2-Bromo-lysergic acid diethylamide hydrogen tartrate (BOL 148) (2–4 mg/kg) produced drowsiness, hypotonia and excessive salivation for 20–60 min. The highest dose suppressed both the myoclonic and the paroxysmal e.e.g. responses to ILS.

Methergoline (FI 6337), a powerful central antagonist of 5-hydroxytryptamine (Beretta, Ferrini & Glässer, 1965; Mawson & Whittington, 1970), at 4 mg/kg produced some hypotonia and increased salivation. Myoclonic responses to ILS were reduced 15 min after the injection but cortical spikes and waves persisted.

LSD, psilocybin and dimethyltryptamine have complex effects on activity in the visual pathways which may contribute to the observed change in responsiveness to ILS.

Among the lysergic acid derivatives which antagonize some of the actions of 5-hydroxytryptamine (methysergide, BOL 148 and Methergoline), the reduction in myoclonic response to ILS correlates with the degree of sedation and loss of muscle tone produced by the drug. However, the possibility that both groups of compounds act by a common mechanism cannot yet be excluded.

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Acute toxicity of heroin, alone and in combination with cocaine or quinine

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Cherubin (1968) states that more than 70% of deaths in heroin-dependent persons in New York are due to " overdose—in reality sudden collapse after intravenous injection with the major finding at autopsy being pulmonary oedema ". Fulton (1965) showed by analysis of confiscated drug samples that adulterants are commonly present in illicit samples of heroin. Quinine is one such substance. Addicts frequently combine heroin with cocaine. Heroin, heroin with cocaine, and heroin with quinine were dissolved in a solution of sodium chloride (0·9% w/v). The acute toxicity was determined by injection into the tail vein of male white mice of 20 g weight, kept at 30° C, at a rate of 0·1 ml/min until fatal collapse occurred. Control mice were injected with an equal volume of saline and killed by dislocation of the neck. The lungs were removed from all animals, blotted dry and weighed.

The acute toxicity of heroin hydrochloride (calculated as base) was 56·7± 2·4 mg/kg (mean±S.E. of mean) and the lung weight of 5·59±0·06 g/kg did not differ from that of controls. The mean lethal dose for cocaine hydrochloride (calculated as base) was 30·7±1·7 mg/kg and quinine hydrochloride (calculated as base) 137·8±3·3 mg/kg.

The acute toxicity of mixtures was determined by the method of Chen & Ensor (1953, 1954) in which the toxicity of solutions containing the two drugs in fixed percentages of their respective lethal doses is determined. Low proportions of cocaine were found to antagonize the lethality of high proportions of heroin, while high proportions of cocaine potentiated the lethality of low proportions of heroin. Addicts generally use a mixture of equal parts by weight; in mice the lethality of heroin in this combination was potentiated. The lung weights of treated mice did not deviate from normal. The lethality of combinations of heroin with quinine was chiefly additive. Quinine by itself caused a significant increase in lung weight over controls ($P<0{\cdot}001$) and this effect persisted and was sometimes enhanced when it was given with heroin. The gross appearance of the lungs was that of congestion rather than that of exudative pulmonary oedema.

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Alprenolol and propranolol in hyperthyroid tachycardia

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β-Adrenoceptor blockade with propranolol reduces the heart rate of hyperthyroid patients. Dose response curves for pronethalol, oxprenolol and practolol are markedly different from that for propranolol; however, this could be due to their intrinsic sympathomimetic activity to which hyperthyroid patients may be particularly susceptible (Turner & Hill, 1968). Consistent with this suggestion is the recent demonstration (Ekue, Lowe & Shanks, 1970) that MJ1999, which is free of intrinsic sympathomimetic activity, produces a dose-dependent slowing of hyperthyroid tachycardia.

TABLE 1. *Comparison between effects of propranolol, alprenolol and normal saline on hyperthyroid tachycardia*

Treatment	Mean difference in fall in heart rate %	S.E.	*t*	*P*	Difference in mean heart rates (beats/min) after treatment	S.E.	t	*P*
Ten patients								
Propranolol 5 mg *v.* alprenolol 5 mg	2·0	1·40	1·40	N.S.	5·5	2·28	2·41	$<0{\cdot}05$
Propranolol 10 mg *v.* alprenolol 10 mg	6·0	1·34	4·47	$<0{\cdot}01$	8·0	2·93	2·73	$<0{\cdot}05$
Propranolol 10 mg *v.* propranolol 5 mg	3·8	1·82	2·09	$\simeq 0{\cdot}05$	5·0	1·80	2·77	$<0{\cdot}02$
Alprenolol 10 mg *v.* alprenolol 5 mg	0·2	1·77	—	N.S.	2·5	3·76	0·70	N.S.
Seven patients								
Propranolol 5 mg *v.* normal saline	10·4	2·51	4·16	$<0{\cdot}01$	9·4	5·2	1·8	N.S.
Alprenolol 5 mg *v.* normal saline	7·6	2·0	3·80	$<0{\cdot}01$	5·3	5·7	0·90	N.S.