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ON THE FUNCTION OF MYOEPITHELIAL CELLS IN SALIVARY GLANDS

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SUMMARY

1. In dogs under chloralose-urethane anaesthesia the submaxillary duct was cannulated and connected either to an open outflow system, in which saliva displaced water, or to a closed pressure recording system.

2. The secretory cells, which are supplied with β-adrenoreceptors, were stimulated with isoprenaline, adrenaline or sympathetic nerve stimulation. Myoepithelial cells, supplied with α-receptors, were activated with phenylephrine, adrenaline or sympathetic stimulation, and also with bradykinin. To abolish α-receptor stimulating effects of adrenaline and sympathetic nerve stimulation, dihydroergotamine, phenoxybenzamine and phentolamine were used.

3. When the secretory cells were activated alone, saliva flowed from the salivary duct, but the flow started late and only a moderately high pressure could be produced in the closed system. Saliva appeared much earlier in the duct when secretion was combined with myoepithelial contraction, and a much higher pressure could be built up in the duct system.

4. It is concluded that rapid emptying of saliva in the mouth and a maintained flow at a high rate of the viscous saliva is promoted by contractions of the myoepithelial cells.

INTRODUCTION

It has been known for a long time that myoepithelial cells are present in salivary glands, just as in mammary glands, and they can be activated by electrical stimulation of glandular nerves (see Babkin, 1950; Emmelin, Garrett & Ohlin, 1968). The functional significance of myoepithelial contractions, is, however, much less known in salivary than in mammary glands. The main reason for this is very likely that it is difficult to distinguish between effects of secretory and motor activity elicited by stimulation of salivary gland nerves; for instance, myoepithelial contractions can be recorded as pressure rises in the salivary ducts, but classical experi-

ments by Ludwig (1851) suggested that pressure rises can be due to secretion also.

In the submaxillary gland of the dog sympathetic nerve stimulation causes secretion which is elicited via β-adrenoreceptors and myoepithelial contraction mediated by α-receptors (Emmelin & Holmberg, 1967; Emmelin, Ohlin & Thulin, 1969). By using appropriate stimulating and blocking drugs it is therefore possible to study, in this particular preparation, secretory and motor responses separately or together. It has also been found that bradykinin stimulates the myoepithelial but not the secretory cells in this gland (Emmelin, Garrett & Ohlin, 1970).

The starting point of the present investigation was the observation that flow of saliva from the dog's submaxillary gland takes a remarkably long time to start following stimulation of β-receptors by injection of isoprenaline. It could be hypothesized that this long latency is due to lack of support from myoepithelial cells. In one series of experiments the time required for saliva to appear at the tip of a salivary cannula after sympathetic stimulation or drug injection was measured. A preliminary account of this work has been published (Emmelin & Gjörstrup, 1972). In a second series the effects of nerve stimulation or drugs on the pressure in the salivary duct was recorded in a closed system.

METHODS

The experiments were made on twenty-one dogs weighing 5–19 kg and anaesthetized with chloralose-urethane (50 + 500 mg/kg) which was given I.V. after induction with ether. Additional doses of anaesthetics were given when required. Tracheal cannula was inserted. The chorda-lingual nerve and the vagosympathetic trunk were cut and stimulated electrically at supramaximal voltage (8–25 V), a duration of each shock of 2 msec and frequencies which varied but were mostly 20/sec. Drugs were usually injected through a cannula in a femoral vein. Phenylephrine was in some dogs also injected continuously from a motor-driven syringe through a cannula in the opposite femoral vein. In some experiments drugs were administered intra-arterially to the submaxillary gland by injection through a cannula in the lingual artery.

The submaxillary duct was exposed in the neck and a polyethylene tube of widest possible bore was tied into it. The tube was connected to an outflow bottle filled with distilled water. The tip of the outlet tube from the bottle was situated about 1 cm above the salivary gland and the level of the water was adjusted so as to fill partly the final, narrow segment of the outlet. Movement of the water meniscus could then easily be detected. The moment a drug was injected or nerve stimulation began was marked on a rapidly running smoked drum, using an electromagnetic signal which was operated manually. The same signal was used to record the moment the meniscus started to move in the outlet tube. Another signal recorded each drop that fell from the tube when saliva replaced water in the bottle. Out of 1 ml. distilled water the system formed 52 drops. A third signal marked the time as minutes on the drum. After the experiment the time intervals were measured between drug

injection or beginning of nerve stimulation and (*a*) the commencement of the movement of the meniscus, and (*b*) the fall of the first drop.

