one alleged great discovery of which we speak no more today; who knows if soon it will not be the same with ether?—Whether a patient suffers more or less, is this a thing which offers interest to the Academy of Sciences?—I maintain that there is a multitude of operations where it is essential that the patient suffer and feel pain.—Pain always is useful. What will become of the woman in childbirth if you take away from her the pain necessary for the completion of the parturition?"

The antagonism to the new procedure expressed here was, of course, quickly dissipated as the novelty of the idea wore off; but the incident reveals the resistance which a valuable new concept oftentimes has to crash through before gaining general acceptance.

There have been many episodes similar to this, where sudden realization of the significance of a phenomenon, previously known to many, has resulted in an abrupt change in some phase of medical practice. The fact that cocaine could numb sensation was well known before 1884. It had undoubtedly come to the personal attention of everyone who had chewed coca leaves, and was known to many of the scientists working on the alkaloid cocaine, such as Niemann (6), Von Anrep (7) and Moreno y Mayz (8). But only when Koller accidentally rubbed some cocaine into his own eye, realized that this could be used for painless surgery in the eye, and demonstrated its clinical value on patients, was practical local anesthesia born (9).

Another similar sharp break in medical practice, brought about by a dramatic situation, was the introduction of ephedrine by Chen and Schmidt in 1924 (10). Natural and synthetic alkaloids of the general

type of ephedrine had been known for over twenty years, some of which had been available commercially. Yet aside from epinephrine there was no special interest in them and none had won more than a very minor use. However, when K. K. Chen appeared before numerous American audiences and reported the brilliant researches of himself and those of Carl Schmidt, the circumstances of Dr. Chen's presenting new information on a valuable drug from his native Chinese materia medica dramatized the scientific data to a point where interest was aroused beyond that ordinarily resulting from research of a more colorless type. Overnight everyone began to use ephedrine and, as soon as they became available, other synthetic alkaloids with related actions.

The introduction of the sulfanilamides is fresh enough in our own memory to be quoted as another example. Here information which was of tremendous interest to small groups of men in certain laboratories, and which was known to them in part at least for several years, did not break forcibly into medical consciousness until its significance was dramatized by the application of the drug to save the life of the President's son. Undoubtedly if this event had not called the profession's attention to the value of the sulfa compounds in connection with a matter of national interest, the drugs would have been introduced into medical practice only gradually, overcoming by a slow process of development the suspicion, lack of faith, and inherent conservatism with which physicians traditionally receive news of each new panacea.

Recognition of the fact that medical progress may at times be explosive is being emphasized here because I believe that scientific workers are figuratively sitting on a safety valve which has the potentiality of opening up at any moment with a tremendous release of energy. We are all on the frontier of medical progress, peering ahead into an undeveloped Promised Land of unimagined richness, which may be opened up to us at any moment when we are able to seize some new fact, realize its significance, and use it to break out into new ground. The time when a new frontier is to be crossed is largely up to our research scientists, but it also devolves on others to play their role by seizing on new information and transforming it into practical clinical reality. Therefore, I would like to spend some time discussing the places where it seems to me that frontiers exist, and, therefore, where we should look for the advances of tomorrow.

GENERAL ANESTHESIA

With the introduction a century ago of nitrous oxide, ether, and chloroform within a very few years of one another, the major agents in anesthesia were available from the very beginning. However, in recent times there has been renewed interest in the development of liquid and gaseous agents of increased potency which might have an

improved margin of safety. The first big break in this direction was made by Luckhardt and Lewis who in 1923 introduced ethylene (11). Then came the clinical introduction of cyclopropane by Waters and his group (12). This latter gas seems to have special prospect of becoming increasingly valuable because of its high potency which permits adequate oxygen intake levels. In the continuing search for a liquid anesthetic which might combine the desirable properties of several previously available materials, Leake and his colleagues developed divinyl oxide or vinylene, which promises to have an increasing use in its special field of application (13). On a par with these, from the standpoint of the long range development of anesthesia, was undoubtedly the evolution by D. E. Jackson of rebreathing, or carbon dioxide absorption apparatus and procedures (14). When Ralph Waters applied this to clinical anesthesia, the control of the anesthetic over the anesthetic procedure became much more flexible (15). Through this technic modulations in the depth of anesthesia are possible to the skilled anesthetist which bring within the range of feasibility hitherto unduly hazardous operations.

