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Implied in a title such as this one is an obligation to determine the present "state of the art," or science, if you will, and to elucidate, in a manner of speaking, where we are, why we are, and in which direction we may be going. To perform such a function in perspective, we must return to the past. Then one wonders, how far into the past? How much of the past is really relevant to today?

Our reflection will go back thirty years to 1942, in Montreal, Canada, to the sphere of McGill University. In those days, Montreal was on a full wartime basis: there was rationing of food and gasoline; soldiers, sailors, and airmen were nudging each other on the streets; the news on the radio was grim except for the occasional sparkle and lift from Winston Churchill; and in the midst of this, four young men, of whom only one is alive today, had been directed by the Canadian Army to pursue a course in anesthesia. The instructors have now become legend. Wesley Bourne was a teacher supreme, whose every sentence and intonation added knowledge to those who would listen, whose every movement at the head of the table was a superb action on a stage. Digby Leigh was the man who breathed life into the pediatric patient when it would appear none was there; he is the man who forged the subspecialty of pediatric anesthesia to make it what it is today. And Harold R. Griffith who is best known to all of us, probably not because of his quiet, lovable, unassuming, Rock-of-Gibralter character, but because in that year, 1942, he demonstrated to the world that curare, or intocostrin, as the preparation was called, could produce reversible relaxation of muscles and so immeasurably aid the performance of anesthesia and surgery.

In passing, it is worth noting that "Uncle" Harold, as he is known, was primarily a clinician. If he had been a habitué of the laboratory, the introduction of curare into practice might have been delayed. Doctor Lewis Wright, the eminent anesthesiologist from New York, had told him that curare had a bad record in dogs, producing marked salivation and significant hypotension. But Dr. Griffith, with his clinical acumen, recognizing that humans are indeed different from dogs, assayed the drug in his patients, his surgeon brother being a cooperative partner, and found it not wanting in desirable attributes.

It is fair to say that 1942 was a major turning point in our philosophy concerning anesthesia care for patients. Today it is rare for a patient to undergo major surgery without the benefit of muscle relaxant drugs. But other factors helped to shape the destiny which makes anesthesia the independent specialty it is at present. Out of the misery and suffering of the Second World War was spawned the anesthesiologist as a specialist; the man or woman who could preserve vital functions both during and after the ordeal of surgery, the individual who could balance, by dint of pharmacologic knowledge, a mixture of drugs, none to a toxic level, which would provide the correct degree of hypnosis, analgesia, muscular relaxation, and obtundation of reflexes for the performance of surgery.

The ubiquitous cautery forced a change in the habits of the anesthetist also. The standard ethyl ether, which had served so well for so long, and the almost angelic properties of cyclopropane were pushed into the background, albeit with some measure of distaste in certain quarters. The value of intravenous narcotic analgesics, to supplement the analgesia of nitrous oxide, became established first in 1953, and then with a vengeance in recent times. But in the interim came the overwhelming tide of

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the halogenated compounds best exemplified by halothane, which to some anesthetists has been all things to all patients, except for a little thiopental and muscle relaxant thrown in from time to time.

This period of growth and development was paralleled by a sharpened interest in what effects anesthetic drugs had on the vital functions of respiration, circulation, and renal and hepatic metabolism. Sophisticated experimentation in laboratories became the order of the day, and much valuable insight has been gained. In the operating rooms, monitoring has become a concomitant of drug administration, and the variables associated with arterial blood determinations and central venous pressures, to say nothing of an infinite variety of ventilators, are lending an aura of science to our pursuits.

And so we come to February 25, 1972. Where do we find ourselves today? If one looks at this program, if one listens to any series of papers discussing anesthesia practice, one finds a querulous note, a feeling approaching dismay, an uncertainness of attitude, a tone of belief that almost encourages disbelief. It appears that we are standing on the brink of change. But what change and in what manner?

