

## TEN YEARS OF PENTOTHAL SODIUM INTRAVENOUS ANESTHESIA; AN EVALUATION OF ITS PAST, PRESENT AND FUTURE \*

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THE story of intravenous anesthesia has been fascinating throughout its years of development. The inherent drama associated with its administration and effects has, from its inception, had an appeal to the anesthetist, the patient and to the surgeon. However, this dramatic side of intravenous anesthesia may have been overstressed and in some instances it certainly has worked to the detriment of the method. Dramatic results almost invariably lead to misconceptions, premature conclusions and dangers. The evolution of intravenous anesthesia reflects the trials and tribulations, the build-ups and let-downs and the enthusiasm and controversy that have beset the evolution of the science and art of anesthesiology.

The history of intravenous anesthesia is now well known, as are the principles of the various methods. However, we sometimes wonder if the lessons learned and set down by our predecessors have been fully taken to heart, for not infrequently we are making the same blunders they warned us against. These mishaps may be partly ascribed to the misuse and misinterpretation of such catch phrases as "ideal anesthetic," "simple administration," "no experience necessary," "no contraindications" and a multitude of others that have done the method harm rather than good and that often have planted false concepts in the minds of physicians since intravenous anesthesia first was known.

We do not propose to rehash the multitude of historical, chemical and pharmacologic data concerning the numerous anesthetic agents that can be administered intravenously, or their relative merits and demerits. These are well known and have been written about and talked about exhaustively. Rather, we propose to consider and reflect on certain fundamental principles of the method which have stood the test of time and which, in our opinion, are essential to its safe and satisfactory clinical use. It goes without saying that one who has had extensive experience with an agent or method may at times digress from standard criteria and use a method which in some hands would be hazardous. However, when a method is being used thousands of times a day (as intravenous anesthesia is being used today) by physicians, dentists, nurse anesthetists and the varied personnel of the

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medical corps of the armed forces, we who teach and write about intravenous anesthesia must lay down rules for the average anesthetist rather than for the skilled specialist. For example, the casual anesthetist is seldom bold enough to take over a gas machine with which he is unfamiliar and administer a potent gas such as cyclopropane, the effects of which he knows but vaguely, but he has little or no hesitation in picking up a syringe and injecting an anesthetic agent into a vein for anything and everything, although his knowledge of intravenous anesthesia may compare with his knowledge of the gas machine. There is little doubt that the use of pentothal sodium is the greatest advance that has been made in anesthesiology in the last decade. In the light of this statement, the foregoing remarks could be construed as contradictory and paradoxical, but if one will stop to consider thoughtfully that in the past five years intravenous anesthesia has displaced inhalation, spinal, local and regional and rectal methods by approximately 25 to 50 per cent in civilian practice and often in excess of this in military practice in World War II, the question of the future of intravenous anesthesia is one that cannot be lightly passed over.

#### THE PAST

Since pentothal sodium was introduced in 1934, it has been obvious that it has much to offer over other agents used for intravenous anesthesia. Evipal soluble, which is the only other drug that approaches pentothal sodium in efficacy, is an excellent substitute but, in the light of our present knowledge, modern intravenous anesthesia has become synonymous with pentothal sodium.

The principle of injecting an anesthetic agent into the venous system always has been rational, provided the agent has had the necessary desirable characteristics. The gases and the volatile anesthetic agents, together with agents administered by rectum, all must find their way to the blood stream for distribution to the central nervous system. With inhalation anesthesia, many things may prevent the agent from reaching the blood stream or from being absorbed by it; with rectal anesthesia, similar possibilities exist. It, therefore, is logical that a method whereby the anesthetic agent is deposited directly into the blood stream obviates certain drawbacks inherent in the other methods. If we stop at this point and carry the comparison no farther we lay ourselves open for trouble right at the start. Intravenous anesthesia is but another form of general anesthesia and, as such, it is subject to most of the difficulties and drawbacks associated with general anesthesia. What is more important, however, is a realization of the fact that to combat these drawbacks it may be necessary to have available most of the equipment considered necessary for the administration of an inhalation anesthetic. Failure to give these factors due consideration has accounted for a fair proportion of the morbidity and mortality associated with intravenous anesthesia.

Perhaps the most important single factor that became apparent early in the development of pentothal sodium anesthesia was the widely divergent tolerance of patients for the drug. This was found to have many ramifications. Not only do the dose and effect vary for normal, healthy individuals but they also may vary widely in the same case in both health and disease. These facts must be appreciated to administer pentothal sodium safely, because on them are based the various criteria for dosage, method of administration, contraindications, use of supplementary methods and so forth. The lives of many patients have been endangered or lost because the intravenous anesthesia has been managed as if the patients were average risks. This has been brought home to us in the past in connection with shock and intravenous anesthesia, particularly in military casualties. We know now that pentothal sodium *per se* is not any more hazardous than any other anesthetic in cases in which the patients are in shock. It is, however, dangerous when administered according to ordinary standards and in so-called average doses.