What can we look forward to in the field of general anesthesia? Where are our frontiers? It seems that there are many desiderata which can be hoped for. In the first place, a gaseous anesthetic of high potency, which is nonexplosive, should be developed. This compound should be active at levels of 75 per cent concentration or less, so that oxygen supply could be well maintained. It should produce complete skeletal and muscular relaxation without the necessity of deepening the anesthesia to the point of impairing respiration or cardiac function. It also is not too much to ask that our research chemists create a gaseous anesthetic with a predilection for depressing the neuromuscular system more than the sensory apparatus. At the present time we have to obtain complete muscular relaxation by premedication, by the use of curare, or by deepening the anesthesia much beyond that needed for sensory blackout. Therefore, an anesthetic which would give muscular relaxation at low concentrations would be definitely advantageous for many purposes. It is also desirable that the new ideal anesthetic have no power to increase the irritability of the heart. With several anesthetics the danger of producing abnormal cardiac rhythm is such as to limit the procedures that can be carried on and, particularly, resuscitative measures that may be employed in case of emergency. It is not necessary that an anesthetic render the heart hyperirritable. Therefore, this property would not be present in the ideal general anesthetic.

Another field of development in general anesthesia which needs to be explored more intensively is that of intravenous anesthesia by the use of special short-acting barbiturates, or other new chemical groupings yet to be synthesized. There should be a definite place for an ultra-short barbiturate, the action of which is so brief that the level

of anesthesia could be varied rapidly by increasing or decreasing the rate of inflow through an intravenous drip set-up. There is no reason why, if the anesthetic agent has a short enough duration of action, it might not be possible to control anesthesia administered intravenously as flexibly as is now the case with gas anesthesia. Experiments along these lines are under way.

Chloroform is an extremely valuable anesthetic for many purposes. However, its use is limited in part by its toxic effects on the liver. Now that we know that choline, methionine and possibly other substances can protect the liver from damage by such fat soluble materials, would it not be in order to consider the wider use of chloroform in special cases in patients whose livers have been put in a better defensive state by premedication with large doses of these protective materials? Could procaine intravenously also be used to minimize the possibility of acute cardiac failure?

TOPICAL ANESTHESIA

The first attempts to produce topical anesthesia are shrouded in the haze of past centuries. We know from inscriptions on Egyptian monuments that pressure on nerves was applied very early. Cold was also used through exposing a part to the weather, or packing it in snow and ice when this was available. Cold was applied in the dental field fairly early, by surrounding a tooth to be extracted with crushed ice. This was later changed by Richardson to spraying the tooth with a highly volatile liquid, which first was ether then rhigolene, a very volatile type of gasoline, and later ethyl chloride. The application of cold has even caused a flurry of interest more recently, but is obviously too limited in its applicability to achieve general use. Topical anesthesia with cocaine was introduced by Koller in 1884 (9) as the result of an accident occurring to one with a prepared mind. From this beginning there were developed, within a relatively short period of years, numerous other topical anesthetics of which benzocaine has remained the most popular one, followed by, in most recent times, such compounds as butyn, nupercaine and pontocaine.

Is there a frontier in this field of topical anesthesia? The answer is obviously yes. In the first place, none of the topical anesthetics now available penetrate the mucous membranes as well as could be desired. The concentration required to force enough anesthetic through the epithelial surface is so high in proportion to the anesthetic activity of the compounds as to create the possibility, under special circumstances, that too much may be absorbed and poisoning occur. Therefore, there is needed a topical anesthetic which passes more readily through the surface to get at the nerve endings beneath, which must be anesthetized. There are no reasons why such an agent would have to be unduly irritating to the tissues locally or hazardous from systemic absorption.