As one surveys the scene, it is discouraging to see that a significant mortality still is attached to the process of anesthesia. One out of every 2,000 to 2,500 patients who submits to anesthesia becomes a statistic due in part to what anesthetists do or do not do. However effective the anesthesia administered, it is still not safe to the degree to which air travel, for example, has become. As a matter of fact, the risk of anesthesia today is probably of the same order as it was in 1942. There is pride that more extensive surgical procedures can be accomplished and that the elderly can survive a sojourn in the operating room, but cardiac arrest carts seldom manage to accumulate dust, and the morbidity-mortality conferences are still an active feature of training programs.

Of course, an element of risk will probably exist until the secret of the state called anesthesia becomes unraveled to some extent. Whatever we do now is associated with physiologic trespass, and what is needed is specificity of action that will not be associated with deterrents such as cardiovascular or respiratory depression.

We are losing faith in cherished pharmacologic traditions. Until seven or eight years ago, the stability of the inhalation anesthetics, except for trichloroethylene, was accepted as an inviolate statute. Then it became recognized that biodegradation was a problem with which to reckon, and that such metabolism could be influenced by numerous factors. Some of these were perhaps genetic in origin, some were related to other drugs acting as enzyme inducers, and at times even an anesthetic was acting as its own inducer of metabolism. The full significance of the fact that so-called stable anesthetics can be metabolized has yet to be delineated, but in the meantime the caution flags are being displayed, and our former confidence in these drugs is being shaken.

Not so many years ago, America's leadership in pharmaceutical discoveries was second to none. In 1958, for example, some 60 diagnostic and therapeutic compounds were marketed; by 1969, however, this number had dwindled to five or six. The principal stumbling block in this decline and fall has been the federal Food and Drug Administration. Efforts to satisfy the requirements and demands of this agency relative to a New Drug Application have become so frustrating that few pharmaceutical companies believe realistically that the time and work involved are worth the problems which must be surmounted. Anesthesiology is one of the specialities suffering from this frustration. The situation at the moment is that a number of new drugs are in actual use in many parts of the world but are not available to physicians in the United States. For example, a new muscle-relaxant drug, pancuronium, has supplanted d-tubocurarine in a number of countries, and bupivacaine, a long-acting local anesthetic, has been heralded in Europe; but both drugs are banned from general use in this country at the moment. Inability to participate in clinical trials of therapeutic compounds has dampened the enthusiasm of many anesthesiologists.

Also of deep concern to practicing anesthesiologists is the almost lackluster interest in the specialty by both the public and neophyte physicians even though, and perhaps because, our malpractice premiums are the highest in the medical profession, ranking with those of our surgical colleagues. It is discouraging to see some of our leaders forsaking the field for administrative pursuits. Paradoxically, others are fleeing the operating room to become specialists in intensive care or inhalation therapy. The rationale for this escape is that the graduating medical student is more likely to be attracted to this specialty if the anesthesiologist accepts more responsibility outside the operating room, if he becomes recognized as the authority in acute medicine throughout the hospital. But what about the patient with the "cardiac arrest" back in the operating room?

Because of the foregoing, it is appropriate to say that in 1972 everything in anesthesiology is not wine and roses. Nor is it, of course, in the entire medical profession. The specter of National Health Insurance hangs heavy in the offing, the peer review system is rearing its head, and the recertification threat is ruffling the equilibrium of some. But how can we set our sights in anesthesia so as to rid ourselves of the indecisions, the frustrations, the lack of satisfaction with what we are doing, and move forward to provide safe pain relief for all patients in this country?

As noted, the arsenal of drugs upon which we have come to rely is being reduced in number and breadth of application. And one finds a trend in many centers toward the use of drugs which are administered parenterally. It is perhaps worthwhile to explore this shift to see if indeed safe and efficient anesthesia can be provided by this means.

For purposes of discussion, certain ground rules will be established which will serve to shape the nature of the search. First, let us suppose potent inhalation anesthetics will be discarded. Second, it will be assumed that the anesthetists can adequately assist or control ventilatory exchange. Third, a primary aim will be to maintain cardiovascular dynamics, with preservation of the preexisting blood pressure and, one hopes, perfusion of blood to the organs in the normal preferential manner. Fourth, the central nervous system will be sufficiently obtunded so the patient will have no memory of the anesthetic or surgical procedure, and painful stimuli will not be reflected in abnormal reflex reactions. Fifth, adequate conditions will be provided for the contemplated surgery, with sufficient signs being presented early to indicate the need for blood volume replacement. And last, there will be rapid restoration of central nervous system function at the conclusion of surgery, with the patient oriented to time, place, and person, and showing evidence of normal respiratory and cardiovascular functions. Ideally, analgesia will be extended into the postoperative period.

