CURRENT COMMENT AND CASE REPORTS

CURRENT COMMENT is a section in ANESTHESIOLOGY in which will appear invited and unsolicited professional and scientific correspondence, abbreviated reports of interesting cases, material of interest to anesthesiologists reprinted from varied sources, brief descriptions of apparatus and appliances, technical suggestions, and short citations of experiences with drugs and methods in anesthesiology. Contributions are urgently solicited. Editorial discretion is reserved in selecting and preparing those published. The author's name or initials will appear with all items included.

COMPATIBILITY OF NEUROMUSCULAR BLOCKING AGENTS WITH BARBITURATES

The development of the use of neuromuscular blocking agents for the production of relaxation to facilitate endotracheal intubation prior to the administration of general anesthesia has led some to the use of a combination of a barbiturate such as hexobarbital (evipal®) or thiopental (pentothal®) with the neuromuscular blocking agent.

This combination, either in the same intravenous syringe or by injection of the neuromuscular blocking agent into the infusion tubing of the barbiturate, enables the physician to combine the initial peak effectiveness of the relaxant with the period of maximal depth of unconsciousness of the barbiturate. To give successive injections might be attended with sufficient delay to permit partial recovery of the patient before adequate relaxation is achieved.

These combinations have been used successfully by the Department of Anesthesiology of the Medical College of Georgia with salts of tubocurarine, decamethonium, dimethyl tubocurarine and flaxedil®, using both hexobarbital and thiopental.

However, when this technic was used in the evaluation of two new neuromuscular blocking agents,* the drugs were found to have been rendered ineffective, although the anesthetic properties of the barbiturate were not noticeably altered.

* OC1130-2602, supplied by Dr. Karl H. Beyer, Research Division, Sharp and Dohme, Glenolden, Pa. Succinylcholine supplied by Dr. Edwin J. de Beer, Wellcome Research Laboratories, Tuckahoe 51, New York.

These questions, therefore, arose:

(1) What quality of the barbiturate solution is responsible for the damage to the drug?

(2) Are the drugs partially or completely destroyed by the barbiturate?

(3) Are drugs previously thought stable in such combination to any degree altered by the combination?

In order to answer these questions a series of laboratory experiments was set up, using anesthetized dogs, with the gastrocnemius muscle intermittently stimulated through the sciatic nerve and recording from the Achilles tendon on a kymograph, as a guide to curariform activity.

These animals were given the curariform agents, with doses controlled to produce a reproducible degree of muscle twitch depression sufficiently slight for complete recovery in ten or fifteen minutes. Mixtures of the agent with barbiturate were tried, with solutions of the agent at pH levels ranging from 6.0 to 12.0, these levels being controlled with buffer mixtures of sodium hydroxide, disodium phosphate and citric acid.

Tubocurarine chloride produces a white, flaky precipitate when added to solutions of thiopental sodium in which sodium carbonate is present as a buffer. In spite of this, there was no evidence of reduced potency of the curare in such mixtures, with pH from 10.5 to 10.8. Mixtures with hexobarbital having a pH 11.5 to 11.7 are clear and likewise of undiminished potency. Tubocurarine chloride solutions varying from a pH of 6.0 to 12.2 were found to be equipotent.

Dimethyl tubocurarine iodide does not produce this precipitation. Solutions in thiopental, hexobarbital and at hydrogen ion concentration similar to that used with tubocurarine had potency equal to solutions in distilled water.

Flaxedil® (Lederle) was also unaffected by either barbiturate or by a wide range in hydrogen ion concentration.

Mytolon® (Winthrop) was not noted to show precipitation or diminution of potency under similar conditions.

Decamethonium bromide in the same solutions was observed to have unreduced potency.

Succinylcholine dichloride, also known as diacetylcholine, is an agent whose effect lasts about five minutes, and from which recovery, in the pentobarbital-anesthetized dog, is nearly complete, even with continued administration. It is destroyed almost immediately by a pH of over 11.0, more slowly between pH 9.5 and 11.0, and little at all below 9.5.

Thus, mixtures with thiopental, if given immediately, are effective, but in five minutes the potency is reduced considerably.

Hexobarbital mixtures (effective dose in two volumes of 10 per cent hexobarbital) are destroyed immediately, but by increasing the proportion of succinylcholine to hexobarbital, this can be delayed five or ten minutes.

OC 1130–2602 is 3-trimethylamoniumpropyl p-trimethylamoniumbenzoate dibromide. Its duration of action and many of its effects in experimental animals are similar to those of decamethonium. In the anesthetized human being moderate fasciculation has been noted. The length of action of this drug compares more favorably with *d*-tubocurarine rather than decamethonium bromide. No tendency toward tachyphylaxis or marked respiratory depression has been noted in 50 clinical patients. It is rendered ineffective slowly below pH of about 11.0, not at all below 9.0. Above pH 11.0 it appears to be completely and rapidly destroyed. Therefore, in solution with hexobarbital (pH 11.7) it is ineffective. In solution with thiopental (pH 10.7) it may produce the predicated paralysis, if given promptly.

It is desirable to emphasize that this procedure does not give a precise quantitative estimate of curariform activity, but is thought to give a more adequate visual record than can be obtained clinically. The preparations were tried in mice, by intraperitoneal and intravenous routes, using inability to hang on a wire screen as an end point, to illustrate that the same results could be obtained with another procedure.

This study was thought useful, not so much as a test of the compatibilities of the compounds in established usage, but to caution against the use of drug mixtures in the evaluation of new agents.

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THE USE OF SUCCINYLCHOLINE FOR ENDOTRACHEAL INTUBATION

Recently, the use of succinylcholine,* an ultra-short acting, "depolarizing" (1) type of muscle relaxant was introduced to anesthesiology (2–5). Succinylcholine differs from the previously employed muscle relaxants in that it is hydrolyzed by both the plasma cholinesterase (nonspecific cholinesterase) and the acetylcholine esterase (true cholinesterase) (6–10). Owing to this enzymatic hydrolysis the duration of the effect of a single intravenous dose is very brief. This circumstance makes succinylcholine suitable for the production of muscular relaxation of short duration.

Succinylcholine was used for the production of muscular relaxation prior to endotracheal intubation in 317 unselected pa-

* Succinylcholine in the form of succinylcholine diiodide was employed in these studies and was made available to us through the courtesy of Dr. E. J. de Beer of Burroughs Wellcome & Co.