Another very obvious need is for a local anesthetic material which will penetrate the unbroken skin. The limitations of the materials now available for this purpose must be evident to anyone who has tried to assuage the sensitiveness of severe hyperemia from sunburn by the use of present anesthetic materials. When the skin is unbroken, only phenols penetrate well enough to produce any perceptible numbing effect, and this action is accomplished only at the expense of using such a high concentration of phenol as to create the possibility of systemic poisoning after absorption and the danger of caustic effects in the area of application. The other surface anesthetic agents have only a very weak effect at the best. They are far from being a satisfactory answer to the need for the relief of pain from the unbroken skin, where a local anesthetic material of high lipoid solubility and rapid powers of penetration and diffusion would seem to be indicated.

An incompletely explored approach to this problem of introducing an anesthetic through epithelial membranes is possible with the use of new synthetic vehicles, such as the polyethylene glycols, carbowaxes or other synthetic solvents. These have unusual solvent and wetting properties, which may lead to increased penetrating power. The developments during the last few years of other groups of synthetic surface-active compounds provide many possibilities for new types of combinations which are certain to have novel properties and applications.

INJECTION ANESTHESIA

Morphine was probably the first drug to be injected for local anesthesia some years before the advent of cocaine (16). However, immediately after the realization of the value of cocaine as an anesthetic, Halsted and his staff began experimenting with injections of cocaine solutions for blocking nerves by infiltration or conduction (17). These experiments were immediately successful, although there were difficulties with cocaine from the standpoint of toxicity and habituation, which all too soon became tragically manifest. The search for synthetic compounds began immediately, so that soon novocain (procaine), introduced by Einhorn in 1904, proved to be an almost complete answer to the needs in this field (18). Fifty years of research have not succeeded in the creation of a local anesthetic capable of displacing procaine from the dominant position it holds as an injection agent. Many compounds have been developed, which have valuable applications for special purposes, but there can be no doubt that the over-all position of procaine still remains without serious challenge.

Where are our frontiers in this field? Again only an uncritical person would say that improved materials are not needed. We obviously need an anesthetic agent which will produce prompt anesthesia at lower concentrations and, at the same time, without having an increased toxicity disproportionate to the greater anesthetic potency.

Long duration of local anesthesia is nearly always a desirable property, since through this the perception of pain is postponed and minimized to the fullest extent. At the present time increased potency of the local anesthetics has been achieved, but at the expense, in at least some compounds, of causing irritation of the tissues in the area of injection, or of producing adverse systemic effects. If our local anesthetic could have such a high preferential solubility in nerves that it would concentrate in these fibers and leave the other tissues unaffected, this might diminish the amount of local irritation.

The question of potency of the anesthetic is of greater importance than is sometimes realized, particularly when so many injections are being made that the occasional or unusual response percentage-wise occurs often enough to be an ever-present source of danger. It is true that nearly all local anesthetics now generally used will produce the desired abolition of sensation when they are injected directly into the nerve or very close to it. However, because of anatomical variations or the presence of areas of infection, there are times when even the most competent operators are not successful in getting the anesthetic directly to its preferred site of action. A similar incomplete anesthesia may also be obtained under entirely normal conditions by less skillful operators. Therefore, there is a need for the greatest anesthetic potency which is compatible with safety, so that the concentration reaching the nerves by diffusion from the area of injection will still be adequate to produce a complete block. If this increase in potency is achieved without a corresponding increase in clinical toxicity, there would seem to be no logical objection to it, and, on the other hand, many reasons why it would add to the efficiency and certainty of surgical and local anesthetic procedures.