Actually, there is nothing really novel in these aims. In 1953, in Liverpool, England, Cecil Gray described in detail what has come to be known as the "Liverpool Technique," which incorporates a "sleep" dose of thiopental, approximately 250 mg for a 70 kg adult; a moderate dose of d-tubocurarine (35 to 40 mg) to facilitate endotracheal intubation and provide muscle relaxation; and a 70:30 high-flow mixture of nitrous oxide and oxygen, plus hyperventilation, to provide analgesia and central nervous system obtundation. The hyperventilation is important in this sequence as it contributes to the cerebral obfuscation. Anesthesiologists in America have questioned this technique on several counts. Thiopental is a direct cardiac depressant and is capable, even in small doses, of producing cardiovascular depression, particularly in geriatric patients. Relatively large doses of d-tubocurarine can also produce marked reductions of blood pressure in some patients, particularly when used in association with thiopental. Administration of only 30% oxygen, especially in patients with preexisting pulmonary dysfunction, has been shown to result in critically low arterial oxygen tensions during the course of anesthesia. Hyperventilation, if carried to the point of reducing arterial carbon dioxide tension to less than 25 mm Hg, may result in a degree of cerebral hypoxia. And finally, there are a number of reports in the literature which attest to the fact that with this technique patients can on occasion recall events which transpired during surgery.

Because of questions such as these, anesthesiologists are modifying their approach to the Liverpool Technique. The basic soundness of using nitrous oxide for its amnesic and analgesic properties is not being questioned, and indeed it forms the foundation upon which the anesthetic structure is mounted. (Incidentally, there is no evidence at the moment that nitrous oxide undergoes biodegradation in the body.) However, it is recognized that nitrous oxide is not all things to all patients and that the degree of amnesia and analgesia which it confers varies from one person to another. Moreover, its actions are dose-related, so that if it is believed necessary to provide a patient with 40 or 50% oxygen during surgery, the benefits from nitrous oxide will be reduced accordingly.

One of the more striking applications of an intravenous drug to modern surgery has been the use of the tried-and-true morphine in open heart procedures, certainly a type of surgery which taxes the skill of all concerned. The doses employed are not niggardly (1 to 3 mg per kg), and there is now reasonable evidence that, at least in the normal heart, doses of this order have little effect in depressing cardiac output. However, problems can arise with this approach. Some patients in incipient cardiac failure develop hypotension with only small doses of the drug, and careful titration is necessary. Although the analgesic properties of morphine are obvious, its propensity to produce amnesia is not great, and one wonders at times about recall by the patient. Another difficulty which is seen frequently, particularly in patients having coronary artery bypass procedures, is a worrisome degree of hypertension. There is concern about such increases in blood pressure; something which we have not had to worry about since the days of cyclopropane. One wonders if there is to be an alteration of blood pressure under anesthesia whether it is safer to have an increase rather than a decrease of 30 to 40 mm Hg. The reason for the increase in blood pressure is unknown at present. The two most likely causes are an augmentation in cardiac output and/or peripheral vascular resistance. The underlying etiology could be an increase in catecholamine release, perhaps due to the direct action of the drug or to reflex responses, which would imply an inadequate degree of anesthesia. Whatever the reasons, various ways of reducing the blood pressure have been employed. The administration of a low concentration of halothane (0.5%) is corrective, perhaps because of its sympatholytic effect or because of the added anesthesia it provides. The ganglion-blocking action of trimetaphan (Arfonad®) will often result in a reduction of blood pressure, and the adrenergic-blocking effect produced by chlorpromazine, and to a lesser extent by droperidol, will tend to restore the pressure toward normal levels.