In three of the dogs the chorda-lingual nerve was cut about 3 weeks before the acute experiment. This operation, carried out in ether anaesthesia, was done in order to increase the secretory responses of drugs, particularly the relatively short-acting adrenaline. Parasympathetic decentralization of the submaxillary gland of the dog has been shown to cause a supersensitivity of the secretory cells not only to cholinomimetic, but also to β-adrenoreceptor stimulating drugs (Emmelin & Lenninger, 1967).

Recording of the pressure in the submaxillary duct was carried out in eight of the dogs, all with normally innervated glands. The salivary cannula, which was made as short as possible, then ended in a three-way tap. One way was connected to the outflow bottle system described above, the other to a closed system containing a pressure bottle, a mercury manometer and a strain gauge transducer, operating a potentiometer writer. The pressure in the salivary duct was set at the desired level from the bottle, usually 10–15 mm Hg. When the saliva was particularly viscous it was found useful to expose the gland for half a minute to a pressure of 50 mm Hg as described earlier (Emmelin *et al.* 1969) and then to lower the pressure to 10–15 mm. A tap was then turned so that the gland was no longer connected to the mercury manometer and the pressure bottle but only to the transducer, and the effect of drugs or nerve stimulation was studied. After each pressure recording the duct was connected to the open outflow system and often the chorda-lingual nerve was stimulated for a brief period.

RESULTS

A. Experiments with the open system

The saliva produced. The saliva flowing from the submaxillary gland was usually very thick, particularly after sympathetic stimulation. On stimulation of the chorda-lingual nerve it often appeared as a clear, transparent string in the outflow bottle. After stimulation of the vago-sympathetic trunk it became whitish and cloudy. When the chorda-lingual nerve was then again excited, the first portion of saliva was often also cloudy; sometimes the meniscus in the outlet tube started late to move and the first drops were formed slowly. On continued parasympathetic stimulation the saliva became clear and the flow rapid. The impression was that organic material secreted during sympathetic stimulation blocked the flow and had to be washed out by the parasympathetic saliva. The fluid produced by isoprenaline or adrenaline injection looked like that secreted during sympathetic nerve stimulation. Because of these observations periods of stimulation of the chorda-lingual nerve at 20 shocks/sec during 30–60 sec were regularly interposed between the periods of sympathetic stimulation; in those experiments in which the chorda-lingual nerve had been cut in advance, methacholine (0·5–2 μg/kg) was injected I.V. instead. The interposed periods of standardized parasympathetic activity also served the purpose to fill the salivary duct system to the same extent each time before the responses to sympathetic

nerve stimulation or sympathomimetic drugs were studied. Under these conditions the latency between the onset of sympathetic nerve stimulation or injection of drugs and the start of the flow in the outlet tube usually remained remarkably constant during a day's experiment. In several experiments the importance of the interposed chorda stimulation period was demonstrated by the fact that the sympathetic responses were found to be greatly delayed when not preceded by a chorda stimulation period.

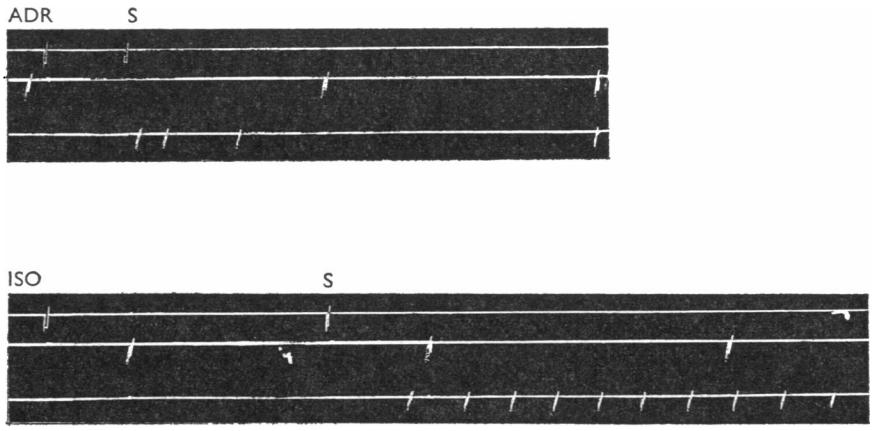

Fig. 1. Responses to adrenaline, 20 μg/kg (ADR) and isoprenaline, 20 μg/kg (ISO). Records from above in each section: signal to mark the injection of the drugs and the start (S) of movement of the water in the outlet tube; minute marks; drops of water from the outlet tube. Isoprenaline produced a more rapid secretion than adrenaline; the short distance between the two first drops following adrenaline is at least partly attributable to extrusion of saliva by myoepithelial contraction.

