SUMMARY AND CONCLUSION
In anaesthetized rats oxotremorine produced hypotension and bradycardia but this effect was abolished by pretreatment with atropine methyl nitrate which does not pass the blood brain barrier. This was indicative of a peripheral site for the cardiovascular action of the drug. Anti-histaminics like mepyramine and ganglion-blocking agents failed to abolish the hypotensive effect. High doses of oxotremorine following atropine produced a hypertensive effect. The participation of $\alpha$-adrenoceptor in the pressor response to oxotremorine was evident from the blocking of the effect by dibenzyline. The vasopressor effect of oxotremorine was inhibited by pretreatment with bretylium or guanethidine. The pressor effects persisted to the extent of 33.4% after ganglionic blockade, suggesting the locus of action to be either the ganglia or the central nervous system. The participation of the adrenal gland was suggested by the abolition of the response in adrenalectomised animals, and a central mechanism by the absence of the response in pithed rats. These experiments thus showed that the vasopressor effect of oxotremorine is mediated through a central mechanism bringing about liberation of noradrenaline from the adrenal medulla. This was confirmed by the diminution
of the response by depletion of tissue catecholamine stores by reserpinisation. The role of an indirect mechanism was also supported by the observation that the pressor response was tachyphylactic in nature.

The facilitation of responses to sympathetic stimulation by oxotremorine was found to be more marked in hypogastric-nerve vas deferens preparations than in transmurally stimulated vas deferens, confirming the ganglio excitatory effect of oxotremorine. In these experiments oxotremorine had no influence on the adrenergic receptors. The liberation of noradrenaline from tissue storage sites was evidenced by the failure of oxotremorine to produce sympathetic facilitation in reserpinised preparations. This was also confirmed by the development of partial tachyphylaxis of the facilitatory effect on repeated administration. The results indicate that oxotremorine may cause sympathetic activation through indirect release of transmitter in addition to its centrally mediated effect.

To examine the role of the cholinergic link in the facilitatory effect of oxotremorine on sympathetic responses, the interaction between oxotremorine and hemicholinium-3 (HC-3) was investigated. Prior incubation with HC-3 antagonised the facilitatory effect, indicating cholinergic mediation.
The neuromuscular blocking effect of oxotremorine was found to be potentiated by physostigmine. Oxotremorine was also found to cause a fall in the acetylcholine level of peripheral tissues. These observations and the blocking of the neuromuscular effect of oxotremorine by drugs like morphine which reduce acetylcholine release and HC-3 which inhibits its synthesis suggest that the action of oxotremorine at the myoneural junction may be mediated by an increased release of acetylcholine.

*C_{10}Dichol* was found to antagonise the oxotremorine and acetylcholine induced contraction of guineapig ileum by 62.6 and 41.5 percent. HC-3 also antagonised the spasmogenic effect of oxotremorine more markedly than that of acetylcholine. In rat colon preparations *C_{10}Dichol* antagonised oxotremorine induced contraction but was without effect on the response to acetylcholine. HC-3 antagonised the response to oxotremorine more markedly than that to acetylcholine. In preparations of rat urinary bladder *C_{10}Dichol* and HC-3 antagonized the response to oxotremorine while potentiating that to acetylcholine. On isolated rabbit atrium *C_{10}Dichol* completely abolished the negative inotropic effect of oxotremorine, but that of acetylcholine only partially. These observations taken together suggest that the mechanism of the peripheral parasympathomimetic effects of oxotremorine is an indirect one.
mediated through release of acetylcholine from the peripheral sites. It is of interest that the time course of increase in the level of acetylcholine in brain and decrease in peripheral tissues induced by oxotremorine corresponded to the development and duration of the pharmacological effects.

In the present work oxotremorine was shown to increase the serotonin level in the intestine but had no effect on the brain serotonin level. The increase in serotonin level of peripheral tissues suggests a role for serotonin in the peripheral autonomic effect of oxotremorine. Oxotremorine produced a marked fall of histamine concentration in blood and tissues after an initial rise in blood histamine level. However the present results do not permit the postulation of an independent role for histamine in the parkinsonimimetic action of oxotremorine, though they indicate a partial role for the amine in the complex biochemical events involved.

The glycogenolytic effects of oxotremorine on muscle and liver were found to be maximal at 40 min after administration. The contribution of this metabolic effect to the tremorigenic action of oxotremorine however requires further study.
The antagonism of oxotremorine-induced tremor by HC-3 in adult mice indicating that beside the central cholinergic system the peripheral cholinergic system is also involved in the mechanism of tremorogenic action of oxotremorine. The antagonism of the tremor effect of oxotremorine by morphine which was found to inhibit muscarinic effect of oxotremorine at smooth muscle and neuromuscular blockade at skeletal muscle confirmed the participation of cholinergic system in tremorogenic property of the drug. The antagonism of oxotremorine-induced tremor by d-tubocurarine also indicated the involvement of a skeletal myoneural effect in the production of tremor by oxotremorine.

To sum up, the pharmacological effect of oxotremorine consisted in the overactivation of sympathetic and parasympathetic activity and a depolarising type of skeletal neuromuscular blockade. The antagonism of the tremorogenic effect of oxotremorine by drugs which reduce or abolish the sympathetic, parasympathetic and skeletal myoneural blocking effect of the drug suggests an adrenergic as well as cholinergic link in the tremor response as well as some contribution of the effects at skeletal myoneural junctions in the tremorigenic effect of oxotremorine.