TABLE 1. *ED50 in mg/kg against*

Drug	Normal strain	Drug resistant strain
Diminazene diaceturate	2·77 to 10·26	>400*
Amicarbalide diisethionate	0·17 to 0·58	>100*
Imidocarb dihydrochloride	0·03 to 0·09	> 80*

* Maximum tolerated dose.

Rate of development. Analyses of the dose levels used and the time (from the commencement of treatment) at which they were given were made by plotting both sets of figures on arithmetic and logarithmic scales. Only when the logarithm of the dose level was plotted against the logarithm of the time was a straight line obtained, if the first few weeks of treatment, when the dose levels were within the limits of the ED50 of the normal strain, are ignored. The slope of this line, calculated from the usual regression line formula, is different for each drug, giving a figure which indicates the ease with which resistance to the drug can be produced in this parasite.

TABLE 2. *ED50 against drug resistant strains, as a factor of that of the normal strain*

Strain: / Drug	Normal	Diminazine resistant	Amicarbalide resistant	Imidocarb resistant
Diminazene diaceturate	1	>65*	15	15
Amicarbalide diisethionate	1	20	>400*	15
Imidocarb dihydrochloride	1	50	100	>1,000*
Quinuronium sulphate	1	>60*	> 60*	>60*
Phenamidine diisethionate	1	>15*	> 15*	>15*
Gloxazone	1	0·7	0·8	0·3
Aureomycin	1	1	1·2	1·4

* ED50 is greater than the maximum tolerated dose.

The slopes of these lines for Diminazene, Amicarbalide and Imidocarb are in the ratio of 3 : 4 : 5.

Cross-resistance patterns. Babesicidal compounds including Diminazene, Amicarbalide and Imidocarb were assayed against the normal, the Diminazene resistant, the Amicarbalide resistant and the Imidocarb resistant strains of *B. rodhaini* in rats. The ED50 for each drug against the three resistant strains was calculated and compared with its effect against the normal drug sensitive strain of *B. rodhaini.*

The distribution of catecholamines in the nervous system of an Octopoda mollusc

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Noradrenaline and dopamine are known to be present in discrete areas of the vertebrate brain (Vogt, 1954; Bertler & Rosengren, 1959) and thought to be neurotransmitters. The presence of catecholamines has also been demonstrated in the nervous tissue of some Octopoda (Bertaccini, 1961; Cottrell, 1967) but their distribution is not known.

The nervous tissue of *Eledone cirrhosa* was subdivided into the regions shown in Table 1. The parts taken are defined by macroscopic criteria though they are easily

reproducible by dissection. The nomenclature proposed by Boycott & Young (1955) for the nervous tissue of cephalopods was used. The catecholamines were separated by paper chromatography and estimated by a fluorimetric method (Laverty & Sharman, 1965).

Table 1 shows that the highest concentration of dopamine was found in the optic lobes and next in a region which included the superior buccal and posterior buccal lobes. The highest concentration of noradrenaline was also found in this last region. In contrast, in the neighbouring median inferior frontal lobe the amount of catecholamines found to be present was very small and near to the limit of sensitivity of the method. In the suboesophageal ganglia the highest concentration of dopamine was found in its anterior portion, while the noradrenaline concentration was the same in all three subdivisions made. In all the regions examined the concentration of dopamine was higher than that of noradrenaline. Adrenaline was not found to be present in *Eledone* nervous tissue. One day after the administration of reserpine (1 mg/kg) the concentration of dopamine in the optic lobe was decreased to about 40% of its normal value while that of noradrenaline was less modified. The concentration of catecholamines in the supraoesophageal and suboesophageal ganglia was less affected by the administration of reserpine.

TABLE 1. *Concentration of dopamine and noradrenaline in nervous tissue of* Eledone cirrhosa

	Approx. wt. of tissue (mg)	Dopamine (μg/g)	Noradrenaline (μg/g)
		Supraoesophageal ganglia	
Vertical lobe	12·3	1·27±0·05 (6)	0·50±0·07 (6)
Median superior frontal lobe	7·4	1·76±0·34 (6)	0·50±0·03 (6)
Median inferior frontal lobe	5·1	1·31±0·12 (4)	<0·20 (4)
Superior buccal lobe and posterior buccal lobe	10·5	5·34±0·91 (4)	3·49±0·11 (4)
Dorsal basal lobe, median basal lobe and anterior basal lobe	42·7	2·50±0·10 (6)	1·64±0·12 (6)
Optic lobe	376·4	8·53±0·78 (4)	2·03±0·15 (4)
		Suboesophageal ganglia	
Anterior	34·0	3·55±0·31 (3)	0·76±0·10 (3)
Median	31·9	1·00±0·09 (3)	0·63±0·19 (3)
Posterior	56·1	1·57±0·31 (3)	0·72±0·09 (3)

Values are means (±S.E.) in μg/g of fresh tissue and are not corrected for recovery.
Number of experiments in parentheses.

The presence of dopamine and noradrenaline in *Eledone* nervous tissue suggests that these substances may also have a function in invertebrate neurotransmission. A recent investigation of the ultrastructure of the vertical lobe showed that in some nerve terminals there are present dense-cored vesicles (Gray, 1970), which is in agreement with the finding of catecholamines in that lobe.

I thank Professor J. Z. Young for his advice and interest throughout this work. This work was supported by a grant from the Medical Research Council.

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The peripheral parasympathetic innervation of the cat lacrimal gland

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The lacrimal nerve, a branch of the trigeminal, is mainly a sensory nerve but it also conveys secretory fibres to the lacrimal gland (Demtschenko, 1872; Tepliachine, 1894). There is little doubt that these cholinergic fibres (Elsby & Wilson, 1967) are parasympathetic (Botelho, Hisada & Fuenmayor, 1966). They are believed to leave the skull in the Vidian nerve and relay in the sphenopalatine ganglion, from which they enter the infraorbital nerve, a continuation of the maxillary, to be distributed to the lacrimal gland by means of the lacrimal or zygomatic nerves (Jendrassik, 1894; Golding-Wood, 1964). This hypothesis has been examined in the anaesthetized cat.

The Vidian nerve was exposed by resection of the zygomatic arch, the ramus of the mandible and part of the infra-orbital region of the malar bone. The sphenopalatine ganglion and the Vidian nerve were located underneath the most medial aspect of the globe, lying on the muscles immediately above the hard palate. Supramaximal stimulation of the intact Vidian nerve produced an ipsilateral secretion which was collected from the superior conjunctival fornix by sheathed filter paper strips. This secretion was not abolished by section of the infra-orbital nerve. The secretions produced at different frequencies of stimulation of the Vidian nerve were greater than those obtained by stimulating the cut peripheral end of the lacrimal nerve; moreover, stimulation of the intact Vidian nerve still produced a secretion after lacrimal nerve section. The remaining secretion did not come from the lacrimal gland, for it was still obtained after removal of this gland. It was, however, abolished by atropine. In other experiments, the cut central end of the Vidian nerve was stimulated with the nictitating membrane clipped to occlude the ducts of the nictitating membrane gland and the infra-orbital nerve sectioned. In these conditions stimulation before and after removal of the lacrimal gland showed that the secretion originated entirely from the lacrimal gland.

Although lacrimal secretion produced by Vidian nerve stimulation could be due to activation of sensory or secretory fibres, the present investigations in the cat do not support the hypothesis that secretory fibres pass in the infra-orbital nerve to reach the lacrimal nerve. It is probable that the secretory fibres enter the lacrimal nerve proximal to the infra-orbital nerve. Investigations are in progress to determine the site of transfer.

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