

PENTOTHAL-CURARE MIXTURE *

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It is the purpose of this paper merely to describe the preparation of pentothal-curare mixture. Only the analysis of a large number of cases will prove or disprove its worth. As yet I do not have a sufficiently large series to form definite conclusions. Encouraging observations, however, have prompted the continuance of its usage.

There is much to say in favor of pentothal anesthesia, although it has its shortcomings. One of its main faults is the poor muscular relaxation which it produces, especially for abdominal surgery. In 1942 Griffith (1) introduced intocostrin into the field of anesthesiology, not as an anesthetic, but as an agent to be used solely for the production of muscular relaxation. Thus, two useful agents are available, each with its valuable points, each with its shortcomings: pentothal, the pleasant anesthetic, with poor relaxing properties, and intocostrin, not an anesthetic agent, but unsurpassed for producing muscular relaxation. Why not combine the two and have a product with the good points of both pentothal and curare?

This combination has been tried, but unfortunately the two products were incompatible. A 2.5 per cent solution of pentothal sodium is alkaline with a pH of 10.35, while intocostrin is acid with a pH of 5.1 (table 1). When the two solutions are combined, a heavy precipitate

TABLE 1

	pH
Aqueous pentothal sodium 2.5 per cent solution	10.35
Intocostrin	5.1
d-Tubocurarine chloride (100 units per cc.)	2.3

of acid pentothal forms. This precipitate, however, will go into solution when injected into the blood stream, owing to the buffering action of the blood. Nevertheless, this is not advisable because, as yet, the dangers of injecting this precipitate are not known nor can the dosage of the precipitated acid pentothal be accurately gauged.

The process of buffering the solutions to prevent precipitation was considered. Squibb and Company (2) have successfully buffered the solutions with 8 per cent sodium carbonate, but they have not fully completed their studies on the period of stability of the solution. The

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problem then arises of finding a new solvent for the sodium pentothal, which will produce a more stable solution. Evans (3), of the University of Minnesota laboratories, suggested an alcoholic solution.

A 10 per cent solution of ethyl alcohol was used as the vehicle for dissolving the pentothal sodium. To 40 cc. of this 2.5 per cent alcoholic

TABLE 2*

	pH	Precipitation
Dis. water 15 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.25 cc. Intocostin 100 U.	10.15	4 hrs.
Dis. water 15 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.5 cc. Intocostin 100 U.	10.25	8 hrs.
10% Ethyl alcohol 15 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.25 cc. Intocostin 100 U.	10.34	10 hrs.
10% Ethyl alcohol 15 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.5 cc. Intocostin 100 U.	10.45	8 days
5% Ethyl alcohol 15 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.25 cc. Intocostin 100 U.	10.23	14 hrs.
5% Ethyl alcohol 15 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.5 cc. Intocostin 100 U.	10.62	18 hrs.
10% Ethyl alcohol 20 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.25 cc. Intocostin 100 U.	10.7	18 hrs.
10% Ethyl alcohol 20 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.5 cc. Intocostin 100 U.	10.78	None after 14 days
5% Ethyl alcohol 20 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.25 cc. Intocostin 100 U.	10.5	12 hrs.
5% Ethyl alcohol 20 cc. Pentothal 0.5 Gm. 8% Na ₂ CO ₃ 0.5 cc. Intocostin 100 U.	10.55	24 hrs.

* The values shown are only approximate. Attempts were made to simulate conditions which would be encountered in actual practice. For this reason solutions were measured with syringes and medicine glasses such as are found in any operating room.

solution of pentothal, 200 units (10 cc.) of intocostrin was added. A fine precipitate formed. This solution was then buffered with 0.5 cc. of 8 per cent sodium carbonate. The precipitate immediately disappeared, leaving a clear, straw-colored fluid. This solution showed no precipitation for eighteen hours (table 2). It became darker, however, probably because of the breakdown of the pentothal. Later it was discovered that 5 per cent alcohol was equally satisfactory as a vehicle. Buffering the alcoholic solution with 1 cc. of 8 per cent sodium carbonate prevented precipitation for a longer period of time. This was thought unnecessary, however, as the solution became darker with age, similar to that seen in aqueous pentothal solution which stands for several days. For this reason it is not considered advisable to use a solution over twelve hours old.

Recently we received a supply of crystalline d-tubocurarine chloride.* An aqueous solution of d-tubocurarine chloride was prepared, each cubic centimeter containing 100 units of the standard drug. The following mixture was then used: 5 per cent alcohol, 38 cc.; pentothal sodium, 1 Gm.; 8 per cent sodium carbonate, 0.5 cc., and d-tubocurarine chloride, 2 cc. (200 units). This solution remained stable much longer than when intocostrin was used. Later it was discovered that buffering with sodium carbonate was unnecessary to prevent precipitation of the pentothal. Still later, experiments disclosed that the alcoholic solution was unnecessary and that no permanent precipitate formed when the d-tubocurarine chloride was added to 2.5 per cent aqueous sodium pentothal (table 3). At the present time the following formula is used: 2.5 per cent aqueous pentothal sodium, 18.5 cc., and d-tubocurarine, 1.5 cc. (150 units). This mixture showed no precipitation for fourteen days (table 3). Although the solution darkens with age, this change is less pronounced than in the alcoholic solution.