In some of the experiments, in which the saliva seemed particularly viscous, the salivary flow following sympathetic stimulation was initially very small, and this was even more the case with the responses to injected isoprenaline. In these dogs a period of chorda stimulation during 1–2 hr resulted in less viscous saliva and improved responses to sympathetic stimulation and isoprenaline injection. This improvement persisted during the whole of the subsequent experiment.

Effects of isoprenaline and adrenaline. The slow response to isoprenaline is shown in Fig. 1. Movement of the fluid was observed only as late as 1 min after the I.V. injection of the drug. For comparison the effect of combined α- and β-receptor stimulation with adrenaline is shown. Its effect appeared much earlier and the first drop also fell much earlier than after isoprenaline, although the volume of saliva delivered was much smaller. Adrenaline was preferred to noradrenaline because it was found to

have the more pronounced secretory effect. Even with adrenaline, however, large doses were needed to produce secretion. In the glands sensitized by previous parasympathetic decentralization it was possible to reach, for a brief period, the maximal secretory rate obtainable with adrenaline using a dose of 10–20 μg/kg. This flow rate was the same as that attained with isoprenaline, which had to be given in a dose of 2–4 μg/kg to the sensitized glands; in normal glands the dose required for maximal secretion was 20–50 μg/kg. In nine dogs studied the latency between drug injection and onset of the movement of the meniscus was $21 \pm 2{\cdot}7$ sec (mean $\pm$ S.E. of mean) with adrenaline and $49 \pm 2{\cdot}9$ sec with isoprenaline; the comparison was based on doses of isoprenaline causing maximal secretion, whereas the secretion caused by adrenaline was usually submaximal. When the doses of isoprenaline were reduced to cause secretory responses far below maximum the latency was found to be even longer than at or near the maximum.

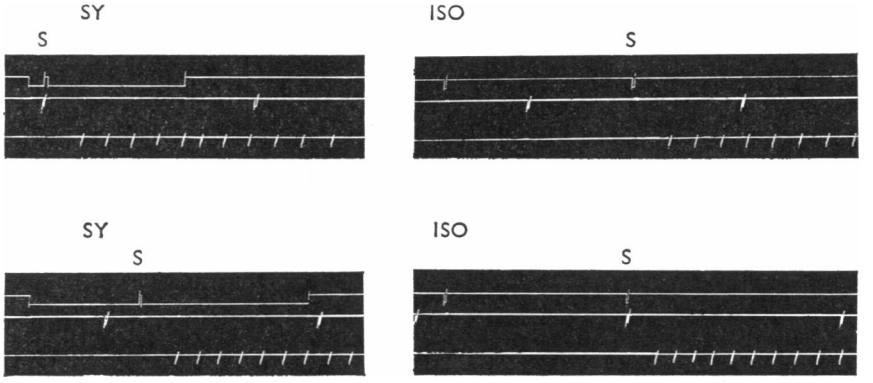

Fig. 2. Responses to stimulation of the vagosympathetic nerve at 20 shocks/sec (SY) and injection of isoprenaline, 20 μg/kg (ISO). Records as in Fig. 1. The upper sections were obtained before, the lower sections after dihydroergotamine, 0·2 mg/kg.

When isoprenaline was administered through the lingual artery instead of by vein the latency was somewhat shortened, but even so it was remarkably long.

Effects of sympathetic stimulation. When the stimulating agent acting both on α- and β-receptors was applied close to the effector cells, by electrical stimulation of the vagosympathetic trunk, the responses appeared even earlier than after adrenaline injection. Fig. 2 shows a comparison between sympathetic stimulation and injection of isoprenaline; the difference in latency and in time to deliver the first drop in the two instances is striking. This effect was seen in all the experiments, whether

maximal or submaximal secretory rates were chosen. In each experiment the frequency of nerve stimulation and the dose of isoprenaline were adjusted so that the same secretory rate was obtained. This was easiest done by working at the maximal level, which was the same for isoprenaline and sympathetic stimulation.

