to what was obtained when the total concentration of 6211 inside was increased without changing the pH (as published previously)[3]. In these experiments when the concentration of 6211 was changed from 1 to 10 mM keeping the pH of the solution at 7, there was a 33% greater block at the higher concentration. Similarily, if the pH was maintained at 8.0, there was a 50% greater block at 10 mM than at 1 mM.

In Figure 2 we have compared on the same axons the effect of changing the external concentration procaine with and without altering the pH of the solution. The solid line represents the results obtained when the concentration of procaine was increased from 1.5 to 4 to 11.8 mM while changing the pH from 8.5, 8.0, 7.5 respectively. As is evident from Figure 2 there is a slight increase in the degree of block as you increase the concentration from 1.5 to 11.8 mM ($\bar{X}$ = 46% at 1.5 compared to 72% at 11.8 mM). If, however, the concentration of procaine is similarily increased externally keeping the pH at 8.0 (dashed line) there is a marked difference between 1.5 and 11.8 mM (35% block at 1.5 mM compared to 97% block at 11.8 mM). It is obvious, therefore, that if the internal concentration of the charged form of the local anesthetic is maintained constant, changing the total concentration by a factor of 8 has little effect on the blocking potency.

The results of these experiments support the concept that it is primarily the charged form of the local anesthetic that is active from inside the nerve membrane. There does appear to be a slight increase in the ability of the local anesthetic to depress the action potential as the concentration of the unchanged form is increased.

Zusammenfassung. Es wird die Annahme gestützt, dass in der Nervenmembran die aktive Form lokal anaesthetischer Mittel die ionisierte Form ist. Die das Wirkungspotential herabsetzende Wirkung dieser Stoffe scheint durch die höheren Konzentrationen der nicht-ionisierten Form bedingt zu sein.

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On the β-Adrenergic Receptors in Salivary Glands of Rat and Dogs

In salivary glands secreting in response to sympathetic stimulation and sympathomimetic drugs, the effect is usually mediated by α-receptors. However, the submaxillary gland of the rat[1] is supplied with some β-receptors also, and, in the submaxillary glands of the dog, the adrenergic receptors belong exclusively to the β-group[2]. LANDS, LUDUENA and BUZZO[3] divide the β-receptors into 2 subgroups, the β_1-receptors (in heart, addipose tissue and small intestine) and the β_2-receptors (in uterus, bronchioles and blood vessels).

Recently salbutamol[4] [2-t-butylamino-1-(4-hydroxy-3-hydroxymethyl)-phenyletanol] was described as a stimulant of β_2-receptors; compared with isoprenaline it is about equipotent in its dilator action on the bronchi, but its chrono- and inotropic actions on the heart are very much smaller[5-7]. In the present experiments this drug was used to study the β-receptors which mediate secretion in the submaxillary glands of dogs and rats.

Materials and methods. 14 rats weighing between 180 and 440 g and 6 dogs between 5.2 and 10.5 kg were used. The rats were anaesthetized with chloralose (100 mg/kg) and the dogs with chloralose-urethane (50 + 500 mg/kg) given i.v. after induction with ether. The submaxillary

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Secretory responses to isoprenaline and salbutamol

Gland	Isoprenaline (0.5 µg/kg)	Salbutamol (20 µg/kg)	Salbutamol (50 µg/kg)	Salbutamol (100 µg/kg)
Normally innervated submaxillary gland of rat	7/7	0/7	1/7	3/6
Decentralized submaxillary gland of rat	7/7	1/7	4/7	4/7
Normally innervated submaxillary gland of dog	3/6	0/3	0/6	0/4
Decentralized submaxillary gland of dog	4/4	1/3	2/4	2/2
Normal parotid gland of dog	0/2	0/2	0/2	0/2

The relation between the number of glands, in which secretion was obtained, and the number of glands studied, is given.

ducts were exposed in the neck and cannulated. In two of the dogs the parotid duct was also cannulated. The following drugs were given. Methacholine (1–10 μg/kg), isoprenaline (0.1–2 μg/kg), salbutamol (1–2 mg/kg). Methacholine was injected between the injections of the other drugs as a control of the functional state of the gland. In 7 of the rats and 4 of the dogs, the right chorda-lingual nerve was cut in order to sensitize the gland cells to secretory agents.

