

## THE SPINAL ANESTHETIC EFFECTS OF BARBITURATES: PRELIMINARY REPORT \* † ‡

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F. H. SHAW (1) of the University of Melbourne, Australia, observed that in mammals, subarachnoid injection of barbiturate solutions produced spinal anesthesia. We endeavored to verify Shaw's observations. According to the technique developed by Bieter et al. (2), aqueous solutions (from 2.5 to 5 per cent) of sodium salts of pentothal, nembutal, evipal, seconal, phenobarbital, and amytal were administered intrathecally to rabbits. Since the results obtained confirmed Shaw's observations, it appeared of interest to give this method a clinical trial. The continuous spinal technic of Tuohy (3) was used in all but 2 of the cases. Of the several barbiturates examined, thiopental sodium (pentothal) and pentobarbital sodium (nembutal) appeared to be the most promising. A 5 per cent solution of phenobarbital sodium produced either minor or questionable sensory changes.

Pentothal sodium was prepared in a 5 per cent solution by dissolving 500 mg. of the sterile powder in either 8 cc. of normal saline, 5 per cent dextrose in water or Ringer lactate solution. Dextrose, 2 cc. of 10 per cent dilution, was added to insure the hyperbaric character of the solution. Five per cent pentothal sodium in the saline solution has a specific gravity of approximately 1.008, and pH of 10.25. The initial dose varied from 3 to 4 cc., and fractional doses were added according to the needs of each patient. The maximum dosage was 850 mg. administered over a period of 150 minutes.

Nembutal was used in a 5 and 6.25 per cent solution, prepared by dissolving 500 mg. of the sterile powder in 8 to 10 cc. of normal saline solution. This solution had a specific gravity of approximately 1.023 and a pH of 9.15. After it was determined that this solution would produce spinal analgesia, 1 cc. of 1:1000 epinephrine hydrochloride was added to determine whether the spinal anesthetic action could be prolonged. The addition of epinephrine made the pH of this solution 8.95, which more closely approximates the pH of spinal fluid, 7.3 to

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7.6. The initial dose of the nembutal or nembutal-epinephrine solution was 3 cc. and fractional doses were added as needed. The maximal dosage of nembutal used was 500 mg. injected in fractional amounts over a period of two hours and five minutes.

Table 1 summarizes the results of pentothal administration in 10 cases. Table 2 summarizes the results of nembutal administration in 27 cases. The onset of sensory anesthesia with both agents requires from three to seven minutes. The onset of motor anesthesia, when present, requires from five to twelve minutes after the introduction of the agent intrathecally. The anesthetic effects are relatively short in duration and it is necessary to inject 1 cc. of solution approximately every twenty to thirty minutes. The addition of epinephrine to the anesthetic solution did not seem to prolong the anesthetic effect. When definite central narcosis becomes evident, however, this interval can be lengthened, particularly when there is no demand for muscular relaxation.

Sensory anesthesia was satisfactory in the majority of cases. In 6 cases it was not sufficient for the surgical procedure. These 6 failures occurred early in this series and, in light of more recent experience, it would seem they were the result either of inadequate initial dosage or of failure to allow adequate time for the onset of sensory anesthesia before attempting the surgical procedure.

In this series the production of motor anesthesia appeared to be somewhat unpredictable. In 15 cases it was not profound, but the operation performed did not require maximal motor relaxation. In the remaining cases motor relaxation was satisfactory, and several abdominal exploratory operations were performed.

TABLE 1  
THE EFFECT OF PENTOTHAL SODIUM AS A SPINAL ANESTHETIC

| Surgery                        | Duration of Anesthesia (in minutes) | Total Dosage (in mg.) | Sensory Anesthesia | Motor Anesthesia | Central Depression | Anesthetic Evaluation | Postanesthetic Complications                |
|--------------------------------|-------------------------------------|-----------------------|--------------------|------------------|--------------------|-----------------------|---|
| Hernioplasty                   | 25                                  | 300                   | Fair               | Slight           | Slight             | Inadequate            | None  |
| Amputation                     | 12                                  | 300                   | Fair               | None             | Slight             | Inadequate            | None  |
| Gastrectomy                    | 20                                  | 250                   | Fair               | Slight           | Slight             | Inadequate            | None  |
| Cystoscopy                     | 60                                  | 300                   | Good               | Slight           | Slight             | Adequate              | None  |
| Amputation, left fifth toe     | 25                                  | 200                   | Good               | Fair             | Slight             | Adequate              | None  |
| Scheduled pilonidal sinus      | 40                                  | 150                   | Good               | Fair             | None               | Surgery not done      | None  |
| Amputation mid-calf            | 85                                  | 630                   | Good               | Fair             | Slight             | Adequate              | Catheterized once first day after operation |
| Hernioplasty                   | 60                                  | 450                   | Good               | Complete         | Asleep             | Adequate              | None  |
| Sequestrectomy first toe, left | 65                                  | 500                   | Good               | Slight           | Slight             | Adequate              | None  |
| Skin graft left leg            | 150                                 | 860                   | Good               | Complete         | Asleep             | Adequate              | Hypesthesia right leg                       |