The use of morphine in large doses also poses a problem related to metabolism in that its respiratory depressant effects persist beyond its period of usefulness in the operating room. This prolonged effect may be advantageous in open heart surgery in which it is planned to maintain the patient on artificial ventilation for a period of time, but it does present difficulties in other types of major surgery when one would like to have the patient self-sufficient in the recovery room. Perhaps the properties of the specific narcotic antagonist, naloxone, can be used to advantage under such circumstances.

Another narcotic combination, Innovar®, has met with varying degrees of success in its application to the state of anesthesia. The advantage of its narcotic component, the potent analgesic fentanyl, lies in its relatively rapid rate of metabolism, a given dose being effective for not more than 30 or 40 minutes. Therefore, with attention being paid to its titration, respiratory depressant effects need not be a problem in the postoperative period. The other component of Innovar, the butyrophenone droperidol, has brought an exciting new dimension to what we are trying to accomplish in anesthesia. Probably acting at the level of the reticular activating system, this drug serves to disconnect the patient from the fear and concerns associated with his immediate environment. However, the degree of associated amnesia is variable from one patient to another, and one cannot count on a given dose of droperidol blotting out remembrance of a procedure. Although it has mild adrenergic-blocking properties, there is no evidence that it is a direct depressant to the myocardium and, if the patient remains supine and does not have a reduced circulating blood volume, vascular homeostasis is preserved with its administration. It also possesses anti-arrhythmic properties which help to stabilize cardiac rhythm during surgery. Unlike fentanyl, droperidol is metabolized slowly in the body, its effects lasting six to eight hours, so that its actions are apparent in the recovery room. These effects are deemed advantageous by some: it is not a respiratory depressant, nor is it an analgesic, but it does appear to alter the patient's reaction to pain so that he does not demand narcotic analgesics.

So far, the drugs discussed have not demonstrated evidence of potent amnesia, or ability to prevent recall—the best has probably been nitrous oxide. But a relative newcomer on the scene, diazepam, shows evidence of providing the desired potency. Administered intravenously, the dose of diazepam required to produce a lack of subjective response by the patient is highly variable, ranging from 5 to 30 mg or more, but amnesia for associated events is usually present after a dose of 10 mg. Best described as an amnestic and hypnotic, in that order, diazepam can produce respiratory depression but has little effect on cardiovascular hemodynamics in the doses required for hypnosis. It can be used safely and with merit in association with narcotics and muscle relaxants.

One compound which has had a mixed reception since its introduction in 1970 is ketamine. Enthusiasts have embraced it because it produces unconsciousness and intense analgesia without associated depression of respiration, except momentarily in some patients, or circulation. As a matter of fact, cardiovascular dynamics appear to be enhanced, as reflected in a moderate increase in pulse rate and blood pressure. Interestingly enough, this cardiac stimulation is not associated with an increase in myocardial irritability; in fact, the drug possesses anti-arrhythmic properties. Equally important is the safety of the compound: more than five times the recommended clinical dose can be given intravenously without untoward effects in a healthy patient. Detractors point to the relatively high incidence of hallucinatory phenomena in adults as they are recovering from the effects of the drug when it has been used as the principal anesthetic. They also emphasize the random movements and increase in muscle tone seen in many patients.

The mechanisms of the action of ketamine have not been well defined, nor is its sphere of usefulness in the field of anesthesia clear at the moment. Does the lack of respiratory and cardiovascular depression in the presence of apparent unconsciousness and intense analgesia imply that this classification of chemical compound allows one to narrow down the actions which one wishes to provide for the anesthetic state? Does the wide margin of safety in dosage imply an inborn compensation for errors of administration? One could validly criticize the upsurge in cardiovascular dynamics associated with administration, as one does with the narcotic drugs. But is such a change as deleterious as the cardiovascular depression so often noted with conventional anesthesia?

If the reasons for the increase in vascular dynamics were known, one might be able to compensate for it directly. Such an increase could result from direct stimulation of the vasomotor center; it could be secondary to an increase in catecholamine secretion; or as Dowdy has suggested, it could be due to an alteration in the baroreceptor mechanism. Whatever the cause, small doses of droperidol (2.5 to 5 mg I.V.) tend to return the blood pressure toward normal levels.

