

THE USE OF PENTOTHAL SODIUM *—PENTOBARBITAL SODIUM COMBINATION † IN PROLONGED SURGICAL PROCEDURES ‡

HUGH FARQUHARSON, M.D., AND FRANK J. MURPHY, M.D.

San Francisco, California

Received for publication November 2, 1949

THE maintenance of smooth anesthesia of a nonexplosive nature, for prolonged surgical procedures in which electrocautery is used, raises the problem of how best to attain this. Of necessity, the choice of agents has been restricted to agents no one of which is 100 per cent potent, with the exception of chloroform. Pentothal with nitrous oxide and oxygen, with minimal oxygen concentration of 20 per cent has proved to be a nontoxic combination. Many technics have been devised to lessen the total quantity of pentothal used and the concentration of nitrous oxide required. Heavy premedication allows an increase of the oxygen concentration in the inhaled mixture. Demerol or morphine, in small divided doses intravenously, has proved satisfactory to aid in the maintenance of smooth anesthesia and lowered pentothal dosage. Pentothal in dilute solution administered by a continuous intravenous drip may be used. More recently procaine, 1 per cent in a continuous drip, with or without pentothal, has been advocated (1, 2). Cullen (3) has reported on the use of pentobarbital sodium with curare for endotracheal intubation in major thoracic and abdominal operations.

The introduction of curare § (4) in clinical anesthesia enables the anesthetist to produce relaxation in a light plane of surgical anesthesia, such as is provided by pentothal, nitrous oxide and oxygen (5). The addition of curare to this combination, particularly when given in apneic doses, makes the determination of the depth of anesthesia very difficult. Indeed, it has been reported (5) that a patient may actually be aware of a surgical procedure being performed on himself, but be unable to protest owing to the paralysis induced by the curare. The use of curare has not actually lessened the need for adequate anesthetization (7). It has made it more difficult to gauge (6).

It was with this problem of smooth maintenance of prolonged anesthesia in mind, that pentobarbital sodium in combination with pento-

* Pentothal sodium (Abbott).

† Nembutal sodium (Abbott).

‡ From the Department of Anesthesiology, University of California Hospital, San Francisco, California.

§ d-Tubocurarine chloride solution.

thal sodium was first employed. Pentobarbital sodium (sodium ethyl (1-methylbutyl) barbiturate is a barbiturate of medium duration of action and is available in ampules of 5 cc. containing 0.25 Gm. For convenience, this then was taken as the total dose of pentobarbital sodium to be used. It is added to a syringe containing 20 cc. of 2.5 per cent pentothal sodium (0.5 Gm.), giving a total volume of 25 cc. Other proportions have not been used. The solution retains the quick action of pentothal sodium but possesses the longer action of pentobarbital sodium.

This paper serves as a report of the use of this combination in 458 cases. It has been used in patients ranging in age from 18 months to 78 years. Its use has been restricted to cases in which the operating time is expected to exceed two hours. In operations of less than two hours it has been found that patients are still well sedated at the conclusion of the procedure. However, even they will regain their pharyngeal and laryngeal reflexes within fifteen to twenty minutes after the cessation of nitrous oxide and oxygen, but they will sleep if undisturbed for three to four hours followed by a further period of two to three hours in a semi-awake state. When the mixture has been used for induction, with or without intubation, additional pentobarbital sodium is not, as a rule, administered. The total dose is restricted with few exceptions to 0.25 Gm. of pentobarbital sodium.

PREMEDICATION

No attempt has been made to establish a routine with regard to premedication when this combined solution is to be used. The one important consideration is that patients are lightly sedated. The average patient receives only morphine, 0.01 Gm. and scopolamine, 0.0004 Gm., about thirty minutes before coming to surgery. When the operation is not scheduled to begin until late in the morning or early afternoon, pentobarbital, 0.1 Gm., may be given orally at 7 or 8 A.M. This provides a period of rest for the patient during the morning while awaiting operation.

Of interest is the observation that, in this hospital prior to the use of pentothal sodium-pentobarbital sodium for induction, the premedication as a rule was heavier. Then the average patient received pentobarbital sodium, 0.1 to 0.2 Gm., orally and morphine sulfate, 0.015 and scopolamine 0.0006 Gm.

In general, the use of this combination has fallen into two main categories:

1. For induction and maintenance.
 - (a) Without intubation—100 cases.
 - (b) Including intubation—289 cases.
 - (c) Including intubation with added curare—44 cases.