Results and discussion. The results are summarized in the Table. It can be seen that in rats salivary secretion was obtained from all submaxillary glands when isoprenaline 0.5 μg/kg was given. In the normally innervated glands, no salivary secretion was obtained when salbutamol 20 μg/kg was injected. In 1 out of 7 of the decentralized glands, salivary secretion was obtained when salbutamol 20 μg/kg was given. With salbutamol 10 μg/kg, no secretion was obtained in this case.

In the normally innervated submaxillary gland of the dog, salivary secretion was obtained in 3 glands out of 6, when isoprenaline 0.5 μg/kg was given. Salivary secretion was obtained from the other 3 glands when isoprenaline 1–2 μg/kg was given. Salbutamol 20, 50 and 100 μg/kg did not cause secretion in these glands. When salbutamol was found to cause salivation in submaxillary glands of rats and dogs, the effect was abolished by propanolol showing that it was mediated by β-receptors. It is not surprising that salbutamol was unable to evoque any flow of saliva from parotid glands of dogs, which lack β-receptors[2]. The secretory effect on the submaxillary gland was very small; it was at most 1/100 of that of isoprenaline and usually much smaller. It is obvious that, in its responsiveness to salbutamol, the salivary glands studied resemble the heart rather the bronchioles or the blood vessels. Using the terminology of LANDS, LUDUENA and BUZZO[3] their β-receptors should in other words be described as belonging to the β_1 subgroup.

Zusammenfassung. Nachweis an Ratten und Hunden, dass Salbutamol, ähnlich wie Noradrenalin, nur in höherer Dosierung, die Speichelsekretion der Submaxillaris, nicht aber die der Parotis erhöhen kann. Diese Wirkung kann durch Propanolol aufgehoben werden, was zeigt, dass sich in der Submaxillaris offenbar β_1-Rezeptoren befinden.

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Responses of the Resistance and Capacitance Vessels Reflexly Induced from the Cardiac Chambers

NEIL[1] suggested that the receptors of the right side of the heart may have a predominant influence on capacitance vessels, the receptors of the left heart having predominant influence on resistance vessels. This hypothesis was supported by ÖBERG[2]. However, there are no experimental data which could conclusively confirm or disprove this conception. While there is certain information on the responses of resistance vessels connected with cardiac reflexes, no information on capacitance vessels is practically available. Distension of the left atrium in cats is known to be followed by dilation of capacitance vessels in extremities and intestine[2]. An increase of blood pressure in the left ventricle in dogs results in a decrease of the venous blood return to the heart[3–6]. This investigation concerns the responses of resistance and capacitance vessels as reflex effects of the distension of the heart chambers.

Method. Experiments were performed on cats under urethane anaesthesia (1 g/kg), with the thorax open, under artificial breathing. Heparine was administered i.v. to prevent blood coagulation. Vasomotor responses resulting from a distension of the left atrium or ventricle were studied in preparations with the right heart bypass. Through catheters introduced into both venae cavae blood was passing to an extracorporal reservoir. By means of a perfusion apparatus the blood was pumped into the pulmonary artery through a catheter introduced in the succession via the right auriculum, atrium and ventricle. The pulmonary artery and the right auriculum were tightly ligatured on to the catheter. Blood entering the right heart chambers through the coronary sinus and thebesian veins was also diverted to the extracorporal reservoir through another catheter. The distension of the right heart chambers was made by inflation of a rubber balloon introduced via the central end of the anterior vena cava into the right atrium. In the course of the experiment the balloon was moved to the right ventricle.

A distension of the left heart chambers was made in the preparations with the bypassed left heart, a donor cat being used. The main pulmonary artery of a recipient cat was ligatured and the venous blood flowed to the donor's lungs through a catheter introduced into the right atrium via the auriculum. The level of the donor cat was 50 cm lower than that of the recipient cat. Blood oxygenated in the donor's lungs moved through a catheter into the extracorporal reservoir; from here it was taken by means of a perfusion apparatus and pumped into the thoracic aorta of the recipient cat through a T-shaped tube. The distension of the left heart chambers was made by an inflation of a rubber balloon introduced into the left atrium or ventricle via the left auriculum.

The responses of the resistance and capacitance vessels in the hindquarter preparations were studied with a method described in a previous communication[7].

Results. The distension of the right heart chambers (9 animals) was found to produce dilation of the resistance vessels and constriction of the capacitance vessels (Figure 1). Distension of the right atrium resulted in a decrease of vascular resistance (by 15.4 ± 3.6% on the average) in 13 experiments out of 14. In one experiment no changes were found. In 9 of 14 experiments an increase of venous outflow (by 6.2±1.2% on the average) was observed, in the other 5 experiments no changes of the venous outflow

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