Letters to the Editor

Sensitivity of aggressive mice to centrally acting drugs

SIR,—Aggressiveness in normal laboratory mice can be induced by isolating them in individual cages for a suitable period of time (Yen, Stanger & Millman, 1959). Recently it was demonstrated that the toxicity of dexamphetamine is much increased in aggressive mice compared with normals, whether the animals are grouped or isolated (Consolo, Garattini & Valzelli, 1965).

Dexamphetamine, beside its activity on the central nervous system, is known to exert peripheral sympathomimetic cardiovascular effects. By contrast, fencamfamin, an amphetamine-like drug, while centrally stimulant (Hotovy & others, 1961), is without any peripheral sympathomimetic activity (Brittain, Jack & Spencer, 1964). We now report that this substance also is more toxic in aggressive animals.

Male Swiss albino mice, about 20 g, were kept six per Makrolon cage with a floor surface of 40 cm^2 at room a temperature of 22° and a relative humidity of 60%. Aggressive mice were obtained by individual isolation for a period of 4 weeks in single cages of the same size with opaque walls.

The drugs were given intraperitoneally to 48 normal mice grouped and to 48 aggressive mice grouped and the toxicity was calculated after 24 hr according to the method of Litchfield & Wilcoxon (1949). The LD50 (95% confidence limits) mg/kg were for dexamphetamine* 9·0 (8·0–12·0) and 3·7 (2·6–5·3) for the normal and aggressive mice respectively. Corresponding figures for fencamfamin were 52·2 (37·3–73·1) and 8·7 (5·1–14·7).

It is evident that fencamfamin is more toxic in agressive mice; the toxicity of amphetamine increases 2·4 times and that of fencamfamin about six fold.

A similar sensitivity is seen with a barbiturate drug (pentobarbitone) in aggressive mice. Table 1 presents the results obtained measuring the sleeping time after pentobarbitone alone or in combination with chlorpromazine.

TABLE 1. POTENTIATION OF BARBITURATE SLEEPING-TIME (PENTOBARBITONE 55 MG/KG/I.P.) BY CHLORPROMAZINE (2·5 MG/KG/I.P.) IN GROUPS OF 16 NORMAL AND AGGRESSIVE MICE

Treatment	Sleeping-time (in min ± s.e.)	% of sleeping animals
Controls (normal mice)	23′ ± 2′.30″	83
Controls (aggressive mice)	10′ ± 3′.25″	16
Chlorpromazine (normal mice) ..	84′ ± 1′.50″	100
Chlorpromazine (aggressive mice) ..	39′ ± 2′.15″	100

Pentobarbitone alone is less effective in aggressive than in normal mice and chlorpromazine induces a prolongation of pentobarbitone sleeping time more marked in normal than in aggressive mice.

The results reported here show that aggressive animals have a peculiar sensitivity to drugs acting on the central nervous system.

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* Data from Consolo & others (1965).

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The nature of the antagonism of bronchospasm in the guinea-pig by ascorbic acid

SIR,—In a Communication presented to the British Pharmacological Society in July 1964, we showed that ascorbic acid exerted a protective action on anaphylactic shock in the guinea-pig (Dawson & West, 1965). This result has recently been confirmed by Guirgis (1965). We have now found that this protective action seems to be a direct effect of ascorbic acid on the bronchial muscle.

Guinea-pigs were anaesthetised with chloralose (100 mg/kg) intraperitoneally, and artificially ventilated with a constant volume pump through a tracheal cannula. Bronchoconstriction was measured from changes in ventilation pressure in the trachea using a transducer system, and arterial blood pressure was recorded from the external carotid artery. Drugs were injected into the exposed jugular vein. Similar degrees of bronchoconstriction were produced by 5-hydroxytryptamine (5 μg), bradykinin (10 μg), and histamine (5 μg), and all these actions were prevented by previously injecting ascorbic acid (500 mg/kg) in neutral solution within 10 min of the injection of the spasmogens (see Fig. 1).

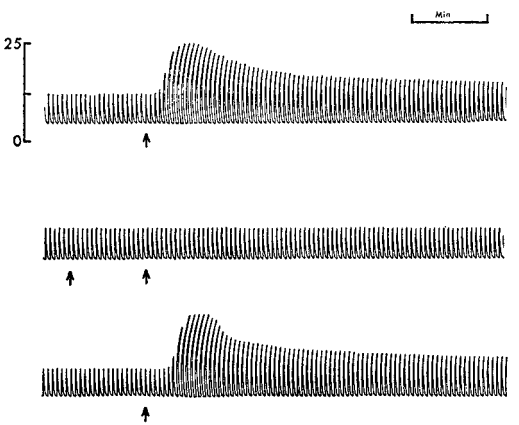

FIG. 1. Record of tracheal pressure of an anaesthetised guinea-pig. Upper tracing, response to histamine (5 μg); middle tracing, effect of ascorbic acid (500mg/kg) given at the first arrow one min before the next histamine dose; lower tracing, response to histamine 30 min later. Time in min. Pressure in mm Hg.

Smaller doses of ascorbic acid (100 and 200 mg/kg) proportionately reduced the actions. Doses of adrenaline (1–5 μg) also abolished the bronchoconstrictor action of the three spasmogens, but adrenaline raised the arterial blood pressure whereas ascorbic acid did not. Pretreatment of the animals with pronethalol