formed radiochemically, using ^{3}H-tyramine as substrate. NCR was estimated both fluorometrically and in the spectrophotometer.

Both MAO and NCR were found to increase with the age of the animal which in the age groups studied, closely paralleled the increase in the weights of the hearts. Following adrenalectomy there was a further increase in enzyme activity superimposed upon that due to the growth of the animal. This increase reached a maximum 14 days after operation. The MAO remained at this level for at least a further 14 days, but the NCR activity began to fall towards normal within a week.

The half-life of the MAO in the hearts of both adrenalectomized and normal animals was measured by irreversibly inhibiting the enzyme with pargyline (25 mg/kg, S.C.) and following the synthesis of new enzyme over a period of several days. Three groups of adrenalectomized rats were used together with matched controls. The first group, with a mean body weight of 155 g, were given pargyline immediately after operation. The half-life of the MAO was 6·2 days compared with 6·7 for the controls. The second group were pargyline treated 13 days after adrenalectomy. The MAO half-life was now 10·1 in the operated animals compared with 10·2 for the controls, for a mean body weight of 230 g. In the third group, with a mean body weight of 340 g, the MAO half-lives were 15·4 and 17·6 days in adrenalectomized and control animals respectively. At no time was there a significant difference in the half-life of the enzyme between operated and control rats.

Calculations of the half-lives of both MAO and NCR from the changes in enzyme activity following adrenalectomy gave values of 6·3 and 6·5 days respectively for the two enzymes in animals weighing 155 g. The breakdown of NCR calculated from its return to the normal level gave a half-time of 11·5 for rats weighing 260 g. All values obtained for the half-lives of both enzymes showed a close linear relationship to either the body weight or to the heart weight of the animals.

As the rats grow older, the rate of destruction of both MAO and NCR decreases, which may account for the observed increase in enzymic activity seen with age. Adrenalectomy has no apparent effect upon this ageing process.

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Catecholamine induced contractures in denervated muscle

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Chronically denervated skeletal muscle has been shown to produce contractures in response to applied catecholamines both *in vivo* (Bowman & Raper, 1965;

Turkanis, 1969) and *in vitro* (Bhoola & Schachter, 1961; Paterson, 1963). In innervated muscle catecholamines do not cause contractures but indirectly affect evoked twitch tensions through both a pre- and a post-synaptic action (Bowman & Raper, 1966; Kuba, 1970). Following denervation, mammalian skeletal muscle also produces a contracture in the presence of acetylcholine, and it has been demonstrated that this response is the result of the development of cholinergic receptors over the entire muscle fibre surface, a process believed to be linked to protein synthesis (Axelsson & Thesleff, 1959; Grampp, Harris & Thesleff, 1972). The present experiments have been designed to investigate whether a similar development of adrenergic receptors can explain the catecholamine evoked contracture of denervated skeletal muscle.

Our results show that denervated mouse diaphragm regularly contracts to the catecholamines (−)-adrenaline, (−)-noradrenaline and (±)-isoprenaline, (4×10^{-7}–4×10^{-6}M) in mammalian Ringer solution at 37° aerated with 5% carbon dioxide in oxygen. The denervated muscle failed to contract in the presence of histamine, 5-hydroxytryptamine, bradykinin and vasopressin.

The appearance of the response to catecholamines occurs 2–3 days after section of the motor nerve, and reaches a peak within 10–14 days; however, the response is absent in tissues denervated for periods longer than 90 days. This is in contrast to the development of acetylcholine sensitivity, which develops over a similar period of time, but which is still evident several months after denervation.

The development of catecholamine sensitivity can be prevented by injecting the animals intraperitoneally with the protein synthesis inhibitor actinomycin D (0·5 mg/kg) within the first two days after nerve section.

The response of the denervated muscle to catecholamine was unaffected by (+)-tubocurarine and atropine in concentrations which block the acetylcholine response. However, the contracture was inhibited by lowering the temperature by 2:4 dinitrophenol (10^{-6}M), KCN (10^{-6}M), ouabain (10^{-4}M) and strophanthin k (10^{-4}M), all of which had no effect on the response of the muscle to acetylcholine.

These results suggest that synthesis of adrenoceptors probably occurs after muscle denervation, but that contracture of the muscle, unlike that produced by acetylcholine, is mediated via an intracellular process. Experiments are in progress to determine whether this process is electrogenic.

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