Effects of α-blocking agents. In the experiment of Fig. 2 the effects of isoprenaline and sympathetic stimulation were also studied after I.V. injection of dihydroergotamine. This α-receptor blocking drug did not change the response to isoprenaline, but the sympathetic response was greatly delayed, although the secretory rate was maintained; the movement of fluid started later, and the first drop fell later after than before

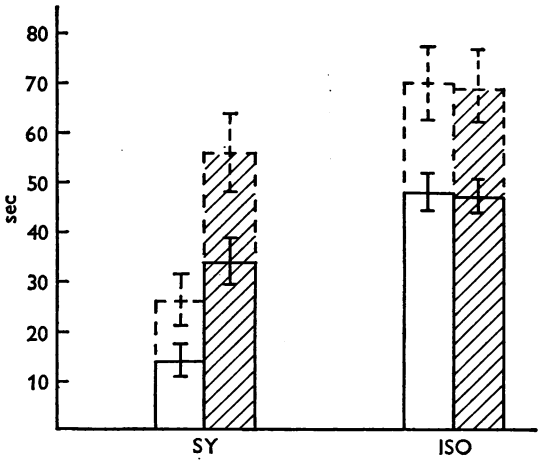

Fig. 3. Time intervals in sec (ordinates) between onset of sympathetic stimulation (SY) or I.V. isoprenaline injection (ISO) and the start of the movement of fluid (continuous lines) or the fall of the first drop (continued with dotted lines). In each pair of columns the left one represents the responses before, the right one after an α-blocking drug. Mean of seven experiments. The vertical bars give the S.E. of means.

dihydroergotamine. Other α-receptor blocking compounds, phenoxybenzamine (2–5 mg/kg) and phentolamine (2 mg/kg) had the same effect as dihydroergotamine (0·2–0·4 mg/kg). Fig. 3 summarizes the results of seven experiments, showing the delaying effect of α-blocking drugs on the responses to sympathetic stimulation but not to isoprenaline.

Similarly, the responses to adrenaline were delayed by α-receptor blocking drugs, as shown in four experiments in Fig. 4.

In the doses used, dihydroergotamine and phentolamine did not affect the secretory responses to chorda stimulation. When phenoxybenzamine (5 mg/kg) was given to a dog with a sensitized gland the secre-

tory effect of methacholine was found to be markedly reduced, and the atropine-like action which this drug is known to possess could then be demonstrated during chorda stimulation in normal glands; it was very slight, however, and could only be detected when the nerve was stimulated at a frequency evoking a slow secretion. In the same sensitized gland phenoxybenzamine (5 mg/kg) was found to have a very small secretory effect and when this dose was repeated, saliva started to flow at a rate of about 1 drop/10 min. This flow continued for about 2 hr without much decline, and it was increased to 1 drop/3 min after a further dose of 5 mg/kg. The secretion was not influenced by atropine (0·1 mg/kg) but was abolished by propanolol (2 mg/kg). It thus seemed to be due to β-receptor stimulation of the secretory cells, but the mechanism of action was not further analysed. In the normal glands such an effect of phenoxybenzamine (2–5 mg/kg) did not appear, to interfere with the results of the α-blocking action.

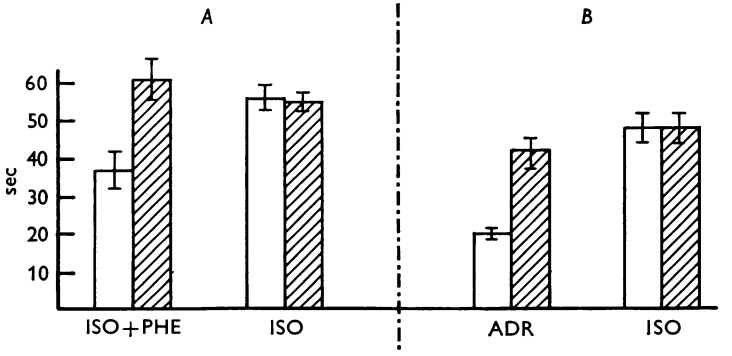

Fig. 4. Latencies between drug injections and onset of movement of fluid. In four experiments the effects of isoprenaline + phenylephrine (ISO + PHE) were compared with those of isoprenaline alone. In four other dogs the effects of adrenaline and isoprenaline were compared. In each pair of columns the left one corresponds to the effect before, the right one after an α-receptor blocking drug.

