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STUDIES ON THE PHARMACOLOGY OF SUCCINYLCHOLINE

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Succinylcholine, a choline ester of succinic acid, is a short-acting neuromuscular relaxant. A review of its chemical, pharmacological, and clinical properties has been published elsewhere (Bourne, Collier, and Somers, 1952). Previous studies on the pharmacology of this compound have been largely confined to the dog and rabbit, and a closer study of its actions in the cat seemed desirable. Organe, Paton, and Zaimis (1949) showed that the actions of decamethonium in the cat are more closely related to those in man. Chemically, succinylcholine shows a close structural relationship to acetylcholine, and it was important to ensure, before clinical trial, that succinylcholine was free from muscarine-like actions.

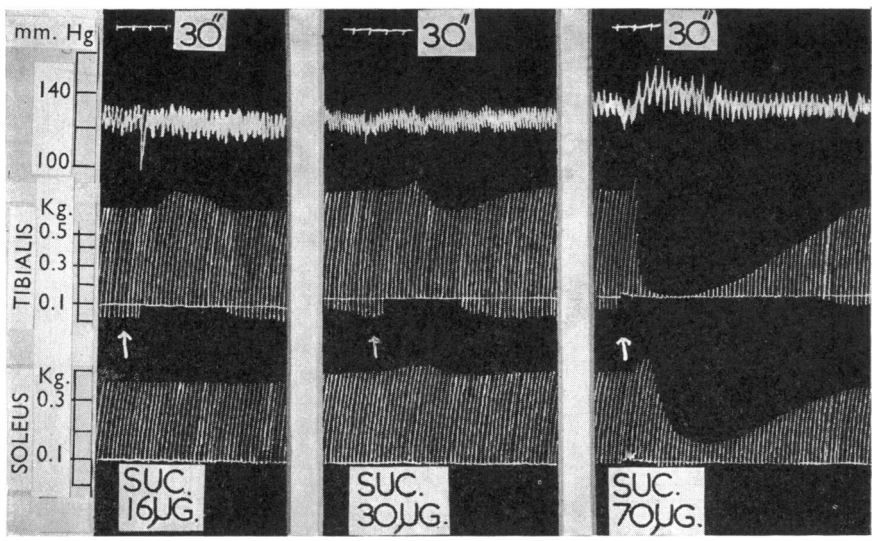

FIG. 1.—Cat, chloralose. Records of blood pressure (above), and of the contractions of tibialis anterior (middle) and soleus (below). Injections of succinylcholine 16, 30, and 70 μg. intravenously.

METHODS

Four cats were anaesthetized with chloralose (80 mg./kg.). Twitches of the soleus and tibialis anterior muscles, stimulated with supramaximal shocks applied to the peripheral end of the sciatic nerve in the thigh, were recorded with a flat spring myograph as described by Paton and Zaimis (1949). All injections were made intravenously and the doses recorded are those for succinylcholine chloride per kg. body weight. Salivary flow was recorded in three cats and two dogs, anaesthetized with chloralose, by a drop recorder (Gaddum and Kwiatkowski, 1938) after cannulation of Wharton's duct.

RESULTS

Neuromuscular Blocking Activity.—Fig. 1 shows the effects on the soleus and tibialis muscles of increasing doses of succinylcholine. Like decamethonium, succinylcholine first caused an increase in the twitch tension and fasciculation of the muscles. This was followed by a brief period of paralysis, much shorter in duration than that caused by decamethonium. Doses could be repeated at

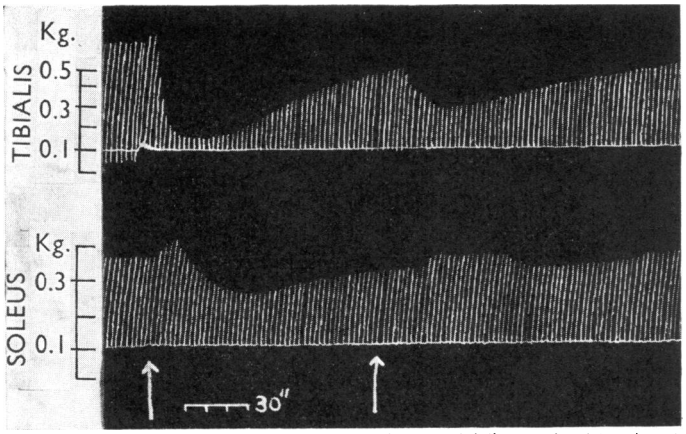

FIG. 2.—Cat, chloralose. Records of contractions of tibialis anterior (above) and soleus (below). At first arrow succinylcholine 50 μg. intravenously; at second arrow neostigmine 20 μg.

30-minute intervals without a cumulative action. Of particular interest was the difference in the sensitivities of the tibialis (" white " muscle) and soleus (" red " muscle), which was much less than that observed after administration of decamethonium (Paton and Zaimis, 1951). A dose of 70 μg. of succinylcholine, which did not completely paralyse tibialis, depressed the twitch tension of the soleus by 75% ; whereas a dose of 20 μg. of decamethonium, which caused a 75% depression of tibialis, actually increased the twitch tension of soleus.