TABLE 2  
THE EFFECT OF NEMBUTAL AS A SPINAL ANESTHETIC

| Surgery                         | Duration of Anesthesia (in minutes) | Total Dosage (in mg.) | Sensory Anesthesia | Motor Anesthesia | Central Depression | Anesthetic Evaluation | Postanesthetic Complications          |
|---------------------------------|-------------------------------------|-----------------------|--------------------|------------------|--------------------|-----------------------|---------------------------------------|
| Skin graft abdominal            | 48                                  | 248                   | Good               | Fair             | Asleep             | Adequate              | None                                  |
| Hernioplasty inguinal           | 70                                  | 430                   | Good               | Complete         | Asleep             | Adequate              | None                                  |
| Skin graft abdominal            | 28                                  | 310                   | Poor               | Slight           | Asleep             | Inadequate            | None                                  |
| Hernioplasty inguinal           | 37                                  | 310                   | Fair               | Slight           | Slight             | Inadequate            | None                                  |
| Skin graft thigh                | 90                                  | 280                   | Good               | Fair             | Asleep             | Adequate              | None                                  |
| Subtotal gastrectomy            | 130                                 | 310                   | Good               | Complete         | Asleep             | Adequate              | Catheterized first day                |
| Hernioplasty inguinal           | 78                                  | 372                   | Good               | Complete         | Asleep             | Adequate              | None                                  |
| Hydrocelectomy                  | 75                                  | 372                   | Good               | Complete         | Asleep             | Adequate              | Catheterized first day                |
| Amputation great toe            | 65                                  | 310                   | Good               | Fair             | Marked             | Adequate              | None                                  |
| Subtotal gastrectomy            | 270                                 | 435                   | Good               | Good             | Asleep             | Adequate              | None                                  |
| Tubal ligation                  | 12                                  | 248                   | Poor               | Poor             | Asleep             | Inadequate            | None                                  |
| Tubal ligation                  | 60                                  | 310                   | Good               | Complete         | Asleep             | Adequate              | None                                  |
| Skin graft thigh-leg            | 55                                  | 250                   | Good               | Complete         | Marked             | Adequate              | Catheterized first day                |
| Hernioplasty inguinal           | 19                                  | 250                   | Poor               | Slight           | Asleep             | Inadequate            | None                                  |
| Sequestrectomy foot             | 35                                  | 372                   | Good               | Complete         | Asleep             | Adequate              | Hypesthesia right leg                 |
| Sequestrectomy foot             | 110                                 | 434                   | Good               | Poor             | Marked             | Adequate              | Postoperative catheterization, 4 days |
| Abdominal hysterectomy          | 99                                  | 434                   | Good               | Good             | Asleep             | Adequate              | None                                  |
| Amputation thigh                | 83                                  | 310                   | Good               | Good             | Asleep             | Adequate              | None                                  |
| Hemorrhoidectomy                | 60                                  | 372                   | Good               | Fair             | Asleep             | Adequate              | None                                  |
| Hernioplasty inguinal           | 64                                  | 372                   | Good               | Fair             | Marked             | Adequate              | Pulmonary atelectasis                 |
| Abdominal hysterectomy          | 120                                 | 372                   | Good               | Good             | Asleep             | Adequate              | None                                  |
| Hernioplasty inguinal           | 50                                  | 310                   | Good               | Fair             | Asleep             | Adequate              | None                                  |
| Dilate urethral stricture       | 30                                  | 208                   | Good               | Poor             | Marked             | Adequate              | None                                  |
| I & D perirectal abscess        | 35                                  | 208                   | Good               | Poor             | Slight             | Adequate              | None                                  |
| Abdominal hysterectomy          | 80                                  | 500                   | Good               | Good             | Asleep             | Adequate              | None                                  |
| Lumbar sympathectomy, bilateral | 120                                 | 434                   | Good               | Good             | Marked             | Adequate              | Pulmonary atelectasis                 |
| Excision ovarian cyst           | 125                                 | 500                   | Good               | Good             | Asleep             | Adequate              | None                                  |

Nembutal seemed to produce more rapid anesthesia and a little better quality of anesthesia than pentothal, although the latter was not used as extensively and a more thorough investigation may not support this impression.

One of the most striking effects in the use of either pentothal or nembutal was its central depressant action. This effect was noted in all patients who received nembutal, and in all but one patient who received pentothal. It varied from mild soporific effects, particularly with pentothal, to marked central narcosis in a number of patients to whom nembutal was given. The central effects were noted in approximately eight to thirty minutes after the initial injection of the barbiturate. We could not correlate the rapidity of onset of the central action with either the presence or absence of epinephrine, the amount of spinal fluid present, or posture of the patient on the table. It may be that more extensive studies will reveal some relationship between onset of central effects and spinal fluid dynamics.