2. For aid in maintenance only.
 - (a) General anesthesia—19 cases.
 - (b) Continuous spinal anesthesia—6 cases.

The 100 cases in which pentothal sodium-pentobarbital sodium mixture was used for induction and maintenance, without intubation, were for the most part extraperitoneal procedures such as long orthopedic operations, radical mastectomies and vaginal plastic procedures. The technic has been to administer the mixture in 2 to 3 cc. doses until the patient is asleep, then nitrous oxide, 4 liters, and oxygen, 1.5 liters, is started by face mask. The injection of the mixture is continued until the patient exhibits loss of the corneal reflex and relaxation of the jaw, which usually occurs after 15 to 25 cc. has been given. In short, the total induction dose may reach 500 mg. of pentothal and 250 mg. of pentobarbital sodium. It never exceeds this. As a result of the light premedication, it is frequently found necessary during the first thirty to forty-five minutes of operation to add 2 to 3 cc. of pentothal, 2.5 per cent, and demerol, 25 mg., intravenously. Thereafter, added doses of pentothal, 2.5 per cent, are given as required. However, they have been needed rarely, apparently because almost basal narcosis is supplied by the pentobarbital sodium used in the induction. When the operative time exceeds two or three hours, the patient awakes readily after the nitrous oxide is removed. Pharyngeal and laryngeal reflexes are rapidly regained. During the immediate postoperative period, the patient rests comfortably and quietly in the absence of disturbing extraneous stimuli.

Particular mention should be given to the use of this combination in anesthesia for pneumoencephalograms. The immediate postoperative period is characterized by severe headaches. Avertin has been used and recommended because of its prolonged action. Disadvantages to avertin are many and well known. Pentothal sodium alone permits easier administration and maintenance associated with controllability, but awakening occurs rapidly, requiring further sedation and narcotics for control of the headache. The addition of pentobarbital sodium in the same manner as described gives a prolonged sedative effect, carrying the patient past the peak of the reaction to the pneumoencephalography. The entire diagnostic procedure requires approximately one hour including the roentgenologic examination. To date this has been used in seven pneumoencephalograms. Total dosage of pentothal sodium is about 1 Gm. and pentobarbital sodium, 0.25 Gm.

Early in our experience with pentothal-pentobarbital sodium, it was found that after 18 to 20 cc. of the 2.5 cc. solution was administered, relaxation of the jaw was adequate for intubation. To aid in the control of pharyngeal reflexes, which are not always completely obtunded by this dose, a 2 per cent pontocaine spray is used. Only the region down to and including the epiglottis is sprayed prior to induction and

intubation; no attempt is made to spray the larynx. The pentothal-pentobarbital sodium mixture is then injected intravenously in doses of 2 to 3 cc. every thirty to forty-five seconds until general relaxation is thought to be adequate for laryngoscopy and intubation. The passage of the tube into the trachea is usually marked temporarily by some coughing and transient laryngospasm which responds readily to the injection of an additional 5 cc. of solution. Prolonged spasm and breath-holding do not follow administration of pentothal-pentobarbital sodium solution.

Although the laryngeal and tracheal reflexes are not depressed, the severe spasm that may be encountered with pentothal alone has not as yet been seen with this combination. Indeed, the cough reflex remains active and has proved very useful in facilitating blind nasal intubation. These may be performed after injection of 6 to 10 cc. of the solution. The technic employed is to give just sufficient anesthetic agent to allow passage of the tube through the nose into the pharynx. From there it is a relatively easy procedure to pass the tube into the trachea when the patient coughs, as a result of the irritation produced by the endotracheal tube.

In this series, anesthesia has been induced and intubations, either orally or nasally, have been performed in 289 cases with the pentothal-pentobarbital sodium mixture, preceded by partial topical in 265 cases. In an additional 37 cases, a small dose of curare has been given. The curare in 60 to 80 unit dosages has been injected after administration of the initial 5 cc. of pentothal-pentobarbital sodium. Curare was added for the obvious reason of increasing relaxation of the jaw and laryngeal muscles. In the occasional robust individual or in the presence of prominent upper front teeth or gold inlays, this has been thought to be necessary since, in most cases, the intubations were being performed by residents in training in anesthesia. Oxygen by face mask is administered almost routinely during the induction prior to intubation.

Pentothal-pentobarbital sodium mixture is indicated in certain selected cases for aid in maintenance only. For sedation during continuous spinal anesthesia, as used in 6 cases, this combination has been particularly useful. Given a supplementary dose of 2 to 3 cc., the interval between injections has ranged from fifteen to forty-five minutes whereas using pentothal alone the interval would have ranged from five to fifteen minutes.

Maintenance of anesthesia in prolonged neurosurgical operations upon infants and children has been similarly facilitated. Anesthesia has been induced with ether and then nitrous oxide, 6 liters, and oxygen, 2 liters, were administered in a nonbreathing system using a Leigh valve for maintenance. In such cases the duration between the 1 to 3 cc. supplementary doses may extend up to sixty or ninety minutes. A similar use has been found in intrathoracic surgery in chil-

dren. In these cases a nonexplosive technic is used with nitrous oxide-oxygen, with curare in apneic doses, and controlled respiration maintained throughout the duration of the intrathoracic surgery. Judicious use of the pentothal-pentobarbital sodium mixture in 0.5 to 1 cc. doses repeated at thirty to sixty minute intervals aids in the maintenance of smooth anesthesia. In cases such as exploratory laparotomy or thoracotomy, in which the duration of surgical procedure is initially in doubt, shorter acting agents such as pentothal-curare or cyclopropane are preferred for induction and intubation. If it should then become necessary for the duration of anesthesia to exceed two hours, pentothal-pentobarbital sodium may be used to aid in maintenance.