Effects of α-receptor stimulation on isoprenaline responses. The late response to isoprenaline could be hastened by injection of the α-adrenoreceptor stimulating phenylephrine (10–50 μg/kg). Fig. 5 shows such an experiment. Phenylephrine was given I.V. within 10 sec after isoprenaline. This shortened the latency and the first drop fell earlier than after isoprenaline alone. In eleven experiments the isoprenaline latency was found to be shortened by phenylephrine from $57 \pm 2{\cdot}8$ sec to $30 \pm 2{\cdot}7$ sec. This effect of phenylephrine was abolished by α-receptor blocking drugs, as illustrated in Fig. 4.

When the gland was already secreting after injection of isoprenaline, the

rate of flow, even if maximal for isoprenaline, could be temporarily increased by injection of phenylephrine, as shown in Fig. 6.

Injected alone phenylephrine caused an effect only when the gland had been secreting recently and the duct system could be assumed to be filled with saliva, for instance, after a previous period of secretory activity induced by nerve stimulation or isoprenaline or methacholine injection. Under such conditions phenylephrine produced some movements of the

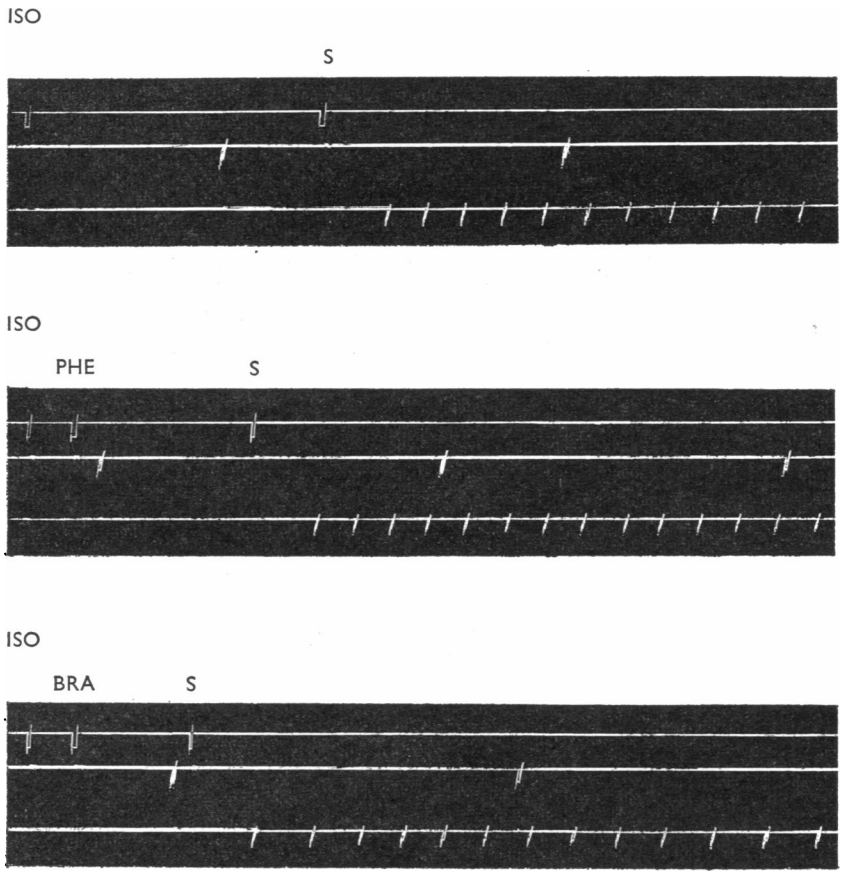

Fig. 5. Effects of phenylephrine (PHE), 20 μg/kg I.V., and of bradykinin (BRA), 5 μg/kg intra-arterially, on the responses to isoprenaline (ISO) 20 μg/kg I.V. Records as in Fig. 1.

meniscus in the outlet tube, and sometimes a few drops fell quickly. Repeated injections of phenylephrine, however, were without effect even if the doses were greatly increased, indicating that phenylephrine lacked secretory and had only a motor effect.

According to previous experience (Emmelin, Garrett & Ohlin, 1969) myoepithelial contractions elicited via α-receptors can be produced in submaxillary glands of dogs by stimulation of sympathetic fibres at a frequency too low to evoke secretion. This was made use of in the present investigation. Sympathetic stimulation at 0·2–0·5/sec in experiments in which 2 shocks/sec were needed for a minute secretion was found to quicken the response to injected isoprenaline. This effect disappeared after injection of an α-blocking drug, suggesting that it was due to myoepithelial contraction and not, for instance, a subthreshold secretory response via β-receptors, increasing the effect of the isoprenaline.

