cytes the α-1,4-glucosidase activity varies with the pH-value, having maxima at pH 3.2, 4.5 and 6.2, we measured the variations of α-1,4-glucosidase activity with pH in 2 cases of POMPE's disease in adults.

Ensuring the diagnosis of POMPE's disease, we could not find α-1,4-glucosidase activity at pH 4,0 in the muscles obtained from the two male, non-related patients. The clinical features will be published elsewhere.

As can be seen from the Table, we found α-1,4-glucosidase activity at pH 4.0 and 4.5 in both the lymphocytes and leucocytes of the two patients. At these pH-values the α-1,4-glucosidase activity was measured by ILLINGWORTH-BROWN and ZELLWEGER[19] and by HUDGSON et al.[13]. The differences were more pronounced for the leucocytes (mixture of granulocytes and lymphocytes) than for the lymphocytes alone.

Studying the variation of activity with pH we obtained the results shown in the Figure. Only the curves obtained for the leucocytes are presented, but for the lymphocytes we obtained a similar picture. Perhaps the α-1,4-glucosidase activity of the leucocytes and the lymphocytes of the two patients with POMPE's disease at pH 4.0 and 4.5 may be explained as residual activity of the enzymes active at pH 3.2 and 6.2, whereas the enzyme with maximum activity at pH 4.5 seems to be absent or at least diminished in the white blood cells. In the muscles there was no activity at pH 4.0.

The results presented suggest that determination of the variation of α-1,4-glucosidase of leucocytes and lymphocytes with the pH of the assay is a useful tool in the diagnosis of POMPE's disease, especially when a muscle biopsy is rejected.

Zusammenfassung. Die Messung der Aktivität von α-1,4-glucosidase in Lymphozyten und Leukozyten in Abhängigkeit vom pH ergab bei 2 erwachsenen Patienten mit POMPE'scher Erkrankung Aktivitätsmaxima bei pH 3.2 und 6.2. Bei den Kontrollpersonen wurde ein weiteres Maximum bei pH 4,5 gefunden.

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Analysis of Vasodilatation in the Submaxillary Gland Using Potentiators of Acetylcholine and Kinins

The problem of the resistance of certain parasympathetic nerve effects to inhibition by atropine is unexplained. Perhaps the most classical example is the vasodilatation in the submaxillary gland of the cat and other mammals, which accompanies stimulation of the parasympathetic nerve, the chorda tympani. This has led to views that mechanisms other than cholinergic ones mediate the vasodilatation. Thus, HILTON and LEWIS[1-3] concluded that the enzyme kallikrein, via the release of kinin, is the mediator of this vasodilatation in the salivary and other glands. SCHACHTER et al.[4-6], however, hold the view that kallikrein plays little or no role, and suggest that this parasympathetic effect may be cholinergic despite its resistance to atropine. The possibility that it is mediated by an unknown neurotransmitter is difficult to exclude absolutely; in fact, it has recently been suggested[7] that the parasympathetic atropine-resistant contraction of the urinary bladder is due to the release of a purine nucleotide, possibly adenosine triphosphate.

A classical experiment demonstrating that acetylcholine is a parasympathetic transmitter at least to some cellular elements of the submaxillary gland was done in a simple but dramatic way by BABKIN et al.[8]. They showed that stimulation of the chorda tympani nerve in an eserinized cat produced a fall in the systemic arterial blood pressure after a delay which corresponded to the circulation time. This hypotensive effect was obtained only in the presence of eserine and was prevented by prior injection of atropine.

A group of peptides has recently been synthesized wich potentiates markedly the effects of kinins[9,10]. It now seemed possible to us, therefore, to perform experiments similar to those done by BABKIN et al.[8], but using a kinin potentiator, as well as eserine. Although we found one of these new compounds to be more effective in potentiating the hypotensive effect of bradykinin than eserine was in potentiating that of acetylcholine, we were unable to demonstrate even a trace of bradykinin release during stimulation of the chorda tympani nerve.

Methods. Cats weighing 2.6 to 4.8 kg were anaesthetized with chloralose (60 mg kg^{-1} i.v.). Nerve stimulation, collection of saliva, and blood pressure measurements were carried out as described previously[8]. Drugs were given either close arterially via a lingual artery, or i.v. via a femoral vein. Blood flow was measured via a forced convection flowmeter with a probe in an external jugular vein[11]. Heparin (2 to 10 mg/kg^{-1} i.v.) was given at the beginning of the experiment with further doses as necessary. Bradykinin potentiators were the pentapeptide (PCA-Lys-Trp-Ala-Pro) and the nonapeptide (PCA-Trp-Pro-Arg-Pro-Gin-Ileu-Pro-Pro). The latter was much more effective and was therefore used in 3 of the 4 experiments. The following drugs were used: acetylcholine choloride, atropine sulphate, eserine sulphate and heparin