With the intravenous drugs which are at present being used to supplement the Liverpool Technique, it is apparent that full reliance must be placed on muscle relaxant compounds to provide satisfactory operating conditions for the surgeon. What Griffith began in 1942 will probably continue in full force, no doubt with substitutions for d-tubocurarine from time to time.

One would like to elaborate on one modification of the nitrous oxide, curare technique which is being presently evaluated. It pertains to the substitution of ketamine for thiopental. Following conventional narcotic or Innovar premedication, induction of anesthesia is with ketamine 2 mg per kg intravenously, followed by d-tubocurarine approximately 0.5 mg per kg, endoctracheal intubation in about three minutes with topical analgesia to the larynx and trachea with lidocaine 4.0% solution, and then maintenance with nitrous oxide and oxygen in a 60:40 mixture. Increments of ketamine 20 to 30 mg are given just before the skin incision and at intervals thereafter. Total dose of ketamine for a three-hour procedure is about 300 mg. Controlled respiration with moderate hyperventilation is maintained, and increments of d-tubocurarine 6 to 9 mg are administered as required to maintain muscle relaxation. Neostigmine reversal is carried out at the end of surgery, and the patient is usually oriented and answering questions before leaving the operating room. In 50 such experiences, there have been no instances of hypotension. In a few patients, increase of systolic pressures of the order of 30 to 40 mm Hg has been controlled by small doses of droperidol (2.5 to 5.0 mg I.V.). In no patient has there been unusual reaction following surgery, and in none has recall of the surgical procedure been elicited.

It is apparent that there are a number of ways in which one can approach fulfillment of the criteria posed. None is perfect, and probably none will be until the secret of anesthesia is unmasked. In the interim, each of us can and must work toward the goal of effective and safe anesthesia.

If indeed we turn our backs on the potent inhalation anesthetics, or use them perhaps only as a second line of defense, we will no longer have need for the cumbersome anesthetic apparatus in use at present. Our gas machines are imposing and perhaps awesome to the non-anesthetists in the operating room, maybe even lending an aura of mystery to our operations at the head of the table. But such displays of one-upmanship are really no longer necessary in our profession. So one would propose scrapping the conventional flowmeters and de-emphasizing the anesthetic machine as a central focus and substituting primarily a ventilating apparatus. Such a ventilator would be volume controlled, pressure variable, simple and foolproof in construction, and capable of being sterilized with ease. It would also be capable of providing positive to atmospheric, positive to negative, or positive to positive pressures, with such pressures immediately identifiable on a rugged but accurate pressure gauge. The rate of respiration per minute would be under the control of the anesthetist, as would the tidal volume to be delivered, this tidal volume being constantly displayed on a ventilation meter. The length of the inspiratory and expiratory phases of ventilation would also be subject to variation by the anesthetist, although the standard to be employed would be the 1:2 ratio proven to be so satisfactory by Cournand a number of years ago. Of vital importance would be a means of manually ventilating the patient at a moment's notice, and of being able to alternate in a simple manner between mechanical and manual ventilation.

The gases to be supplied to the ventilator would be nitrous oxide and oxygen, utilizing one meter to determine the total flow rate per minute and a mixing valve by means of which one could vary the percentage of each gas being supplied to the patient. This mixing valve would be unable to provide less than 25% oxygen and would of course have a fail-safe mechanism incorporated into it. In the gas supply line distal to the mixing valve would be an oxygen analyzer which would constantly record the percentage of oxygen in the mixture being delivered to the patient.

It is unlikely that a carbon dioxide absorber would be necessary in this ventilator-oriented apparatus—particularly with our present knowledge regarding controlled ventilation in the anesthetized patient—if the flow rate of the mixture supplied to the patient were not less than six liters per minute. However, an important monitor in this apparatus would be a carbon dioxide analyzer which would intermittently, or on demand, record on a scale both the inspired and expired concentrations of carbon dioxide.