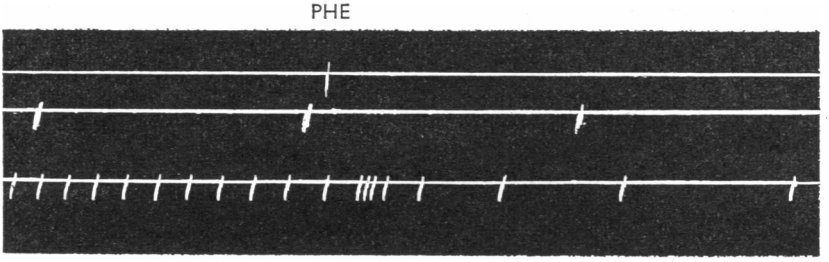

Fig. 6. Effect of phenylephrine (PHE), 20 μg/kg I.V. on the salivary flow produced by I.V. injection of isoprenaline 1½ min before the tracing shown. Records as in Fig. 1.

Effects of bradykinin. When injected through the lingual artery in retrograde direction bradykinin in a dose of 5 μg/kg (no other branches of the arterial tree had been tied off) caused movement of the fluid, but only if the duct system had been filled in advance. Furthermore, it shortened the isoprenaline latency, like phenylephrine (Fig. 5), but unlike this drug it was active even after injection of an α-blocking agent. Consequently, it was in addition able to shorten a latency to sympathetic stimulation that had been prolonged by administration of an α-blocking drug. For instance, in one experiment the sympathetic latency, 27 sec, was increased to 58 sec after phenoxybenzamine but when, still under the influence of the blocking drug, bradykinin was given a few sec after the start of the sympathetic stimulation, the latency was reduced to 24 sec.

B. Experiments with the closed system

The eight experiments with pressure recording in a closed system revealed a striking difference between the reactions to isoprenaline and to stimulation of the sympathetic nerve. This is demonstrated in Fig. 7. After injection of isoprenaline in a dose, which in the open system evoked the maximal secretory response, there was a distinct latency and the

pressure then slowly and gradually rose. Repeated doses of isoprenaline, which in the open system were sufficient to guarantee a secretion maintained at the maximal rate, could usually cause some further small rise of the pressure but a maximum was soon reached, in the experiment of Fig. 7 at 45 mm Hg and in the remaining seven experiments at 23–43 mm Hg. When, on the other hand, the vagosympathetic nerve was stimulated at a frequency of 20/sec, which in the open system produced the same maximal secretory effect as isoprenaline, a very quick, steep pressure rise ensued. A pressure of 76 mm Hg was rapidly reached; in the other experiments the corresponding figures were 32–72 mm Hg. There was then,

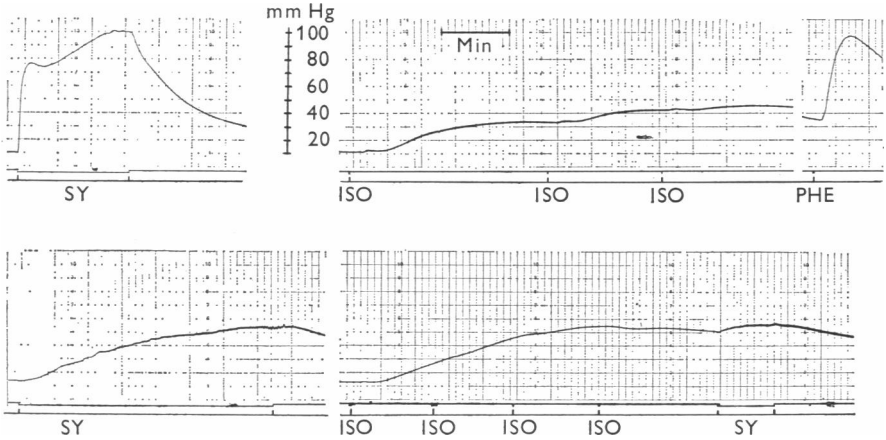

Fig. 7. Pressure in the submaxillary duct system (mm Hg). SY: stimulation of the vagosympathetic nerve at 20 shocks/sec. ISO: I.V. injection of isoprenaline, 50 μg/kg. PHE: of phenylephrine 50 μg/kg. The lower panel shows the effects after intravenous injection of dihydroergotamine, 0·4 mg/kg.

