mice, for although with isolated mice at dose levels in the region of the LD50 there was a marked increase in body temperature in no case did it rise above 41·8°.

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Neuromuscular Blocking Action of Succinyldicholine Stereoisomers

SIR,—An interesting fact has come to light during an investigation of the neuromuscular blocking action of a series of succinyldicholine compounds. On the cat gastrocnemius preparation, the isomers of succinyldi-(β-methyl)-choline had very little activity compared with that of suxamethonium; the L(+)-isomer was 1·35 times as effective as the D(−)-isomer on a molar basis, and the DL meso-mixture occupied an intermediate position (Table I).

TABLE I

COMPARISON OF POTENCY ON CAT GASTROCNEMIUS PREPARATION

Substance	Isomer	No. of mols of substance equivalent to 1 mol. of suxamethonium
Succinyldi-(β-methyl)choline	L(+)- D(−)- DL-meso-	887 1,200 913

The nature of this neuromuscular blocking action was further investigated, using the isolated innervated biventer cervicis muscle of the chick (Ginsborg and Warriner, 1960). Two points of note emerged. By contrast with all isomers of both the methiodide and the ethiodide series of succinyldi-(α-methyl)choline, both the L(+)- and the D(−)-isomers of succinyldi-(β-methyl)-choline were curare-like (Fig. 1), that is, they produced a reduction in twitch height without causing contracture. On a molar basis (+)-tubocurarine was 175 and 400 times as potent as the L(+)- and D(−)-isomers respectively. On the other hand the DL-meso-mixture produced a typical suxamethonium-like response, that is, it caused a contracture, which was found to be referable entirely to the meso content of the mixture. (Suxamethonium was 270 times as potent as the mixture in this action.)

The chick nerve-muscle preparation was selected since both the reduction of twitch height and the contracture are simultaneously available for comparison. In fact it appears that for suxamethonium-like neuromuscular blocking agents reduction of twitch height always runs parallel to contracture. Occasionally, however, a reduction of twitch height is observed shortly after the application

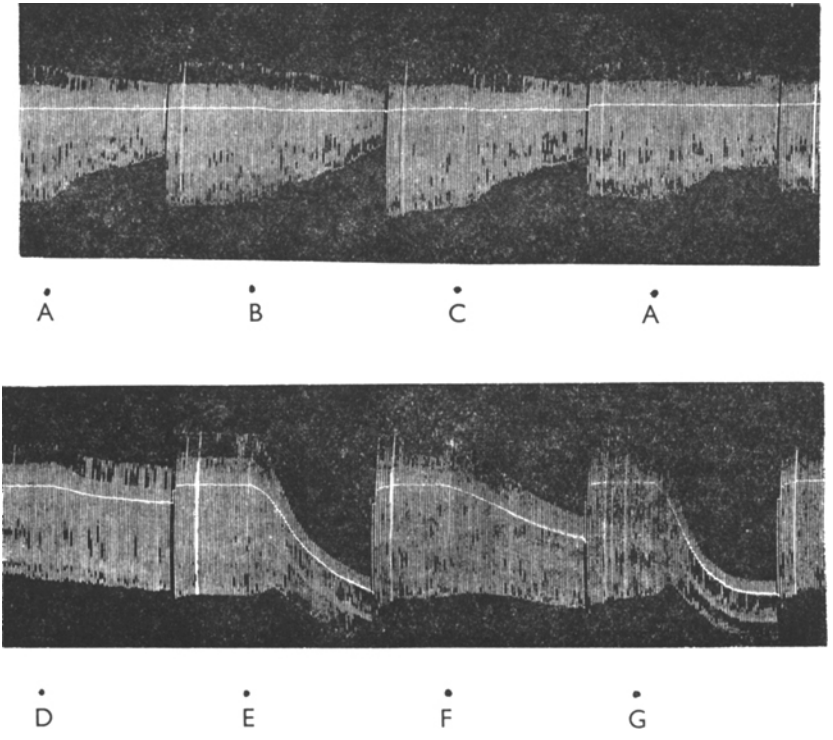

FIG. 1. Record of twitch produced by supra-maximal stimuli applied at a frequency of 12/min. Doses were given as follows:

A. 120 μg. of (+)-tubocurarine chloride.
B. 40 mg. L(+)-succinyldi-(β-methyl)choline iodide.
C. 40 mg. D(−)-succinyldi-(β-methyl)choline iodide.
D. 4 μg. suxamethonium iodide.
E. 2 mg. DL-meso-mixture succinyldi-(β-methyl)choline iodide.
F. 1 mg. DL-meso-mixture succinyldi-(β-methyl(choline iodide.
G. 8 μg. suxamethonium iodide.

of the drug, but this is rapidly swamped by the onset of contracture (Fig. 1: E and G).

All the succinyldicholine compounds used were synthesised by Mr. J. W. Clitherow in the Pharmaceutical Chemistry department of Chelsea School of Pharmacy.

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