The type of operation suitable for intravenous anesthesia has been a most controversial subject. Most anesthetists have felt and continued to feel that pentothal sodium leaves much to be desired in producing satisfactory muscular relaxation—particularly of the abdominal wall and throat and glottic region. In certain other types of operations the use of intravenous anesthesia has not been as controllable as one could wish, as, for example, in operations on the upper part of the respiratory tract, owing to the problem of the airway. When used for many of the aforementioned types of operations the desirable features of pentothal anesthesia are neutralized by the potential hazards involved.

Consequently, as the use of intravenous anesthesia expanded, anesthetists began to devise ways and means whereby pentothal sodium might be used for major and specialized operations and to minimize the complications that might occur when pentothal sodium was used as the sole anesthetic. The accessory methods varied but in the main consisted in either supplementing or complementing pentothal anesthesia with some other agent or method or combination of agents and methods. This began with the simultaneous use of oxygen by inhalation during the intravenous anesthesia, followed by the use of oxygen and nitrous oxide. Perhaps the most important combinations were those with local, regional and block anesthesia with or without oxygen or oxygen and nitrous oxide. The use of intravenous anesthesia with spinal anesthesia has many possibilities. The value of topical anesthesia prior to and during intravenous anesthesia has increased with the years for intraoral and laryngeal operations.

The maintenance of a clear airway was one of the earliest problems under pentothal anesthesia, particularly during operations about the head, neck, face and for intranasal or oral or laryngeal operations.

The increasing use of an intratracheal tube, preceded by cocainization of the glottis, has largely solved this problem. Sometimes a nasopharyngeal tube may be used as a substitute. All these improvements have done much to increase the useful scope of pentothal sodium anesthesia and have permitted anesthetists to take advantage of its many excellent qualities for a variety of operations for which they formerly would have considered it to be contraindicated.

These gradual changes and improvements throughout the first decade of pentothal sodium anesthesia have made it necessary for us to alter our opinions and concepts of the method from time to time. As far as the use of pentothal sodium as the sole anesthetic is concerned, our attitude is the same as when we first started to use it. During the past ten years, the valuable chemical and pharmacologic investigation carried out by many investigators on pentothal sodium has clarified many of the details of its action. Many problems still remain, perhaps the most important of which is the site of its detoxication and the factors which govern the speed of its detoxication.

#### THE PRESENT

Few anesthetic agents during the first ten years of their development have reached the widespread and extensive use that pentothal sodium enjoys today. This acceptance has been deserved, for, while pentothal sodium lacks many of the qualities of the ideal anesthetic, it still possesses many of them. World War II has provided a great impetus to the use of pentothal anesthesia and this agent has played a most important part in medicomilitary anesthesia. Further comments on its use in military practice will be made later in this article. Since pentothal sodium has become widely known by both laymen and physicians and since it is now being administered by all types of medical personnel from anesthesiologists to general practitioners, it is important that its administration should be taught on a sane, common sense basis.

Many persons, both physicians and nurses, are administering pentothal sodium today, with or without supervision, who perhaps have had inadequate training in its use and who, in less unusual times, would not have been administering it at all. Whether anesthetists feel this to be right or wrong is beside the point. The fact remains that the already widespread use of pentothal anesthesia will progressively increase in the next few years, and it seems likely that more and more inexperienced individuals will be administering it. Over this state of affairs anesthesiologists have little or no control for it will be used anyway. Since this appears to be the case, the only alternative is to teach its correct administration and its dangers and limitations. One must teach its use in the average case in which it is most suitable, leaving its finer and more specialized application to the experienced anesthetist.

It may be well to look briefly at a few of the present-day concepts of pentothal anesthesia. In most places the use of a 2.5 per cent solution has become routine. Although more dilute solutions, administered as an infusion, are being used in some places, this method does not appear to have any advantages over the injection technic and the possibility of errors during the administration seems to be somewhat greater. Equipment for administration is varied and depends on the ideas of the anesthetist and what suits his particular needs. In our hands, the apparatus which offers the greatest simplicity for both administration of the anesthetic and maintenance of parts is a type of extension tubing which permits single-handed administration. This can be hooked up rapidly and there are few parts to sterilize and maintain.

The use of the combined type of intravenous anesthesia has increased steadily from year to year. It has not only increased the surgical field of the method but it has widened the margin of safety. Such combinations have been largely instrumental in cutting down the large doses that often have had to be used and, as a result, the desirable features of pentothal sodium may be enjoyed while the undesirable ones, respiratory depression, difficulties with the airway, large doses, poor relaxation and prolonged postoperative sleep and so forth, are either prevented or minimized. One must never forget that the desirable attributes of a so-called ultra-short-acting barbiturate such as pentothal sodium remain desirable just as long as the total dose of the drug remains within minimal limits. As the doses increase in size, the action and effects of the agent come to resemble more and more closely those of the medium-acting and long-acting barbiturates.