on continued sympathetic stimulation, a secondary slow pressure rise, the slope of which resembled that seen initially after injection of isoprenaline. In this way a pressure of 100 mm Hg was eventually attained. In the other experiments values of 60–94 mm were found, and it should be noted that in each experiment this level was far above that found after isoprenaline injection. The two phases of pressure rise during sympathetic nerve stimulation were not always quite as distinctly separated from each other as in Fig. 7 (see Fig. 8). A large dose of phenylephrine (50–100 μg/kg) I.V. produced a pressure rise almost as steep as the first pressure response to sympathetic nerve stimulation and of the same order of magnitude; considering the different ways in which the α-receptor stimulating agents were applied in the two cases the similarity between the responses were striking. If phenylephrine was injected while isoprenaline was acting, as in

Fig. 7, a pressure was reached that was of the same order as that attained in the two phases during sympathetic stimulation. A similar effect was obtained by sympathetic nerve stimulation on top of the isoprenaline pressure curve.

In other experiments phenylephrine was first injected slowly from a motor-driven syringe and the rate of injection was raised until phenylephrine produced its maximal pressure rise; this was the same as that seen in the first phase during sympathetic nerve stimulation. The dose of phenylephrine required for this was about 300 μg/kg.min. This rate of injection was maintained while isoprenaline was injected repeatedly.

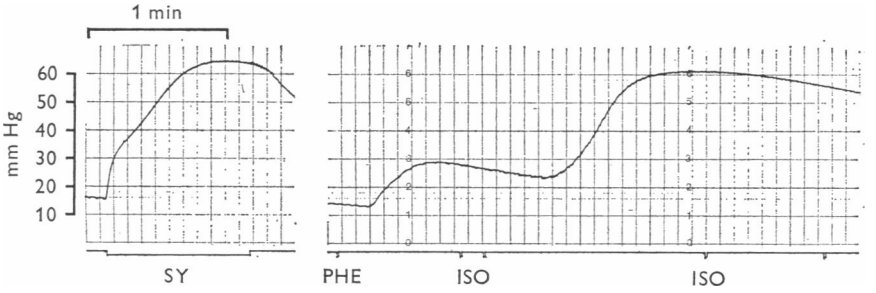

Fig. 8. Pressure rises produced by stimulation of the vagosympathetic nerve at 20 shocks/sec (SY) and of phenylephrine injected from PHE and throughout the section shown, in a dose of 350 μg/kg. min. ISO: I.V. injection of isoprenaline 50 μg/kg (injected 3 times). Injected alone in this experiment this latter drug caused a pressure rise to about 25 mm Hg.

From this pressure level isoprenaline was now found capable of causing a further slow pressure rise, similar to that seen as the second phase during sympathetic nerve stimulation. Fig. 8 shows a comparison between the effects of sympathetic nerve stimulation and of isoprenaline injections during continuous administration of phenylephrine. In this particular experiment the pressure produced by phenylephrine tended to fall in spite of continued injection of the drug; in others the maximal pressure level was maintained for a long time.

Administration of α-receptor blocking drugs did not change the pressure responses to isoprenaline, as can be seen in Fig. 7. The effect of sympathetic nerve stimulation, however, was radically altered. After a certain latency there was a slow, gradual rise of the pressure to a level which was only as low as that reached with isoprenaline. In fact, the picture was almost identical with that produced by isoprenaline. After α-blocking agents phenylephrine did not cause any pressure rise, and phenylephrine or sympathetic nerve stimulation were unable to raise the maximal isoprenaline pressure curve.

These observations indicate that the first pressure rise seen after

stimulation of the sympathetic nerve (in the absence of blocking agents) is due to myoepithelial contraction, mediated via α-receptors, and the second phase due to secretion via β-receptors. The main conclusion from these pressure recording experiments is that during stimulation of the secretory β-receptors a much higher pressure can be built up in the duct system when the myoepithelial cells are contracted than when they are relaxed.

DISCUSSION

It is obvious that activity of the secretory cells, unaided by myoepithelial contractions, is sufficient to cause a flow of saliva through the duct system. In the submaxillary gland of the dog this occurred when only β-receptors were excited, e.g. after injection of isoprenaline or, in the presence of an α-receptor blocking drug, during sympathetic nerve stimulation or administration of adrenaline. Concomitant contraction of myoepithelial cells manifested itself, in the experiments with the open system, in a quickened response. This was seen when both α- and β-receptors were activated at about the same time: when (in the absence of α-blocking agents) the sympathetic nerve was stimulated at a moderate or high frequency or adrenaline injected, or when isoprenaline was combined with phenylephrine or sympathetic nerve stimulation at a low frequency.