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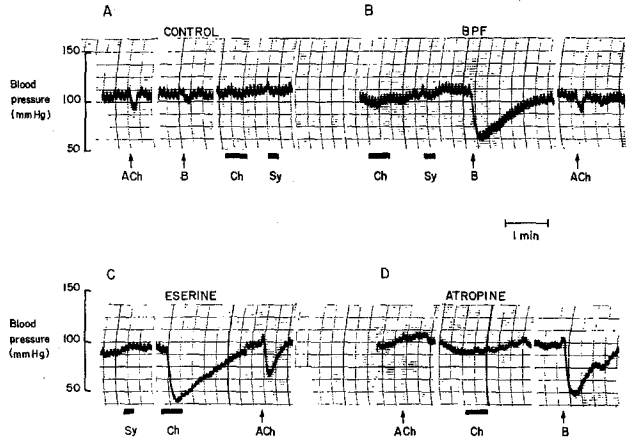
Results. Effect of chorda lingual nerve stimulation on systemic blood pressure before and after eserine and BPF. 2 experiments were carried out with the objective of stabilizing either acetylcholine or kinin released locally in the submaxillary gland so that the systemic affects of a released transmitter or mediator could be detected. In one experiment, eserine was given in a cumulative dose of 400 $\mu g/kg^{-1}$ i.v. over a 5-min period; in the other experiment, the dose was s single one of 100 $\mu g/kg^{-1}$ i.v. Large doses of eserine may cause convulsions some time after administration. These may be reduced or eliminated by increasing the depth of anaesthesia. The more potent nonapeptide kinin potentiator was used in both experiments in a dose of 2 mg/kg^{-1} i.v. Whereas prior administration of eserine readily demonstrated the systemic 'spill-over' of acetylcholine following stimulation of the chorda lingual nerve, the nonapeptide failed to reveal any overflow of bradykinin despite the fact that it potentiated the hypotensive effect of bradykinin injected i.v. to a greater degree than eserine enhanced the effect of injected acetylcholine. Detailed results of one of these experiments are shown in the Figure.



Blood pressure of cat (2.7 kg) under chloralose anaesthesia. ACh, 0.01 μg acetylcholine. B, 1.0 μg bradykinin. Ch, stimulation of chorda lingual nerve. Sy, stimulation of cervical sympathetic nerve. Trace A: Control, showing effects of i.v. injection of acetylcholine, bradykinin and of chorda lingual and sympathetic nerve stimulation. Trace B: After injection of bradykinin potentiating factor (BPF), synethetic nonapeptide, 2 mg/kg^{-1} i.v. Marked potentiation of effect of injected bradykinin but there are again no systemic effects following stimulation of the chorda lingual or sympathetic nerves. Trace C: After injection of eserine, 400 $\mu g/kg^{-1}$ i.v. Chorda lingual nerve stimulation now results in a marked fall of the arterial blood pressure after a latency of approximately 10 sec. The effect of injected acetylcholine is also greater than in the control panel. Sympathetic nerve stimulation produces no systemic effects. Trace D: After injection of atropine, 250 $\mu g/kg^{-1}$ i.v. The effects of injected acetylcholine and of chorda lingual nerve stimulation are now completely blocked. Injected bradykinin is still potentiated.

In a second experiment, eserine (100 $\mu g/kg^{-1}$) was injected before the kinin potentiators. In this experiment, both the pentapeptide and the nonapeptide were injected (total dose, 4 mg/kg^{-1}) and the systemic effects of bradykinin were enhanced to an even greater degree than in the first experiment. Nonetheless, the systemic blood pressure revealed no trace of systemic overflow of kinin; again, however, overflow of acetylcholine on nerve stimulation was readily demonstrated after injection of eserine.

Effect of chorda lingual nerve stimulation on vasodilatation before and after BPF. In 2 other experiments, an attempt was made to potentiate vasodilatation in the submaxillary gland resulting from chorda lingual nerve stimulation by prior administration of a kinin potentiator. In one experiment, the nonapeptide was infused close arterially via the lingual artery (1 mg/kg^{-1}) and in the other the pentapeptide was injected i.v. (1 mg/kg^{-1}). Although the systemic hypotension to the intravenous injection of bradykinin was increased in both experiments by the potentiator, vasodilatation in the gland resulting from nerve stimulation was unaffected.

Discussion. Our results show that under equivalent conditions of potentiation of acetylcholine and kinin, although the release of acetylcholine following stimulation of the chorda lingual nerve can readily be demonstrated, there is no evidence of kinin release. We conclude, therefore, that kallikrein has no involvement in the mediation of the vasodilatation which occurs in the submaxillary gland during stimulation of the chorda lingual nerve. The physiological significance of salivary kallikrein remains obscure. The problem of the marked difference in sensitivity to atropine of the secretory and vasodilator effects of chorda lingual nerve stimulation has still not been resolved and also requires further study. It has been suggested, however, that the secretory and vascular smooth muscle cells both possess different cholinergic receptors but with markedly different sensitivities to atropine[4].

Zusammenfassung. Nachweis, dass bei Reizung des N. chorda lingualis der Katze ein Blutdruckeffekt ausbleibt, wenn ein Bradykinin potenzierender Faktor (Präparat BPF) zuvor gegeben wurde.

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The Effects of Cholinergic Drugs on the Motility of the Alimentary Canal of *Blennius pholis* L.

In view of the complex and unresolved problems which remain in understanding the control of gastrointestinal motility in teleosts[1,2] a study was undertaken in intact fish to explore the effects of drugs likely to influence motor activity of the alimentary tract. A locally available fish, *Blennius pholis* L., was selected principally because it is an example of a fish with no histologically defined stomach[3] and the results can be compared with in vivo studies on other fish, possessing stomachs, which have been reported from this laboratory[4].