nerve is thought to take place in the region of the sphenopalatine ganglion (Jendrassik, 1894). Recent observations (Arenson & Wilson, 1970) have shown that in the cat the secretory fibres do not run in the sphenopalatine and infra-orbital nerves to reach the lacrimal gland, as previously thought. In the current investigation, the role of the Vidian nerve and of the sphenopalatine ganglion has been examined in the anaesthetized cat to elucidate the parasympathetic pathway.

After bilateral cervical sympathectomy and removal of the nictitating membrane by cauterization, the brain stem was exposed by removing the occipital bone and cerebellum.

Supramaximal stimulation of the brain stem induced a secretion which was collected from the superior conjunctival fornix by sheathed filter paper strips. This secretion did not occur after removal of the lacrimal gland, showing that under the experimental conditions used, secretion was produced entirely by this gland. In further experiments, section of the Vidian nerve with the lacrimal gland intact reduced the secretion to amounts which were similar to the resting values. The secretion induced by brain stem stimulation could also be reduced or abolished by painting the sphenopalatine ganglion with a solution of nicotine (2%).

The results of this study show that the Vidian nerve contains secretory fibres which relay in the sphenopalatine ganglion. Since it has been shown that the Vidian nerve must be stimulated in a central direction to activate the lacrimal gland (Arenson & Wilson, 1970), it is concluded that the secretory fibres in this nerve must be postganglionic. The site at which these fibres transfer to the fifth nerve is central to the sphenopalatine ganglion. Experiments are in progress in an attempt to determine whether the site is intra- or extracranial.

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## The effect of isoprenaline on the responses of the guinea-pig isolated heart to vagal stimulation and to acetylcholine

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Guinea-pig isolated hearts with or without the right vagus nerve were used to study the effect of isoprenaline on the bradycardia elicited by vagal stimulation or by the addition of acetylcholine to the perfusate. The coronary vessels were perfused with a constant volume (7·0 ml/min) of McEwen solution at 29° C. The vagus nerve was stimulated supra-maximally with rectangular pulses of 1 ms duration at the following frequencies: 1, 2, 5, 10 and 20 Hz for 30 s. The heart rate was measured by recording the electrical activity of the sinus node through electrodes attached to the left atrium. Acetylcholine in increasing doses (0·2, 0·4, 0·8, 1·6 and 3·2 $\mu$g) was injected into the perfusion cannula.

Isoprenaline ($5–20 \times 10^{-9}$ g/ml) decreased the slowing of the heart response to vagal stimulation and to exogenous acetylcholine. The duration of action of this latter acetylcholine effect was shortened by isoprenaline. The $\beta$-adrenoceptor blocking agent 4-(2-hydroxy-3-isopropylaminopropoxy) indole (LB46) ($2 \times 10^{-8}$ g/ml) abolished the effect of isoprenaline in reducing vagal bradycardia. This seemed to exclude the possibility of the damage or fatigue of the vagus nerve as well as the exhaustion of the acetylcholine stores, provided that LB46 did not exert some unsuspected " facilitation " upon nerve activity or transmitter release. In control experiments in the absence of isoprenaline, there was no tachyphylaxis to acetylcholine, which accords with the view that the inhibition of the acetylcholine effect was due to isoprenaline.

**Acetylcholine receptors of invertebrate neurones**

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In this study we have compared the acetylcholine receptors in the nervous systems of three species. The neurones tested were the giant cells (Retzius, 1891) in the ventral nerve cord of *Hirudo medicinalis*, cells in the visceral ganglion of *Helix aspersa* and cells in the sixth abdominal ganglion of *Periplaneta americana*. Action potentials were recorded intracellularly by methods previously described (Kerkut & Walker, 1967; Kerkut, Pitman & Walker, 1969; Walker & Hedges, 1968). Drugs were applied either by addition to the bath or iontophoretically. The potencies of the agonists are expressed as equipotent molar ratios relative to the carbachol threshold. The drugs used were carbachol, acetylcholine (ACh), 1,1-dimethyl-4-phenylpiperazinium (DMPP), 4-(*m*-chlorophenylcarbamoyloxy)-2-butynyltrimethyl ammonium (McN-A-343), muscarone, nicotine and furmethide (furtrethonium).

In the snail there are two types of cell responsive to acetylcholine. Some neurones (called D cells) are depolarized and excited by acetylcholine, whereas other cells (called H cells) are hyperpolarized and inhibited by acetylcholine. Our results (Table I) suggest that each type of cell contains both muscarinic and nicotinic receptors, although McN-A-343 has little effect on D cells.

In the cockroach sixth abdominal ganglion all of the neurones tested were depolarized and excited by acetylcholine. Nicotinic agonists were powerful stimulants of these cells, but muscarinic agonists were less potent, indicating that the receptors are mainly nicotinic (Table 1).

In the Retzius cells of the leech the nicotinic agonists produced a depolarization similar to that produced by carbachol. In contrast the muscarinic agonists muscarone, furmethide and McN-A-343 caused inhibition when added in threshold amounts. In higher concentrations the muscarinic agonists sometimes produced excitation.

In all three species the effects produced by the iontophoretic application of carbachol were similar to those obtained when the agonist was applied by addition to the bath.