Effect of Neostigmine.—Succinylcholine differs from decamethonium in being hydrolysed by cholinesterases (Glick, 1941 ; Bovet-Nitti, 1949). Thus neostigmine, which inhibits cholinesterases, prolongs the action of succinylcholine. Fig. 2 shows the effects of a dose of 20 μg. of neostigmine on tibialis and soleus. The tibialis was further depressed, while the soleus showed only an increase of twitch tension such as neostigmine causes on normal muscle.

Muscarinic and Nicotinic Actions.—The absence of muscarine-like actions was shown on the blood pressure and salivary flow of three anaesthetized cats and two dogs. Small doses of succinylcholine had no effect on the blood pressure, provided ventilation was adequate. In cats under artificial respiration 2 mg. of succinylcholine caused a slight rise in blood pressure and 10 mg. caused a large rise ; this was nicotinic in origin, since it was abolished by ganglionic blocking agents such as hexamethonium and tetraethylammonium chlorides (Fig. 3). Bovet, Bovet-Nitti, Guarino, Longo, and Fusco (1951) reported the hypertensive action of high doses of succinylcholine in the dog, but they also found that it caused a fall of blood pressure in small doses (Bovet, Bovet-Nitti, Guarino, Longo, Fusco, and Marotta, 1949). Succinylcholine did not increase salivary flow in cats or dogs, in contrast with the observations of Bovet *et al.* (1951) and Ginzel, Klupp, and Werner (1951), who reported an increase in the flow of saliva in the dog. Large doses of succinylcholine, 10 mg., slightly decreased the rate of salivary secretion (Fig. 4).

DISCUSSION

Although succinylcholine resembles acetylcholine in chemical structure it shows only the nicotine-like actions and is free from muscarine-like actions. It would appear, therefore, that the larger molecule of succinylcholine is unable to combine with the muscarinic receptors. The neuromuscular blocking action of succinylcholine is similar to that of decamethonium, being preceded by a brief period of stimulation. Unlike decamethonium, however, succinylcholine is slowly hydrolysed by

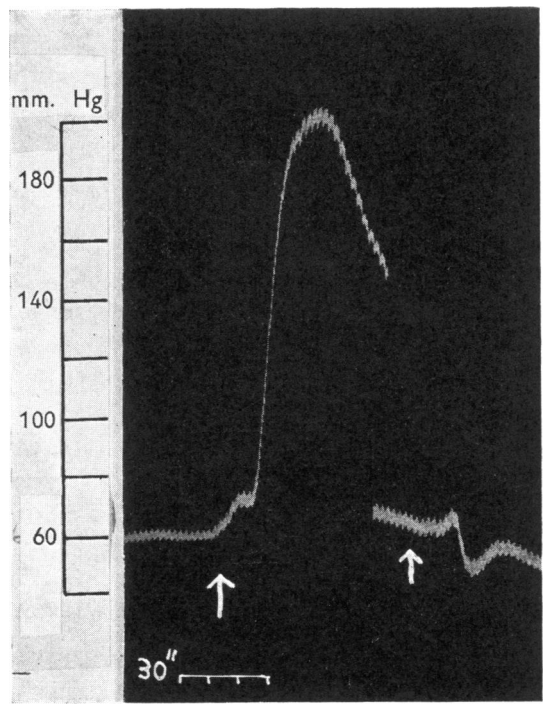

FIG. 3.—Cat, chloralose. Record of blood pressure. At first arrow succinylcholine 10 mg.; at second arrow succinylcholine 10 mg. after 20 mg. of tetraethylammonium.

cholinesterases and its action on the neuromuscular end-plate can be regarded as intermediate between that of acetylcholine and that of decamethonium. The difference in sensitivities of the "red" and "white" muscles is not as great as with decamethonium, which would suggest that succinylcholine will not have the sparing effect on the respiratory muscles claimed for decamethonium (Paton and Zaimis, 1951).

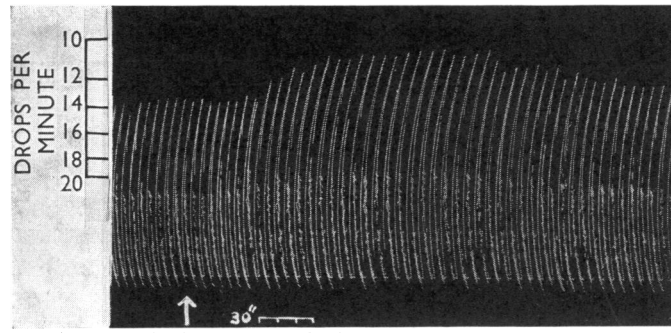

FIG. 4.— Dog, chloralose. Record of salivary flow. At arrow succinylcholine 10 mg. intravenously.

SUMMARY

1. The neuromuscular blocking action of succinylcholine has been studied in the cat. Like decamethonium it first potentiates the indirectly excited maximal twitch, followed by a brief period of paralysis. There is not the same difference in sensitivities between soleus and tibialis as with decamethonium. Neostigmine potentiates and prolongs the paralysing action of succinylcholine.

2. Although closely related to acetylcholine in chemical structure, succinylcholine shows only the nicotinic actions and not the muscarinic actions of acetylcholine.

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