CURRENT COMMENT AND CASE REPORTS

CURRENT COMMENT is a section in ANESTHESIOLOGY in which will appear invited and un-
solicited 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 anesthesia. Contributions are urgently solicited. Editorial di-
rection 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 neu-
romuscular blocking agents for the produc-
tion 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 hexo-
barbital (evipal®) or thiopental (pento-
thal®) with the neuromuscular blocking 
agent.

This combination, either in the same in-
travenous syringe or by injection of the 
neuromuscular blocking agent into the in-
fusion tubing of the barbiturate, enables the 
physician to combine the initial peak effective-
ness of the relaxant with the period of max-
imal depth of unconsciousness of the 
barbiturate. To give successive injections 
might be attended with sufficient delay to 
permit partial recovery of the patient be-
fore adequate relaxation is achieved.

These combinations have been used suc-
cessfully by the Department of Anesthesiol-
ogy of the Medical College of Georgia with 
metate of tubocurarine, decamethonium, di-
methyl 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, arise:

(1) What quality of the barbiturate solu-
tion 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 gastro-
enemius 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 de-
pression sufficiently slight for complete re-
covery 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 car-
bonate is present as a buffer. In spite of 
this, there was no evidence of reduced po-
tency of the curare in such mixtures, with 
ph from 10.5 to 10.8. Mixtures with hexo-
obarbital 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 unaltered 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 1130–2002 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 fasciculations have 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 predicted 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-