The effect of pregnancy on the central sympathetic components in angiotensin-induced hypertension

SIR,—Numerous reports have demonstrated that angiotensin has less pressor activity in pregnant than in non-pregnant animals. Mackaness (1959) observed that pregnant rats are insensitive to pressor doses of renin. Also, McCaa, Douglas & Richardson (1966) found the pressor action of angiotensin to be decreased in pregnant dogs. Others found pregnant women resistant to the pressor effects of angiotensin (Chesley, Wynn & Silverman, 1963; Abdul-Karim & Assali, 1961), although renin levels appear to be increased during pregnancy (Brown, Davies, Doak, Lever & Robertson, 1963).

There are also numerous reports which suggest that an intact sympathetic nervous system is required for optimal angiotensin pressor activity, and several laboratories have reported that the peptide may generate increased sympathetic activity by a central mechanism (Buckley, Bickerton, Halliday & Kato, 1963; Benetato, Haulica, Uluitu, Bubuianu, Mocodean, Stefanescu & Suhiciu, 1964; Laverty, 1963; Benelli, Della Bella & Gandini, 1964).

We have observed that the injection of angiotensin into the perfused lateral ventricles of cats anaesthetised with chloralose consistently produces sympathetic activation via a central mechanism (Severs, Daniels, Smookler, Kinnard & Buckley, 1966; Smookler, Severs, Kinnard & Buckley, 1966). We have injected angiotensin, 4 μg, into the perfused lateral ventricles (Bhattacharya & Feldberg, 1958) of approximately 40 cats. Nine of these animals were either in a late stage of pregnancy or were lactating and all were hyporesponsive to the central pressor effect induced by angiotensin. The difference between the mean pressor response of the nine pregnant or lactating cats (19/12 $\pm$ s.e. 2/1) and the mean pressor response of nine cats randomly selected from the non-pregnant animals (58/44 $\pm$ s.e. 5·5) was statistically highly significant ($P = <0{\cdot}001$).

This observation indicates that the decreased pressor response to angiotensin during pregnancy may be due, at least in part, to a decreased sympathetic component in the overall angiotensin effect.

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Rabbit reactivity to cannabis preparations, pyrahexyl and tetrahydrocannabinol

SIR,—Recent work on the chemistry of cannabis constituents and synthesis of tetrahydrocannabinols (Gaoni & Mechoulam, 1965; Taylor, Lenard & Shvo, 1966) will certainly renew an interest in their pharmacological activities, relative potency and stability. Among the biological tests so far proposed for cannabis and related principles, the abolition of the rabbit blink reflex appears to be one of the more sensitive (Gayer, 1928). We believe this test to be suitable for the estimation of one of the central actions of marihuana.

The assay is made in groups of 3–6 rabbits repeatedly injected with a preparation until the blink reflex is completely abolished. In preliminary tests a rough estimate of the potency is made and less reactive animals are discarded. The selected rabbits are restrained in wooden cages, with the head out, and maintained in a noiseless room. The test solution is made in saline with polysorbate 80 and the emulsion slowly injected into the ear vein. Twenty stimuli in each eye are made with a horse hair at 10 min intervals and the number of injections (0·2 ml/kg each) to completely abolish the blink reflex in both eyes is determined. For the estimation of the relative potency of the unknown preparation in terms of a standard, two groups of at least 6 animals each should be employed.

The dried and powdered flowering tops and leaves of the plant cultivated in north-east Brazil or in the neighbourhood of these laboratories were extracted with light petroleum for 4–6 hr. The extract was filtered through activated charcoal, washed with water and evaporated to dryness. The residue was dissolved in acetone and kept in the refrigerator overnight to separate wax constituents. After acetone evaporation the crude resin was dissolved in light petroleum and chromatographed on an alumina column. Elution with light petroleum, light petroleum with benzene, benzene, and benzene with sulphuric ether afforded fractions which were examined in a Beckman DU spectrophotometer at 250 and 280 mμ. Details and properties of the main components are given elsewhere (Valle & Hyppolito, 1964).

The most active fractions obtained after chromatography on alumina columns were those designated Cr19Fr10 and Cr23Fr14. Besides these cannabis preparations, synthetic samples of pyrahexyl and tetrahydrocannabinol (THC) were also assayed.

A sample of cannabis crude resin (0·8 mg/ml) was assayed against THC (0·08 mg/ml) as standard. The results (mg/kg $\pm$ s.d.) were 0·107 $\pm$ 0·013 (6 animals) and 1·143 $\pm$ 0·335 (6 animals) respectively and indicated a relative potency of 0·093 and that the solutions tested did not differ significantly in their activities ($F = 0{\cdot}105$, $P < 0{\cdot}05$). Then, by our procedure, the selected cannabis