($P < 0.05$) but changes in BP, HR, SMVF and JVR were variable and insignificant ($P > 0.30$).

When secretin was infused intravenously in a dose of 0.5 U kg^{-1} min^{-1} to five preparations, the CFC rose by 61.6 ± 10.9% from 0.060 ± 0.009 to 0.095 ± 0.011 ml min^{-1} $mmHg^{-1}$ 100 g^{-1} ($P < 0.02$), and the JV rose by 0.83 ± 0.25 ml/100 g ($P < 0.05$). These infusions resulted in falls in BP (3.4 ± 1.2%), rises in HR (13.5 ± 5.0%), rises in SMVF (17.4 ± 7.2%) and reductions in JVR (16.4 ± 5.5%), changes which were consistent, but not statistically significant ($P > 0.05$). The effects of secretin at this dose on CFC and JV were not modified by pretreatment with hexamethonium (5 mg/kg, i.v.: three experiments) or propranolol (0.1 mg/kg, i.v.: three experiments).

On six occasions in three preparations, intravenous injections of 0.02 to 20.0 U/kg secretin resulted in dose-dependent transient reductions in JVR (maximum: −67.3 ± 3.0%) and increases in JV (maximum: +1.61 ± 0.27 ml/100 g). Doses above 0.5 U/kg additionally caused dose-dependent falls in BP and rises in HR.

As well as reducing small intestinal vascular resistance, intravenous secretin causes an increase in tissue volume over the same dose range, indicating dilatation of capacitance vessels (Folkow *et al.*, 1963). Low dose infusions increase CFC and JV without significant effects on other variables: the rise in CFC indicates either dilatation of precapillary 'sphincters', leading to an increased functional exchange vessel area, or an increased vascular permeability, mechanisms which are not separable by this technique.

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Some preservatives in eyedrop preparations hasten the formation of dryspots in the rabbit cornea

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Three factors are important in the maintenance of the tear film between the replenishing action of the blink. Its adherence to the cornea is aided (a) by the surface microplicae on the epithelial cells, (b) by the surface-tension lowering layer of conjunctival mucus which overlies the epithelium and (c) by an outer layer of oil (secreted by the Meibomian glands) which delays evaporation. Since surface-active substances are often used as preservatives in eyedrop preparations, these experiments were undertaken to examine the effect of such substances on the stability of the rabbit tear film.

Dutch rabbits were anaesthetized with halothane (3%) in nitrous oxide-oxygen (3 : 1). Saline (3 drops of 0.9% w/v) was applied to both eyes at zero time and the excess fluid removed. The time taken for the development of a dry spot on each cornea was measured and was taken as the 'start-control' value (each eye to act as its own control). The tear film was immediately restored by blinking the eyelids three times. Three drops of preservative solution (lowest concentration, in 0.9% saline or suitable vehicle) were then applied, excess fluid removed and the drying time measured again. This procedure was repeated for successive increases in concentration of the preservative solution. Finally, the cornea was irrigated with saline and the eyelids repeatedly blinked for 10 min, before another control determination was made ('end-control').

The start-control value (mean ± s.e. mean) was 151.4 ± 20.1 s (n = 81). Variation in control times from animal to animal greatly exceeded that between L and R eyes of each rabbit, while variation between start-control and end-control times was not statistically significant. Several preservatives, in concentrations equivalent to those used in eyedrop preparations, produced statistically significant hastening of the drying time: 0.01% (w/v) benzalkonium chloride (22.9% of start-control time); 0.03% n-propyl p-hydroxybenzoate (54.1%); 0.3% 2-phenylethanol (53.1%); 0.01% chlorhexidine (38.2). All of these substances produced dose-related decreases in drying time at the lower concentrations tested, in some cases down to one-hundredth the concentration indicated. Two mercurial preservatives, 0.3% (w/v) thiomersal and 0.1% phenylmercuric nitrate, caused no change in the rate of corneal drying.

A time-course study indicated that the effect of applying 2 drops of 0.01% benzalkonium chloride could still be detected 45 min afterwards. The presence of 0.01% benzalkonium chloride also significantly hastened the drying time following application of 0.3% or 1.5% (w/v) hydroxypropylmethylcellulose drops.

An approximate relationship was shown to exist between the ability of these substances to lower surface tension and to hasten the formation of dryspots on the cornea. This indicates that the mechanism of this effect may involve adsorption to, or solubilization of, either the conjunctival mucus layer or the oily Meibomian secretion.

The effect of melatonin on pinealectomy-induced hypertension in the rat

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Surgical removal of the pineal gland has been shown to elevate blood pressure in anaesthetized rats (Zanoboni & Zanoboni-Muciaccia, 1967) and a modest hypertension (20 mmHg) has been described in unanaesthetized rats after electrocoagulation of the pineal gland (Karppanen, Vapaatalo, Lahovarra & Paasonen, 1970). These authors suggest that an increased adrenal steroid level after pinealectomy contributes to the observed hypertension. Karppanen, Airaksinen & Särkimäki (1973) have proposed that melatonin and/or related pineal hormones may act as natural anti-hypertensive agents, possibly by stimulating central inhibitory adrenergic pathways.

In the present study the effect of melatonin administration on hypertension produced by electrolytic lesion of the pineal gland in the rat was investigated.

Male Sprague-Dawley rats (180-220 g), anaesthetized with pentobarbitone sodium (60 mg/kg i.p.), had a 21 g hypodermic needle positioned 2.0 mm vertically below the surface of the skull at lambda. A d.c. current of 40 mA passed between the needle and a negative electrode on the ear for 20 s was found to produce destruction of the pineal gland with minimal damage to surrounding cortical tissue. Destruction of the pineal gland was verified macroscopically in all animals at the end of the experiment. Sham-operated rats had identical electrode placement but no current was applied. Systolic blood pressure was measured indirectly from unanaesthetized rats using the tail-cuff method.

A modest, but statistically significant, hypertension (15-20 mmHg) was seen in the pinealectomized animals (n = 16), compared to sham-operated or unoperated controls, from 1 week after operation until at least 7 weeks. Melatonin administered in the drinking water [1 mg/ml in 1.25% ethanol vehicle started immediately after operation] prevented the emergence of pinealectomy-induced hypertension and significantly depressed the blood pressure to below that of vehicle-treated control animals. Replacement of drug treatment with vehicle alone resulted in the development of hypertension in these pinealectomized animals. Administration of melatonin to animals in which hypertension had become established resulted in a significant fall of blood pressure to below sham-operated levels after 2 weeks of treatment. It was estimated that the average daily intake of melatonin for each rat was approximately 100 mg/kg.

These results suggest that the hypertension caused by pinealectomy is, at least in part, due to the lack of normal melatonin secretion by the gland.

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