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THE ALKALI IN THE PANCREATIC SECRETION*

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There has been some discussion as to whether the alkali in the pancreatic juice is delivered from reservoirs in the gland or whether it is taken direct from the blood during the pancreatic secretion. In 1928, Hammarsten & Jorpes advanced the theory that the alkali is stored in the gland as nucleic acid alkali and that this alkali bound to the nucleic acids is first taken into use when the secretion takes place. Ball [1930], after having observed that changes in the sodium and potassium content of the blood are immediately followed by changes of these ions in the pancreatic juice, concluded that the alkali in the juice is delivered direct from the blood during the secretion.

If the theory advanced by Hammarsten & Jorpes is correct, and the charging of the gland with alkali proceeds at a slower rate than the discharging, with a maximum secretion, their assumption ought to be experimentally verifiable. These investigators, by means of repeated injections of secretin, caused their experimental animals (cats) to secrete maximum amounts of pancreatic juice. The animals' stomachs had been removed in order to exclude all possibility of a simultaneous secretion of gastric juice. Control cats operated upon in the same way and at the same time were used as comparative material. The first experiments were made with a view to finding out whether the secreted amounts of alkali produced any change in the alkali reserve in the blood of the experimental animals, but no such change could be demonstrated. It was also thought that if the pancreas could be worn out by powerful and sustained secretion the accumulation of acid radicals in the gland which, according to their theory, ought to take place, should bring about a reduction in the alkali reserve in the gland; such a reduction, when sufficiently advanced, should cause an increase in the degree of acidity in the gland. Hammarsten & Jorpes produced an extract from the finely cut-up gland and made *p*H determinations on the extract. They observed that the degree of acidity in the extract from a normal pancreas was in all cases lower than that in the extract from the secreting pancreas. From the

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results of these experiments Hammarsten & Jorpes found support for their theory that the alkali in the pancreatic juice is stored in the gland and discharged from these supplies during secretion.

Ball [1930] took as his starting point the assumption that if the alkali in the juice on secretion comes direct from the blood, then changes in the bicarbonate content of the plasma and in the concentration of each individual cation in the blood ought immediately to affect the concentration of the ions concerned in the pancreatic juice. Ball's experiments were made on dogs, the secretion being set in motion by injections of secretin. He administered hydrochloric acid intravenously, and produced a comparatively high reduction in the bicarbonate content of the blood; this was answered by a slight fall in the bicarbonate content of the pancreatic juice. He raised the bicarbonate content of the blood by an injection of carbonate and the bicarbonate radical in the pancreatic juice rose. After this procedure also, a relatively large increase in the bicarbonate content of the blood was obtained but only a slight increase in that of the pancreatic juice. When he increased the sodium and potassium in the blood, these ions rose at once in the pancreatic juice. Thus Ball found that alterations of the bicarbonate radical, the potassium, and sodium in the blood were immediately followed by similar changes of these ions in the pancreatic juice; the pancreas is therefore readily permeable to these ions. He considered he had proved by these tests that the alkalinity of the pancreatic juice originates directly from the blood. Objections may be raised against Ball's experimental method; the alterations in the equilibrium between acids and bases which he produced in the blood of his experimental animals are large, and fall outside the physiological limits. Furthermore, the changes in the bicarbonate content of the pancreatic juice were small in relation to the great changes in the alkali reserve of the serum. In addition, his results are made more difficult to interpret through the fact that, as he himself demonstrated, the bicarbonate content in the pancreatic juice varies according to the secretion rate. When the rate increases the bicarbonate content in the juice increases. His experiments on the effects on the pancreatic juice of alterations in the blood's content of potassium and sodium show, however, that an alteration in the concentration of these ions in the plasma is accompanied by a corresponding change in the pancreatic juice.

As was proven by Montgomery, Sheline & Chaikoff [1941], radioactive sodium given intravenously appears in the pancreatic juice within 3 min. This, of course, supports the theory that the alkali in the pancreatic juice originates directly from the plasma.

In the investigation to be described in this paper, Hammarsten & Jorpes's theory has been subjected to further experimentation.

If the alkali in the pancreatic juice is delivered from a supply of alkali in the gland, one would expect, as Hammarsten & Jorpes pointed out, that this alkali reserve would decrease during intensive secretion. In order to test whether this really occurs the following experiments were carried out.