Such would be the basic components of a new anesthetic apparatus. It would be mechanically simple and incorporate a number of monitors vital to the welfare of the patient which are not an integral part of present-day equipment. Of course, for those who wished to rely in part on the potent inhalation anesthetics, calibrated vaporizers could be placed in series on the patient side of the mixing valve.

One would hope that more specific means of monitoring the integrity of the cardiovascular system in a non-invasive manner will become available in the operating room. Today we rely primarily on the blood pressure and the electrocardiogram. The blood pressure is the result of the interaction between the cardiac output, the peripheral vascular resistance, and the circulating blood volume, and therefore, changes which occur cannot be specifically diagnosed. The electrocardiogram merely reflects the electrical activity within the conduction system of the heart; it reveals little concerning myocardial function or cardiac output per se. The closest one can come to determining the adequacy of perfusion of blood to organs is to observe the urinary output. An adequate flow of urine during surgery reflects continuing renal function and presumably reasonable perfusion of that organ.

In proper care of the patient, increasing reliance is being placed on determinations of arterial pH and blood gas values, and rightly so. But obtaining comparative information over a period of hours or days requires an arterial puncture and usually an indwelling catheter, and because of this degree of invasive sophistication, many patients are being denied therapeutic measures which they might otherwise receive. A non-invasive technique of determining these values is sorely needed and capable of being perfected.

There is one other aspect of anesthetic practice in this country today which demands attention in the effort to enhance the safety and efficiency of our services. We have the unique situation of two groups of professionals, anesthesiologists, some 10,000 in number, and nurse anesthetists, some 14,000 in number, being responsible for anesthetic care. Unfortunately, until recently, for reasons which one hopes are now past history, there was little liaison or rapport between these two groups, even though their daily objective was the same—to provide the best anesthetic care possible for the patient. It is high time we began to communicate meaningfully with each other, recognizing the concept that by working together, by sharing mutual problems, better care will be provided for the patient.

Beginnings have been made in these directions. There is a Liaison Committee of the American Society of Anesthesiologists and the American Association of Nurse Anesthetists which meets regularly in a growing spirit of mutual exchange. Both societies have recognized a joint statement of over all aims and objectives. Meetings such as this one attest to the fact that not only are nurse anesthetists sharing as participants in scientific programs, but they are also attending in greater numbers such programs throughout the country.

But there is more to be done. We need to work together as individuals, as small groups within a hospital, as larger groups within a city or state, and on a national level. Each of these groups has become a national entity in the realm of medicine and will remain so. The proper administration of anesthesia could not survive in this country without the full activities of both groups, and patients who require surgery are dependent on the knowledge and practice of both the nurse anesthetist and the anesthesiologist. It is my sincere belief that by talking together, working together, acquiring knowledge together, the practice of anesthesia in this country will become safer and more efficient.

There is one concrete way in which these mutual efforts could be enhanced. To increase our knowledge and abilities in this day and age, reliance is placed primarily on reading books and journals, and on attending meetings, workshops, and seminars. The latter efforts usually involve leaving one's place of practice and traveling some distance. What one would propose is that the teacher travel to one's place of work, spend a few days in the operating rooms at the head of the table, showing and telling, to put it in the vernacular, and discussing actual or potential problems which could arise. There is a precedent for this type of endeavor in at least one state of the Union in the speciality of obstetrics. It would be worthy of a trial in anesthesiology. One recognizes, of course, the numerous logistical and economic problems surrounding such a suggestion, but a national society or a national foundation could lend its support less wisely in other endeavors.

And so we end the survey of *Anesthesia, 1972*. If it has failed to be glowing and full of sparkle, it is not for lack of confidence that this, the youngest of the true specialties, has inherent within it the greatest challenge for the future. Today we are standing on the threshold of significant discoveries and developments. Everyone in this room will have an opportunity to participate in the exciting advances that are all about us. But while we work and extend our knowledge, may we keep in the foreground the hope and prayer that Sir Robert Hutchison left for us: "From inability to let well alone; from too much zeal for the new and contempt for what is old; from putting knowledge before wisdom, science before art, and cleverness before common sense; from treating patients as cases, and from making the cure of the disease more grievous than the endurance of the same—good Lord, deliver us."