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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$\beta$-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. |

Alprenolol has a β-adrenoceptive blocking potency similar to propranolol when administered intravenously, but possesses intrinsic sympathomimetic activity (Ablad, Brogard & Ek, 1967; Forsberg & Johnsson, 1967; Johnsson, Norrby & Sölvell, 1967). The effects of these two agents have been compared in ten patients with proven hyperthyroidism, all of whom had a heart rate of more than 90 beats/min at rest before the start of the investigation. Two doses of each drug (5 and 10 mg) were given intravenously to each subject, treatments being administered on different days in varying order, the smaller before the larger doses. In seven patients normal saline (5 ml) was also included among the treatments. A resting heart rate was determined by electrocardiogram for 5 min before, and every minute for 5 min and at 10 min after, each injection. Both drugs produced a significantly greater fall in heart rate than normal saline (Table 1), but although the 10 mg dose of propranolol produced a significantly greater fall than 5 mg, the effects of the two doses of alprenolol did not differ significantly from one another. The heart rate 10 min after injection was significantly lower after propranolol (10 mg) than propranolol (5 mg) or alprenolol (10 mg), and propranolol (5 mg) produced a significantly lower heart rate than alprenolol (5 mg). Neither drug produced an arrhythmia or increase in ectopic beats in any patients. These results are further evidence that β-adrenoceptor blocking drugs with sympathomimetic activity are inferior to a compound without such activity in the treatment of hyperthyroid tachycardia.

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## A comparison of the effects of propranolol and practolol on the exercise tolerance in angina pectoris

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β-Adrenoceptor blockade improves the exercise tolerance of patients with angina pectoris (Hamer & Sowton, 1966; Grant *et al.*, 1966; Birkett & Chamberlain, 1966; Wilson, Brooke, Lloyd & Robinson, 1969). Propranolol has β-adrenoceptor blocking and local anaesthetic properties either of which might be responsible for its action. With the development of practolol, a β-adrenoceptor blocking agent devoid of local anaesthetic properties, an assessment of the relative importance of these two actions in the amelioration of the symptoms in angina pectoris can be made.

Six patients with long-standing angina pectoris were exercised on a treadmill to assess the effect of intravenous administration of propranolol (0·15 mg/kg), practolol