Cats were fasted for 24 hr. and anaesthetized with urethane. The duodenal papilla was laid free and 20 doses of secretin [Wilander & Ågren, 1932] were given intravenously every 15 min. for 2–3 hr. By this means a continuous and powerful secretion of pancreatic juice was obtained. The secretin compound had very kindly been placed at my disposal by Ågren & Wilander [1933], and by Hammarsten and his co-workers [1933]. In some of the tests the secreted juice was collected in the manner suggested by Wilander & Ågren and the alkali titrated. Immediately after the conclusion of the experiment the cat was killed and the pancreas removed and freed from fat as completely as possible. The gland was minced by cutting slips 10 μ thick on the freezing microtome, and the process was then repeated. Part of it was transferred to a weighing flask and weighed (2–3 g.). Distilled water (as a rule about 5 c.c.), a few drops of octyl alcohol, and a number of glass beads were added and the flask was energetically shaken. A homogeneous suspension of the gland in water was thus produced. The suspension was then saturated at 38° C. with a mixture of air and carbon dioxide having a carbon dioxide pressure of 40 mm. The alkali reserve in the gland suspension was then determined immediately by Van Slyke's manometric method, on 1 c.c. of the suspension [Peters & Van Slyke, 1932]. Control animals were treated in exactly the same manner, except that they received no secretin injections. The values obtained will be seen in Tables 1 and 2.

In these experiments the stomach was not removed; this did not seem necessary in view of the hypothesis on which the tests were based. The pylorus was tamponated.

TABLE 1. Pancreatic secretion set free by secretin

Cat no.	Alkali reserve mM. $BHCO_3$/kg.			Mean mM. $BHCO_3$/kg.	Collected alkali c.c. of 0·1 N solution
2	18·7	18·5		18·6	6·5
4	21·8	18·7		20·3	10·2
5	18·4	18·2		18·3	2·8
7	18·4			18·4	7·0
8	19·4	18·7		19·1	25
10	20·8	19·9	19·1	19·9	22

TABLE 2. Normal cats

Cat no.	Alkali reserve mM. $BHCO_3$/kg.			Mean mM. $BHCO_3$/kg.
1	18·9	19·0		19·0
3	18·8	18·3		18·6
6	18·9			18·9
9	20·6	20·6	20·1	20·4

The mean figure for the alkali reserve was thus 19·1 mM. of $BHCO_3$/kg. of gland for the secreting cats, and 19·2 mM. of $BHCO_3$/kg. of gland for the normal cats. The alkali reserve of the pancreas therefore does not change during secretion. The experiments point consequently to the fact that the alkali released during the secretion of pancreatic juice is not stored in the gland as was suggested by Hammarsten & Jorpes. The amounts of alkali collected during these secretion experiments exceeded many times over the alkali which, according to the last-mentioned investigators, could be bound by the nucleic acids in the gland of a cat (3 c.c. of 0·1 *N* alkali).

Another way of testing the secretion theory under investigation might be to determine the alkali metals in the gland when at rest and after intensive secretion. I carried out a few experiments of this type.

The experimental animals were cats, and these were operated upon and treated in the same manner as for the preceding experiments. Immediately after the close of the experiment the pancreas was excised and freed as thoroughly as possible from fat and blood. It was divided into two parts and these were weighed and incinerated with perchloric acid. The surplus perchloric acid was evaporated and the ash dissolved in distilled water to make up a certain volume, usually 25 c.c. From the solution the potassium was determined by the method used by Cullen & Wilkins [1933], the sodium by the method of Butler & Tuthill [1931], and of Cullen & Wilkins, and the calcium by Lundegårdh's [1929] method. Table 3 shows the findings.

TABLE 3. Determinations of the alkali in the pancreas

Exp. time min.	Collected pancreatic juice c.c. of 0·1 *N* NaOH	Alkali in the gland tissue			K + Na + Ca m.equiv./kg.
		K m.equiv./kg.	Na m.equiv./kg.	Ca m.equiv./kg.	
180	27·5	112	61	3	176
25	4·4	107	68	3	178
		113	65	3	181
—	0	107	72	3	182
		111	70	3	184

Not even in these experiments could any difference be observed between the pancreas at rest and after secretion. The results support the observations made during the determinations on the alkali reserve.

SUMMARY

1. The alkali reserve of the pancreas of cats after profuse secretion of pancreatic juice is not different from that of the resting gland.

2. The potassium, sodium and calcium content of the pancreas of cats does not change as a result of secretion.

3. The origin of the alkali of pancreatic juice is discussed and it is concluded that it is obtained directly from the blood during secretion.

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