To get increased potency it is not helpful to raise the concentration of procaine beyond 2 per cent. When concentrations greater than 2 per cent are used, the vasodilator action of the anesthetic so relaxes the vessels that even the highest practicable concentrations of epinephrine are not able to keep the local anesthetic locked in the area of injection to maintain an adequate duration of action. Evidence that this is the case can be seen in table 1, taken from some work recently published (19).

Inspection of the figures in this table will show that when the attempt was made to increase the potency or duration of action of the procaine by increasing the concentration from 2 to 3 per cent, bleeding was increased and the average duration of anesthesia was actually shortened, both of which constitute evidence of impaired activity of the anesthetic mixture.

However, it is possible to combine local anesthetic agents so that the potency of the mixture summates the effects of the individual ingredients. It is entirely probable that by this means increases in potency can be obtained without corresponding changes in toxicity. Certainly

when a compound like pontocaine is added to procaine, the resulting combination is more effective and apparently not demonstrably more toxic in patients than is the procaine alone or procaine of such higher concentrations as would theoretically be of the same anesthetic strength (19). There has not yet been adequate exploration of the gains that may be achieved through the use of combinations of this sort. There are possibilities of synergism of action, which would seem to make this kind of combination worthy of extensive study. Perhaps greater activity may also be obtained by synthesizing new local anesthetic agents with vasoconstrictor power of their own.

TABLE 1
INFLUENCE OF INCREASING THE STRENGTH OF THE LOCAL ANESTHETIC SOLUTION ON THE CHARACTER OF THE ANESTHESIA. RESULTS FROM A SERIES OF 1760 DENTAL OPERATIONS UNDER "BLIND TEST" EXPERIMENTAL CONDITIONS (DATA FROM WINTER AND TAINTER, 19).

Solution	Number of cases	Onset of anesthesia, minutes	Duration of anesthesia, minutes	Per cent of cases with more than slight bleeding
Procaine 2% with Epinephrine 1:50,000	330	3.1±0.17	190.3±20.3	51.2±3.0
Procaine 2% with Cobefrin 1:10,000	326	3.3±0.15	175.0±27.3	64.4±2.8
Procaine 2%, Pontocaine 0.15% with Cobefrin 1:10,000	561	3.5±0.13	215.0±15.0	69.1±2.7
Procaine 3% with Epinephrine 1:50,000	543	3.3±0.34	136.8±10.9	71.3±2.5

Another very pressing need is for a local anesthetic agent of really long duration. At the present time, the drugs commonly used give local anesthesia lasting only five or six hours. The patient who has had a hemorrhoidectomy, the excision of a rectal fistula, or repair of the pelvic floor would welcome the use of a local anesthetic which would leave the sensory nerve tracts still depressed two or three days after the operation. Procaine base in oil should enjoy a wider application in this particular field. The quinine derivatives that have been used possess at least in part the desired long duration of action, but along with this goes the unfortunate property of producing local irritation of sufficient degree and frequency as to make them only partially useful.

For this particular purpose are needed new anesthetic groupings which will have a duration of action greater than that of the p-amino benzoic acid derivatives, which form the base of most of our present anesthetic agents. If success does not attend the efforts to find an entirely new anesthetic, is there not the possibility that much the same end may be achieved by modifying the pharmaceutical form in which the anesthetic is administered, just as we at present slow down and prolong the action of insulin, pituitary extract, and possibly even of penicillin?

SPINAL ANESTHESIA

When it was realized that a local anesthetic solution could be injected into the tissues, it was not long before injection into the spinal canal was also tested. Probably Dr. J. Leonard Corning was the first to investigate this form of injection, since he published a report on it as early as October 1885, using cocaine as the anesthetic agent (20). Corning is a man whose name has been overlooked altogether too frequently in the distribution of credit for the development of our modern anesthetic procedures. Those interested in his contributions should turn to the excellent discussions of the development of anesthesia published by T. E. Keys in 1941 to 1943 (21). When procaine was made available, this became the drug of choice for spinal anesthesia because of its obvious advantages from the standpoint of safety and anesthetic power. At the present time such newer drugs as pontocaine and nupercaine which have greater potency and more prolonged duration are also used extensively.

