Letters to the Editor

Effect of certain neuromuscular blocking agents on dexamphetamine toxicity in aggregated and isolated mice

SIR,—Since the observation by Gunn & Gurd (1940) that amphetamine is several times more toxic to aggregated than isolated mice, several factors have been found to influence this effect. The major factors are strain and body weight of mice (Chance, 1947; Fink & Larson, 1962), environmental temperature (Höhn & Lasagna, 1960; Askew, 1961; Fink & Larson, 1962; Wolf & George, 1964), noise (Chance, 1946, 1947; Cohen & Lal, 1964), electrical stimuli (Weiss, Laties & Blanton, 1961) and artificially induced aggressive behaviour (Consolo, Garattini & Valzelli, 1965). Greenblatt & Osterberg (1961) attributed the enhanced toxicity of amphetamine aggregation to the enhanced body movements of the mice. Hardinge & Peterson (1963, 1964) reported that amphetamine is as toxic to isolated mice forced to exercise as it was to aggregated mice.

It was reasoned that, if excessive body movements following amphetamine aggregation was a factor responsible for the enhanced lethality, it should be possible to counteract it by pharmacologically induced reduction in the body movements. This aspect was examined by using those neuromuscular blocking agents which act peripherally—(+)-tubocurarine, suxamethonium and gallamine triethiodide—to overcome the excessive movements.

Male albino mice, 25–33 g, were given the drugs or saline injected in 0·01 ml/g body weight. Aggregated mice were placed in plastic cages which allowed 25 cm^2 floor space per mouse, and isolated mice were placed, one mouse per cage with 200 cm^2 floor space. All experiments were made in an air conditioned room at 22–23°.

TABLE 1. INFLUENCE OF NEUROMUSCULAR BLOCKING AGENTS ON DEXAMPHETAMINE TOXICITY IN AGGREGATED AND ISOLATED MICE

Drugs	Aggregation 5 mg/kg dexamphetamine i.p. 10 min later		Isolation 10 mg/kg dexamphetamine i.p. 30 min later	
	No. dead/No. used	% Mortality	No. dead/No. used	% Mortality
Control (Saline)	18/36	50	2/20	10
Tubocurarine 400 µg/kg, s.c. ..	6/12	50	2/10	20
Suxamethonium 2 mg/kg, s.c. ..	7/12	66	1/10	10
Gallamine triethiodide 5 mg/kg, s.c.	5/12	41	0/10	0

From the results of Table 1 it is seen that tubocurarine suxamethonium and gallamine triethiodide do not appreciably alter the lethality of mice in amphetamine aggregation. These results do not, therefore, lend support to the view that reduction in motor activity leads to a decrease in amphetamine aggregation toxicity.

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The spirally cut tracheal strip preparation

SIR,—Castillo & DeBeer (1947) described the tracheal chain preparation for investigating the *in vitro* action of drugs on the tracheal muscle of small laboratory animals. Modifications of this method have since been introduced by Akcasu (1952) and by Foster (1960). The original method is unsatisfactory in that the magnitude of recorded responses is small, and preparation of the chain is laborious. The subsequent modifications have overcome the first objection, but they have not eliminated the tedious preparation of a tracheal chain. The guinea-pig spirally cut tracheal strip, described here, is quickly and simply prepared, and is suitable for the investigation of spasmogens and their inhibitors.

Male guinea-pigs, 350 to 500 g, were used. The excised trachea was placed on gauze soaked with Krebs-Henseleit solution and cleaned of extraneous tissue. It was then cut, one end to the other, in spiral fashion such that 2 or 3 segments of cartilage separated each turn of the spiral. The entire strip can be used, or it can be cut in half thus providing two preparations from one donor. Each strip was suspended in a tissue bath containing Krebs-Henseleit solution at 38° aerated with 95% oxygen and 5% carbon dioxide. The strip was attached to a Grass FT.03 transducer, and contractions were recorded with a Grass polygraph. The tracheal strip contracted against an imposed tension of 5 g; less tension resulted in inconsistent results. Strips were left in the bath for 1 hr before starting an experiment; during this time the bathing medium was changed 3 to 4 times. Contractions to each spasmogen were elicited at 15 min intervals.

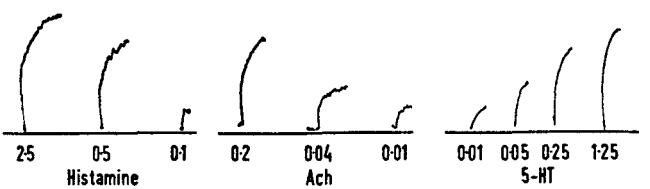

FIG. 1. Contractions of guinea pig spirally cut tracheal strips to: histamine, acetylcholine (Ach), 5-hydroxytryptamine (5-HT). Numbers refer to bath concentrations of spasmogens in μg/ml.

Fig. 1 shows responses of tracheal strips to histamine, acetylcholine, and 5-hydroxytryptamine. The strips were more sensitive to acetylcholine than to histamine. This agrees with Carlyle's (1963) finding with the guinea-pig tracheal chain, and with Jamieson's (1962) results with the isolated intact trachea. It is not in accord with Akcasu's (1952) finding that the tracheal chain is equally sensitive to histamine and acetylcholine. The sensitivity of the spirally cut tracheal strip to 5-hydroxytryptamine was approximately the same