There is a maximal amount of d-tubocurarine that can be added to the pentothal solution without causing precipitation of the pentothal. It was found that 400 units d-tubocurarine per 36 cc. of 2.5 per cent pentothal was approximately the maximal amount that could be added without a precipitate forming (table 3).

A freshly prepared solution of pentothal sodium is necessary to prevent the precipitate from forming when higher concentrations of curare are used. It is advisable to add the curare to the pentothal solution while it is being agitated. If the two solutions are mixed without agitation, a precipitate will form at the point of contact of the two liquids. This precipitate will disappear, however, upon shaking the solution.

Although we are using a pentothal solution which contains 7.5 units d-tubocurarine per cubic centimeter, the optimal amount of curare that should be added to the pentothal solution has not been

* d-Tubocurarine chloride furnished through courtesy of Squibb and Company.

definitely determined. Nevertheless, we are of the opinion that the correct concentration is 5 * to 7.5 units per cubic centimeter of solution.

I have administered pentothal-curare anesthetics—alcoholic and aqueous—in more than 50 cases, with varying degrees of success. The series includes the use of this mixture for patients on whom cholecystectomy, gastrectomy, colectomy, radical mastectomy, and plastic operations are to be performed and for passing an endotracheal tube preliminary to administration of cyclopropane. Patients ranged in age from 17 to 70 years. The usual premedication was morphine, grain $\frac{1}{4}$ and scopolamine, grain $\frac{1}{200}$. All patients received 50 per cent oxygen and 50 per cent nitrous oxide by inhalation. One-half to 1 cc. of

TABLE 3 *

	pH	Precipitation
10% Ethyl alcohol 19 cc. Pentothal 0.5 Gm. d-Tubocurarine chloride 100 units (1 cc.)	10.5	9 days
5% Ethyl alcohol 19 cc. Pentothal 0.5 Gm. d-Tubocurarine chloride 100 units (1 cc.)	10.45	10 days
2.5% Aqueous pentothal 19 cc. d-Tubocurarine chloride 100 units (1 cc.)	10.29	None after 15 days
2.5% Aqueous pentothal 18.5 cc. d-Tubocurarine chloride 150 units (1.5 cc.)	10.16	14 days
2.5% Aqueous pentothal 18 cc. d-Tubocurarine chloride 200 units (2 cc.)	10	6 hrs.
2.5% Aqueous pentothal 17.5 cc. d-Tubocurarine chloride 250 units (2.5 cc.)	9.96	immediate

* The values shown are only approximate. Attempts were made to simulate conditions which would be encountered in actual practice. For this reason solutions were measured with syringes and medicine glasses such as are found in any operating room.

the mixture was intermittently injected intravenously as required to maintain adequate muscular relaxation and depth of anesthesia.

The solution was injected into an accessible vein through a needle connected to a syringe by means of a length of rubber tubing. If intravenous fluids were to be administered to the patient during the operation, the mixture was injected into the intravenous tubing or through a Gilson Y connected to the needle.

It was noted that less pentothal sodium was required than in similar cases in which no curare was added to the pentothal solution. The curare apparently obliterated many of the troublesome reflex movements which are seen during pentothal anesthesia. Because less pento-

* 5 units per cc. solution has proved to be the most satisfactory concentration. At the time of writing, the series numbers over 150 cases.

thal is required, the period of recovery is usually shortened following termination of the anesthetic. If, after operation, the patient shows signs of having received an overdose of curare, prostigmine may be administered to counteract the action of this drug. In the series reported 2 patients received prostigmine.

Induction of the anesthesia and recovery of the patient were without untoward incident. No difference was observed than when pentothal alone was used. Muscular relaxation was adequate in all cases.

Passage of the endotracheal tube is facilitated under this type of anesthesia. Severe laryngospasm was not encountered even though the patient coughed when the glottis was stimulated by the endotracheal tube. This is in contradistinction to the occurrence of laryngospasm when pentothal alone is used. The average amount of solution injected preliminary to passing the tube was 10 to 15 cc. of the mixture.

After passing the endotracheal tube it was usually necessary to resort to artificial respiration for a time to counteract complete apnea or to insure adequate respiratory exchange. Following the initial respiratory depression which lasted from one to ten minutes, depending upon the amount of the mixture injected, the respiratory movements returned to normal. If at any time respiratory exchange was deemed inadequate, the movements were supplemented by compressing the breathing bag on the gas machine.

In 2 cases (gastrectomy and ileocolostomy) hiccups developed while the patients were under anesthesia. The pentothal-curare anesthetic was discontinued and cyclopropane anesthesia substituted.

COMMENT

If, after sufficient study, the pentothal-curare mixture proves successful, another useful anesthetic agent may be added to our armamentarium. This will make available an anesthetic agent which will be pleasant from the patient's point of view, and also one that will produce adequate muscular relaxation to facilitate any surgical procedure. Perhaps more important, it is a non-explosive anesthetic agent which can be used with safety.

Freshly prepared solutions should be used; solutions over twelve hours old should be discarded. Experience undoubtedly will show that older solutions can be used with safety.

SUMMARY

Methods of combining pentothal sodium and curare are described. Experience with pentothal-curare mixtures is discussed.

REFERENCES

1. Griffith, Harold R., and Johnson, Enid: *The Use of Curare in General Anesthesia, Anesthesiology* 3: 418-420 (July) 1942.
2. Newcomer, H. Sidney, Squibb & Company: Personal communication.
3. Evans, Gerald T.: Personal communication.