Where is the frontier in the field of spinal anesthesia? Obviously, a compound of greater duration is needed for there are some operations in which the anesthesia does not last long enough. Another desideratum for a spinal anesthetic solution might be diminished diffusibility. One of the difficulties of injecting a local anesthetic solution into the spinal canal is that the extent of the diffusion may vary, with the result that occasionally there may be some interference with intercostal respiration or even depression of the medullary respiratory centers. The level of anesthesia can generally but not invariably be controlled by the position of the patient, selection of the volume of solution injected, and the area of the spinal puncture. However, if an anesthetic agent had such a high affinity for nerve tissues that it did not diffuse appreciably from the area of injection, then the effects could be sharply localized to a preselected region, with advantage to both surgeon and patient. The same effect might be secured by preventing diffusion through change in the physical nature of the anesthetic solution, such as making it too viscous to spread freely up and down the canal.

It is my personal impression that the role of vasoconstrictors in controlling the course of spinal anesthesia has not been adequately explored. Perhaps with these there can be beneficial modifications in the duration. Attention might also be directed at developing an antidote for the local anesthetic whereby the anesthesia could be terminated at will.

Very stimulating types of study are those of Lemmon and Julia Arrowood (24), in which the duration is controlled by what might be called a continuous drip, after a preliminary sequence of intermittent injections. Is it possible that, if we had a local anesthetic agent of extremely brief duration, a continuous intraspinal drip procedure

could be as flexible as previously suggested for intravenous anesthesia? This would deliver the control of the anesthesia directly into the hands of the anesthetist, since by lowering or increasing the rate of inflow of the anesthetic solution the extent and depth of the anesthesia produced could be modified at will.

A brilliant special application of this general concept was made by Hingson and his coworkers in the development of his procedure for caudal analgesia (22). This has resulted already in the saving of untold amounts of needless pain in childbirth. As skill in this technic becomes so widespread that it is used by practically all those doing obstetrical work, we can look forward to the pain of parturition being reduced to a negligible minimum. Here again there exists a definite frontier. The studies of Hingson and his colleagues, and of many others as well, as vigorous and as extensive as they have been, have not yet explored completely the question of the optimum anesthetic solution for this purpose. There are many local anesthetic agents which might, on theoretical grounds, be tested for caudal injections and which have yet to be studied sufficiently. Pontocaine is a drug which seems, as it becomes more thoroughly evaluated, to have definite prospect of being extremely useful for this particular purpose.

Again the question might be raised whether a very short-acting compound with which continuous drip inflow would be possible might not be the most flexible type of agent to use for the sometimes prolonged and extremely variable course of deliveries. In this caudal anesthesia we need to know much more about the role of vasoconstrictors and what may be their contribution to the achievement of the ideal therapeutic result.

In all varieties of spinal anesthesia the fall of blood pressure that may accompany the block of the sympathetic nerves is an undesired and potentially hazardous phenomenon in at least some patients. Improved means of maintaining the blood pressure level are needed, such as by keeping the sympathetic tonus at a proper level. Since the central pathways are blocked, this will have to be done by a stimulant that acts on the peripheral sympathetic mechanisms. It is, perhaps, not too much to hope that in this development of new anesthetics we might conceivably find a solution which does not affect the sympathetic fibers in the same way as it does the sensory tracts in the cord. Such a differential action might seem to be fantastically improbable, but there have been many such improbabilities which research has eventually transformed to actualities.

