a well known fact that isolated perfused kidneys will release renin when their blood flow is sharply reduced[5].

Thus, a reduction of the effective blood volume may give rise to the release of renin by two mechanism: a) by a reduction of the renal blood flow, consecutive to arterial hypotension and/or renal vasoconstriction, and b) by the release of an humoral renin releasing factor.

Résumé. L'activité de la rénine de coupes de reins de rats et celle de la rénine libérée par elles pendant une incubation de 2 heures ont été mesurées. Les coupes témoins ont libéré 22% de leur contenu original. Après adjonction d'albumine sérique, la quantité de rénine libérée était de 49%.

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Comparison of the Blocking Potency of Local Anesthetics Applied at Different pH Values

There has been some question as to whether the uncharged molecule of local anesthetic or the charged form is responsible for the nerve blocking action[1,2]. In a recent series of papers we have concluded that in the squid giant axon local anesthetics block the action potential from inside the nerve membrane in the charged form. This conclusion was reached following experiments in which the effect of pH on the action of a given concentration of tertiary and quaternary local anesthetics was studied on both internally and externally perfused axons. Additional experiments have now been completed to test our hypothesis more quantitatively.

Giant axons of the squid *Loligo pealei* were externally and internally perfused as described previously[3,4]. The maximum rate of rise of the action potential was held constant at a slightly hyperpolarized level (−60 to −75 mv) by application of a polarizing current across the nerve membrane to eliminate the effect of resting potential changes on the action potential. One tertiary derivative of lidocaine (6211–2 [N-(2-Methoxyethyl)-methylamino] 2′, 6′ Acetoxylidide · $pK_a = 6.3$) and procaine were used in the study. The purpose of the experiments was to demonstrate that if the concentration of the charged form inside is held constant the degree of block produced by the local anesthetic will be independent of total anesthetic concentration. Calculations for the changes in the pH of the solution needed to maintain the concentration of the charged form inside constant when the total concentration is altered can be made from the Henderson-Hasselbach equation, $pK_a = \text{pH} + \log [BH^+]/[B]$ where $[BH^+]$ and $[B]$ are the concentration of the charged and uncharged forms, respectively.

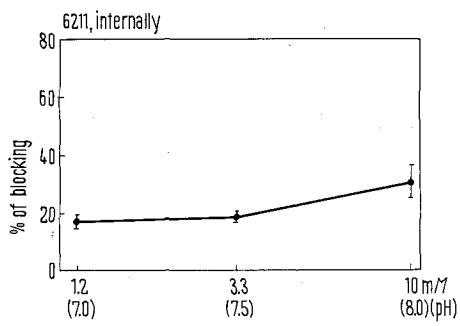

Fig. 1. The effect of changing pH on the blocking potency of different concentrations of 6211 applied inside a squid axon. Each point represents the mean of 4 experiments with the standard error indicated by the bars.

Figure 1 shows the results of experiments in which 3 concentrations of 6211 were applied inside the axon at different pH values. In these experiments the pH of the external solution was held at 8.0 by continuous perfusion. Separate experiments have shown that the pH changes alone, within the ranges used in Figure 1, had no significant effect on the maximum rate of rise of the action potential[3]. As is evident from the graph there is relatively little difference in the degree of block as you go from 1.2 to 3.3 mM if the pH is altered from 7.0 to 7.5. At 10 mM (pH 8.0), there is about a 10% increase in the percent of block as compared to the lower concentrations. There is a marked difference, however, if these results are compared

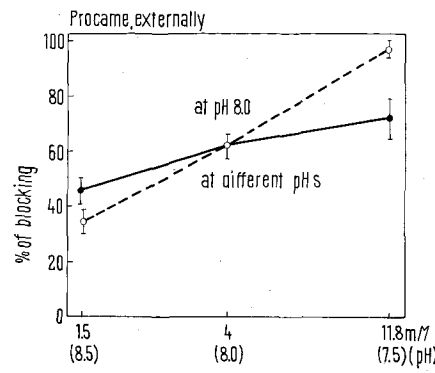

Fig. 2. The effect of pH changes on the blocking potency of externally applied procaine. The solid line represents experiments in which the concentration of procaine was increased from 1.5 to 11.8 mM while changing the pH of the solution from 8.5 to 7.5. The dashed line represents experiments in which the concentration of procaine was similarily increased while keeping the pH at 8.0. Each point is the mean of 5 experiments with the standard error.

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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.