Whereas, in some cases the central effects were desirable from the standpoint of the patient and surgeon, some of the patients who were given nembutal had prolonged central depressant effects which posed definite problems. Two of these patients had pulmonary atelectasis within the first twenty-four hour period after operation. Five additional patients had marked depressant effects lasting from twenty-four to thirty-six hours. These effects were completely out of proportion to what might be expected from either the intramuscular or intravenous administration of an equivalent dosage of the agent. One patient (C. T.), who received only 208 mg. of nembutal intraspinally, had rather marked central depressant effects for some thirty hours after operation.

Dille et al. (4) have shown that, while there is no specific affinity of the brain for barbiturates, after nembutal administration the brain contains more barbiturate than any other tissue. It is well established that at least part of the cerebrospinal fluid is absorbed in the cerebral subarachnoid space (5); also that certain dyes, upon being introduced into the subarachnoid space, can be detected in the blood within a minute. It is reasonable to assume, therefore, that the central effect is, for the most part, mediated by way of blood stream absorption of the barbiturate from the subarachnoid space. In view of the rather prolonged central effects which are frequently observed, however, the possibility that there may be direct absorption of the barbiturate from the circulating cerebrospinal fluid by the brain should not be discounted. Undoubtedly, the cerebrospinal fluid serves as a temporary reservoir permitting prolonged systemic absorption and possibly direct central absorption of the barbiturate. Further studies may determine the practicability of using this method of administration of the barbiturates when prolonged central sedation is desired with a minimum dosage of drug—such as in the treatment of eclampsia, and so forth.

## COMMENT

Nausea or vomiting did not occur in any case with the use of these agents. There was no instance of marked fall in the blood pressure level. It would seem that with the slow onset of anesthesia the circulatory system has time to accommodate itself and any fall in blood pressure is gradual in nature. Vasopressor agents were not administered before or at the time of the initial spinal injection.

Postanesthetic complications, in addition to the 2 cases of pulmonary atelectasis and 5 cases of prolonged central depression previously mentioned, consisted of residual sensory depression in 2 patients and postoperative catheterization which was required one or more times by 5 patients. Two of these 5 patients also had prolonged central depression. One of the 2 patients with sensory disturbances received 850 mg. of pentothal over a period of 150 minutes and had sensory depression over the right leg for a period of five weeks; the other patient received 372 mg. of nembutal over a period of thirty-five minutes and also had sensory depression over the right leg for four weeks. Both patients completely recovered normal sensory perception. These complications indicate the need for more extensive laboratory and clinical study before final evaluation of this method of administering barbiturates.

So far as we know, this is the first presentation of clinical cases in which spinal anesthesia was produced by barbiturates. Of the several barbiturate used, pentothal sodium and nembutal proved to be the most satisfactory, but many other barbiturates and related compounds have not been fully explored and evaluated for this purpose. Several laboratory and clinical investigations are now in progress.

## SUMMARY

Some barbiturates when introduced intrathecally produce typical sensory and motor anesthesia.

These agents also produce a cerebral (soporific) effect when introduced intrathecally. The mechanism of this action may be caused by systemic absorption or by direct action centrally of the barbiturate contained in cerebrospinal fluid.

Motor anesthesia appears to be somewhat more variable than sensory anesthesia.

Certain complications such as bladder dysfunction, hypesthesia, central depression and pulmonary sequelae have been encountered. Considerable investigation should be done to evaluate these complications.

These observations are not only of clinical but of theoretical interest, particularly since, according to a widely held theory, barbiturates have a limited site of action in the central nervous system and in therapeutic doses are considered brain stem depressants (6, 7, 8, 9).

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## FRIDAY

Joint Meeting with Section on Urology.

Symposium on Preoperative Preparation, Anesthesia and Supportive Therapy for Urologic Operations.

Chairman's Address: Prostatectomy in the Aged.  
John Arthur Taylor, M.D., New York.

Anesthesia in Pediatric Urology.

Stevens J. Martin, M.D., and Thomas M. Feeney, M.D., Hartford, Conn.

The Preoperative and Postoperative Management of Aged Patients Undergoing Urological Surgery with Particular Reference to Problems of Nutrition and Body Chemistry.

Richard Chute, M.D., Boston, Mass.

Anesthetic Problems in the Hormonal Disorders of the Adrenal Gland.

E. M. Papper, M.D., and George F. Cahill, M.D., New York.

Infiltrating Carcinoma of the Bladder: Relation of Early Diagnosis to Five Year Survival Rate After Complete Extirpation.

Hugh J. Jewett, M.D., Baltimore, Md.

Renal Tumors.

Lloyd H. Mousel, M.D., and O. A. Nelson, M.D., Seattle, Wash.

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Doctor Daniel C. Moore, Seattle, will address the Section of Laryngology, Otology and Rhinology on "A Technic of Anesthesia for Long and/or Technically Difficult Ophthalmologic and Otolaryngologic Surgical Procedures."