In major abdominal operations, curare is used for relaxation as in other forms of combined anesthesia. Here too, the pentobarbital sodium, used in the induction already described, provides a more even maintenance of anesthesia. For the most part, adequate respiratory exchange is maintained, but failing this, aided or controlled respiration is used as indicated.

Contraindications to this type of combined anesthesia are few. Because pentobarbital sodium is broken down in the liver, it is not used in the presence of known hepatic damage or functional impairment. Prolongation of the period of narcosis would undoubtedly result if it were used.

Patients exhibiting arterial hypertension are not excluded. Slow administration of the pentothal-pentobarbital sodium accompanied by oxygen administration by face mask during induction does not result in undue depression of the blood pressure.

CONCLUSION

This study of 458 cases, in which the combination of pentothal sodium and pentobarbital sodium has been used, has included all manner of surgical procedures and risks. The growing popularity of slow, careful surgical technic has necessitated the development of anesthetic technics designed not only to make the anesthesia safer for the patient, but also to facilitate the work of the surgeon, and last but by no means least, to facilitate the work of the anesthetist. When using such agents as ether or cyclopropane, there are well known classical signs which are continuous guides to the depth of anesthesia. These signs, however, are either grossly modified or abolished when combinations such as the one herein described are used, particularly if curare is added. Nitrous oxide with oxygen serves admirably as a benign basic agent for maintenance, provided the concentration of oxygen is such as to preclude hypoxia at all times, a total flow of 5 liters per minute being considered minimal. The oxygen concentration is increased, depending on the position of the patient, the nature of the surgical procedure and the disease for which operation is being performed. Hence in thoracic surgery the oxygen flow is maintained at between 40 to 50 per cent.

This necessitates the use of more adjuvants to maintain surgical anesthesia. Prior to the use of pentothal-pentobarbital sodium greater doses of demerol intravenously were used. Pentothal, 2.5 per cent, was added more frequently. At the present time, however, demerol is used less frequently and the dosage averages from 50 to 75 mg. per case as compared to 70 to 125 mg. previously employed. This dosage is used for operations averaging at least four to five hours. The time interval between injections of pentothal-pentobarbital sodium has ranged from fifteen to sixty minutes or longer. With pentothal alone, the interval between injections may be as short as five to fifteen minutes. This does not constitute a great advance in anesthesia but it does mean that maintenance is somewhat simplified. More time is left to the anesthetist to observe the patient's general condition during operation. This is of definite value in thoracic surgery using controlled respiration in which the operative time may exceed six to eight hours.

SUMMARY

The use of a combination of pentothal, 0.5 Gm., and pentobarbital sodium, 0.25 Gm. in a total volume of 25 cc., in 458 cases is recorded. The total dose of pentobarbital sodium is restricted to this amount.

Pentothal-pentobarbital sodium is employed for induction with or without intubation, only when the operative time is expected to exceed two to three hours in order to avoid prolonged postoperative narcosis owing to the pentobarbital sodium.

In selected cases such as those in which continuous spinal anesthesia is employed and for prolonged procedures on infants and children, maintenance is aided by the use of small repeated doses of the pentothal-pentobarbital sodium solution.

Impaired hepatic function is considered the only valid contraindication to the use of the pentothal-pentobarbital sodium mixture other than the usual contraindications ascribed to pentothal sodium.

REFERENCES

1. Fraser, R. J.: Intravenous Pentothal-Procaïne Anesthesia, *Anesth. & Analg.* **28**: 203-213 (July-Aug.) 1949.
2. Mackersie, W. G.: Pentothal Sodium With Procaïne For Thoracic Surgery, *Anesth. & Analg.* **28**: 213-218 (July-Aug.) 1949.
3. Carron, H.; Stoelting, V. K., and Cullen, S. C.: Pentobarbital Sodium-Curare Induction for Endotracheal Intubation, *Anesthesiology* **9**: 11-14 (Jan.) 1948.
4. Griffith, H. R., and Johnson, G. E.: The Use of Curare in General Anesthesia, *Anesthesiology* **3**: 418-420 (July) 1942.
5. Knight, R. T.: Combined Use of Sodium Pentothal, Intocostrin (Curare), and Nitrous Oxide, *Canad. M. A. J.* **55**: 356-360 (Oct.) 1946.
6. Apgar, V.: Experience with Curare in Anesthesia, *Ann. Surg.* **124**: 161-166 (Aug.) 1946.
7. Smith, S. M.; Brown, H. O.; Toman, J. E. P., and Goodman, L. S.: The Lack of Cerebral Effects of d-Tubocurarine, *Anesthesiology* **8**: 1-14 (Jan.) 1947.