Adrenoreceptors of the α-type are present not only in the myoepithelial cells but in the vascular bed of the salivary glands also. It is very unlikely, however, that the observations described here result from effects on the vessels rather than on the myoepithelial cells. There seems to be no reason to believe that abolishment with an α-blocking drug of a vasoconstrictor effect of sympathetic stimulation or adrenaline or phenylephrine injection should delay the salivary flow. Furthermore, bradykinin, which like the α-stimulating agents contracts the myoepithelial cells but causes a marked vasodilatation in the gland, was found to quicken the flow. This effect of bradykinin on the flow caused by isoprenaline could possibly be thought to be due to an increased inflow of isoprenaline into the vascular bed of the gland; but it may be pointed out that bradykinin was also able to shorten the latency to sympathetic nerve stimulation when it had been prolonged by an α-blocking drug.

In the closed system the myoepithelial contractions were seen as rapidly occurring, steep and marked pressure rises. It seems reasonable to assume that one role of the myoepithelial cells is to aid in the rapid flow of the viscous saliva, particularly through ducts of small calibre. The contractions may be especially efficient if occurring rhythmically, as seen during sympathetic nerve stimulation at low, physiological frequencies (Emmelin *et al.* 1969).

Physiologically the salivary glands show an often slow, continuous, basal secretion with superimposed periods of suddenly enormously increased activity to fulfil digestive and protective functions. It may be important that saliva can be rapidly emptied into the mouth not only to protect against noxious agents but also to serve digestive functions, considering the short time period the food spends in the mouth. For a slow, basal salivary flow the myoepithelial cells may be less essential. During secretory activity at or near the maximal level the myoepithelial contractions may, however, be important not only to raise the speed of the initial flow but also to maintain the high flow rate. This idea is suggested by the following observations. Repeated injections of isoprenaline, which in the open system evoke a prolonged flow at a maximal rate, were in the closed system able to raise the pressure only to a moderate level; the pressure rise then ceased, probably because back flow of fluid into the tissues balanced the outflow from the secretory cells into the duct. However, when the myoepithelial cells were contracted, by continuous injection of phenylephrine or during sympathetic nerve stimulation, prolonged excitation of the β-receptors was found to be able to raise the pressure to high levels. This suggests that the myoepithelial cells are of importance to support in some way the tissues during secretion at a high rate. It is interesting to note that in the sublingual gland of the cat, in which the machinery of the secretory cells is continuously active, producing a very slow 'spontaneous secretion', the flow decreases and ceases if the outflow level is increased to as little as 15 cm above the gland (Emmelin, 1953); this secretory activity is probably not supported by myoepithelial contractions.

The present experiments were centred on the action of the sympathetic innervation on the secretory and myoepithelial cells, mainly for methodological reasons: it was easy to separate the two actions with the aid of pharmacological tools. It may be that myoepithelial contractions are of special importance for the flow of the very viscous saliva produced by sympathetic nerve stimulation. This saliva is particularly rich in organic material, as demonstrated by Baxter (see Babkin, 1950) and Dische, Kahn, Rothschild, Danilchenko, Licking & Wang (1970), and suggested by the present experiments also; like the secretion of water, the secretion of this material seems to be mediated by β-adrenoreceptors as shown by the fact that saliva produced by isoprenaline was as cloudy and thick as that secreted during sympathetic nerve stimulation. It has been hypothesized that a single axon of a salivary gland nerve may have en-passant contacts with both secretory and myoepithelial cells (Emmelin, 1968, 1969). If this be the case, secretion caused by activity in the sympathetic nerves can be assumed to be accompanied, and even preceded, by myoepithelial

contractions, since the α-receptors of the myoepithelial cells are more sensitive to the chemical transmitters than the β-receptors of the secretory cells and respond to very low stimulation frequencies (Emmelin *et al.* 1969).

It should be emphasized that it is difficult to state whether the present observations reflect occurrences in the non-anaesthetized animal during alimentary or protective reflexes since reflexly evoked contractions of salivary myoepithelial cells have never been recorded. It is even true that the role of the sympathetic system in digestive and other reflexes from salivary glands is obscure. For the moment the present experiments may merely be regarded as models to demonstrate a possible interplay between secretory and contractile processes, and during more physiological events the contributions of the parasympathetic nerves may be of particular interest.

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