RESUSCITATION

If there is success in developing the improved agents suggested previously, the problem of resuscitation will become largely academic. However, in view of the fact that Utopia is not likely to be achieved

in toto overnight, it is worth while to consider the important life-saving procedure of resuscitation. Collapse during an anesthesia, if we exclude convulsions, is the result of impairment of either the respiratory or the circulatory functions. Of these, perhaps the circulatory is the more important, if any distinction may be drawn between two such interdependent functions, because oxygenation can be maintained through artificial respiration or oxygen insufflation, provided the blood is kept moving by the heart.

When respiratory stoppage occurs from overdoses of anesthetic agents, the primary cause is usually a depression of the automatic respiratory centers in the brain. There are a number of analeptic drugs which can be used to increase the irritability of this area and, therefore, perhaps to induce it to send out respiratory impulses again. Carbon dioxide is, of course, one of the normal physiologic stimulants of this center, whether it works directly or indirectly. Also available and well known are such drugs as caffeine, metrazole, picrotoxin, and nikethamide. The difficulty with these stimulants of respiration is that they have to act on a depressed center in order to overcome the impaired function. As a result, the dose required varies with the degree of depression to be antagonized. The dose may actually become so high as to lead to convulsive manifestations during the recovery period. In this case it is possible that the convulsive seizures or increased oxygen use by the muscles are more dangerous to the life of the patient than is the temporary stoppage of respiration, which can be offset by simple artificial respiration until spontaneous breathing occurs. There would seem to be a very definite field for the development of new analeptic drugs which have the power of stimulating the respiratory mechanism without risking at the same time the potentiality of convulsive after-effects. Is it possible that the use of these compounds is actually deleterious, because they increase the oxygen need more than they improve the respiratory volume? Data bearing on this have already been published and the whole subject is one which has to be scrutinized very closely. Therefore, this emphasizes the need for a compound which does not cause increased utilization of oxygen by the tissues. Here indeed is a frontier well worth crossing.

From the point of view of circulation, the situation is somewhat muddled. At times we are too prone to consider the circulation as a static phenomenon instead of a dynamic one. The important thing about the state of the circulation is not the pressure that is being maintained but the volume flow of blood. Hence it is that when there has been blood loss or sudden opening up of vascular areas by shock, the addition of fluid to the blood, in the form of salt solution or transfusions with blood or blood substitutes becomes very valuable.

But filling up the circulatory bed is only one part of the picture. The other requirement is a driving force from the heart to move this fluid volume through the tissues. Epinephrine raises the pressure, but,

because it clamps down the peripheral vessels, does not necessarily increase the mass movement of blood, especially in critical tissue areas.

It would seem that considerable attention should be given to a close relative of epinephrine—ethylnorsuprarenin, which has the same power as epinephrine to augment the force of contraction of the heart, but which, if anything, dilates the arterioles so that the heart is able to pump the blood against a lowered mean peripheral resistance (23). This causes an increased volume of blood flow at the expense of what may be a decreased amount of work and consumption of oxygen by the heart. Here again is a frontier in the field of resuscitation of the circulation worthy of considerable study.

CONCLUSION

These rather random comments on the types of improvements that may be sought in the field of anesthesia have been made in the hope that they will stimulate the medical profession to accept the new developments as they come along, and thereby to hasten their transformation from the fields of speculation to reality. It is also hoped that germs of ideas may have been planted which may eventually stir to life and be fruitful.

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REGULAR MEETING OF THE AMERICAN SOCIETY OF
ANESTHESIOLOGISTS, INC.

NEW YORK ACADEMY OF MEDICINE
2 EAST 103RD STREET, NEW YORK, N. Y.

THURSDAY, APRIL 25, 1946

Business Session: 8:15 P.M.

Scientific Session: 8:30 P.M.

"Stages of Pentothal Anesthesia: Physiological Basis"—40 minutes.
By Benjamin Etsten, M.D., Albany Hospital, Albany, N. Y.

"Anesthesia for Pulmonary Artery Anastomosis"—40 minutes.
By Austin Lamont, M.D., Johns Hopkins Hospital, Baltimore, Md.

General Discussion.