Some of the benefits to be derived by the aforementioned combinations may be exemplified by their use in the following types of operations. Certain operations about the oropharynx and nasopharynx have in the past been considered to be contraindications to the use of intravenous anesthesia owing to the difficulty of maintaining a clear airway, the danger of aspirating blood, mucus, vomitus or pus into the tracheobronchial tree, and the hyperactivity of the pharyngolaryngeal reflexes. The use of an endotracheal tube with the simultaneous administration of oxygen and nitrous oxide has largely taken care of these difficulties and has rendered otherwise hazardous procedures much safer. In addition, this combination of agents and methods is free from the danger of fire and explosion. The cautery is used frequently in cases in which they are employed. A similar example is the use of intravenous anesthesia for laryngoscopic examination and for suspension laryngoscopy. The intravenous anesthesia is preceded by topical application of cocaine to the glottic area; during the operation, nitrous oxide and oxygen is administered by a nasopharyngeal tube. Here again, noninflammable agents only are employed.

Other combinations of pentothal and local or regional anesthesia

are too numerous to mention but at present they are helping to shape the course of the intravenous anesthesia of the future. One gratifying feature of the pharmacologic action of pentothal sodium which becomes more apparent as time goes on is its comparatively low toxicity and freedom from remote untoward effects, provided its administration is correct and the total dose within reasonable limits. This applies not only to healthy organs but in many instances it applies where disease exists. It is difficult to lay down hard and fast contraindications, although we recognize that many exist. These have been mentioned in previous publications. A few of these are absolute but most of them are relative. The choice is more often made from the anesthetist's experience with general anesthesia and its problems rather than on the basis of a few rules that supposedly apply only to intravenous anesthesia.

The impetus that pentothal sodium anesthesia has gained as a result of its use in the present World War cannot be overlooked and there is little doubt that this will play a predominant role in shaping the course and attitude toward the use of intravenous anesthesia in future years. Intravenous anesthesia is adapted to the ever-changing conditions of military anesthesia and its widespread use in the medical services of our armed forces bespeaks its value. It has been one of the outstanding advances in modern military surgery. In spite of the glowing words of praise it has received from military anesthetists these men who have used it over the far-flung battle fronts will be the first to corroborate the statement that it is no more the ideal anesthetic in military practice than it is in civilian practice. The only differences in its use in the two types of practice are that military surgery presents more problems to weigh and possibly more contraindications and precautions to observe.

The trained anesthetist personnel of our armed services has done a most excellent job of carrying out the correct application of pentothal anesthesia. Unfortunately, experienced anesthetists have not always been available. During the course of the war, it has often been reported that the morbidity and mortality under intravenous anesthesia has been excessive and greater than with other forms of anesthesia. We probably will not be in a position to evaluate fully this statement until later. Anesthetists who have returned from tours of duty on the various battle fronts have told us that there are reasons for this in certain sectors. The first is the result of faulty administration by inexperienced personnel or the choice of the method in cases in which it is not the method of choice. The second reason, we have been told, may probably be the result of its very extensive use for casualties who are poor risks for any type of anesthesia. Naturally, the mortality figures will be greatly increased under these conditions. However, medical officers returning from the various theaters of operations still vary in their opinions concerning these things but in the main they leave little

doubt in one's mind as to the general usefulness of intravenous anesthesia in World War II.

### THE FUTURE

There is no doubt that intravenous anesthesia, as it is known today, will continue to play a major role in anesthesiology. Without the advent of the war it would have taken longer for it to attain its present degree of widespread use. Anesthetists who have had extensive experience with pentothal anesthesia for the multitude of problems that war casualties present will be able to teach many things that physicians in civilian practice may have overlooked. The experienced anesthetists of our armed forces have done a great deal to promote the rational use of intravenous anesthesia. While they have realized the many advantages of the method, most of them have been well aware of its limitations and dangers. This attitude, carried back into civilian practice, will be invaluable in promoting its rational use during future years.

Radical future changes and developments of the method will, no doubt, be dependent on the evolution of new and probably different agents. As far as we know there are no such agents in the offing at this time. To be superior to pentothal sodium, a new drug would have to have all the good points of pentothal sodium; in addition, it must produce good muscular relaxation without depressant effects, it should be rapidly detoxicated and eliminated, and should have at least as few toxic side effects as pentothal sodium.

It is likely that the coming years will see pentothal sodium used in combination with more agents than it has been in the past. One of the most recent combinations is the use of curare with pentothal sodium to provide the relaxation that the latter often fails to produce. It would appear that the judicious use of these drugs produces very satisfactory anesthesia without untoward side effects. There are many operations in which this combination is producing good results and it appears to have greater possibilities in the future.

It does not seem reasonable that any type of intravenous anesthesia of the future will be divorced from most of the problems of general anesthesia. As long as a patient is rendered unconscious and relaxed by an anesthetic agent, no matter by what route it is administered, one must face the problems of airway, oxygen and carbon dioxide exchange, hypoxia, anoxia and so forth. These facts, if kept in mind in the future use of pentothal sodium or any other intravenous anesthetic agent that may be evolved, will go a long way toward preventing some of the untoward effects and criticisms that have been associated with intravenous anesthesia in the past.