INTESTINAL SECRETION IN MONKEYS

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At the present time monkeys are widely used experimentally. Nevertheless their physiological processes have not been extensively studied, and this is particularly true of the gastro-intestinal tract. No work has been done on the liberation of secretions and enzymes by the intestine, which reduces the usefulness of these animals for studies of the pathology of the digestive tract.

EXPERIMENTAL METHOD

The experiments were carried out on four Chinese female macaque monkeys from five to eight years old, weighing 4-5 kg. Every care was taken before the experiment to see that they were healthy. To study general secretory and enzymatic function of the small intestine, the Thiry operation was performed. The anterior segment of the jejunum was isolated; the proximal end of the isolated loop was closed blindly and the open distal end was brought to the outside through the abdominal wall and fixed to the skin. The intestine was completed by joining the remaining two ends.

The experiment was begun when the animals had completely recovered, $1\frac{1}{2}$-4 weeks after the operation.

During the experiment the animals stood on a stand to which they were held by special bandage.

All the experiments were carried out with the stomach empty. Intestinal juice reduced by periodic secretion was collected through a funnel into a tube immersed in ice. To investigate the influence of mechanical stimulation of soft rubber tube was introduced into the intestinal loop. Each experiment lasted $3\frac{1}{2}$ to 4 hours.

In the juice collected in this way we determined enterokinase, alkaline phosphatase, saccharase amylase and lipase activities.

The amount of juice secreted was measured every 15 minutes, and enzyme activities were found from the total homogenized juice. The enzymes were measured quantitatively. The enterokinase was estimated by Shlygin's method [7], which depends upon the double coagulating and digestive action of active tripsin on casein; phosphatase was estimated from the decomposition of sodium phosphate using phenol phthalin [3]; saccharase from the breakdown of cane sugar and subsequent polarography, lipase was estimated from the breakdown of tributyrin and subsequent titration for free fatty acids with 0.1 NaOH in 50% alcohol [2]; amylase by a modified Wohlgamuth method [2]. The enzyme concentration was expressed in arbitrary units per gram of juice homogenate.

We carried out 65 experiments on four monkeys and obtained juice while the stomach was empty without the use of local stimulation, and in 43 experiments a local stimulus was used.

EXPERIMENTAL RESULTS

Periodic secretion. After a fast 14-16 hours the intestinal juice from an isolated loop of intestine is liberated in separated portions. The duration of a secretory period is, as a rule, 45-60 minutes and sometimes it is reduced to 30 minutes or extended to $1\frac{1}{2}$ hours. There are pauses of from 15 to 45 minutes. One typical experiment is illustrated in Fig. 1. Cases were observed when secretion from the intestinal fistula failed almost completely for as long as four hours. The mechanism of this phenomenon is not understood.

TABLE 1. Amount of Intestinal Juice and its Content of Solid Matter During Periodic Secretion (mean values)

Number of monkey	Total amount of juice in four hours (in g)						Solid portion as a percentage of total juice	
	total		fluid portion		solid portion			
	mean amount	Limits of variation	mean amount	limits of variation	mean amount	limits of variation	mean amount	limits of variation
3435	1,9	0,22—4,31	1,84	0,20—4,15	0,06	0,01—0,16	3,2	1—5
3434	1,51	0,26—3,5	1,26	0,23—3,33	0,25	0,03—0,83	16,5	2—25
3742	1,6	0,55—3,0	1,44	0,53—2,7	0,16	0,02—0,30	10,0	4—22
3882	1,0	0,44—1,62	0,87	0,4—1,3	0,13	0,04—0,32	12,0	8—20

TABLE 2. Amount of Intestinal Juice and its Solid Content in Response to Local Mechanical Stimulation (mean values)

Number of monkey	Total amount of juice in four hours (in g)						Solid portion as a percentage of total juice	
	total		fluid portion		solid portion			
	mean amount	limits of variation	mean amount	limits of variation	mean amount	limits of variation	mean amount	limits of variation
3435	5,7	1,8—8,9	5,65	1,78—3,8	0,05	0,01—0,16	0,9	0,2—2,5
3434	4,6	2,2—6,4	4,48	2,19—6,28	0,12	0,01—0,29	2,5	0,5—5,6
3742	5,5	2,5—8,7	5,28	2,48—8,17	0,22	0,02—0,5	4,0	0,8—8,5

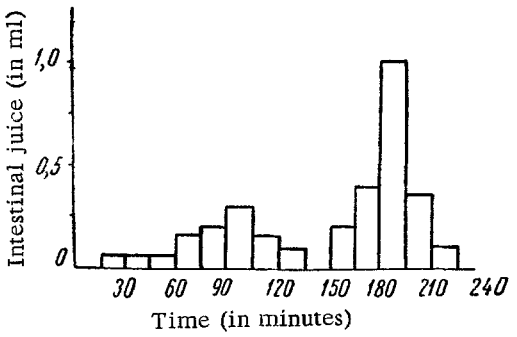

Fig. 1. Intestinal secretion by Monkey No. 3434 in a fasting condition and without mechanical stimulation.

Juice obtained from periodic secretion is an opalescent fluid of a slightly yellow color containing fragments of mucosa suspended in it. A morphological study of this suspension (by M. P. Bochkov) showed that it consisted of degenerating epithelial cells and a small number of lymphocytes.

The reaction of the intestinal juice was alkaline (pH 7.0-9.0). The total amount of secretion and of solid matter (fragments of mucosa) obtained during a four hour period varied not only from one animal to another but also in different experiments on the same animal (Table 1).

Secretion in response to local mechanical stimulation. Under these conditions juice is secreted continuously from an intestinal loop and the rate of secretion is considerably enforced (Table 2).

A comparison of the results shown in Tables 1 and 2 shows that in response to local mechanical stimulation the increase is accounted for entirely by the fluid portion, so that the percentage of solid matter is reduced.

Activity of the enzymes of the intestinal juice. In periodic secretion the mean activity of the enterokinase as estimated from the secretions of all the monkeys was 2,450 units, with a total range from 900-10,000 units. The alkaline phosphatase activity was on average 352 units with a range of variation from 150 to 3015 units. Saccharase activity varied between 20 and 161 units. The indices of activity of such enzymes as amylase and lipase, which are not specific to the small intestine, were 0 to 5 units for amylase, and from traces to 42 units for lipase.

Frequently the amounts of juice obtained were so small as to make it impossible to determine the amount of all five enzymes systematically. Therefore we made the most complete observations on the two enzymes enterokinase and alkaline phosphatase, which we will now describe.

In the juice with the greatest amount of solid matter the enzyme activity was also the greatest.

TABLE 3. Activity of Enzymes in the Intestinal Juice during Periodic Secretion (mean values expressed in arbitrary units per g of juice homogenate)

Number of monkey	Enterokinase		Alkaline phosphatase	
	mean value	limits of variation	mean value	limits of variation
3435	2 039	900—4 545	376	100—759
3434	2 790	1 130—6 700	728	150—3 015
3742	4 590	1 350—10 000	255	150—337
3882	4 237	1 500—8 500	768	337—1 419

TABLE 4. Activity of the Enzymes in Intestinal Juice Obtained in Response to Local Mechanical Stimulation (mean values expresses in arbitrary units per g of juice homogenate)

Number of monkey	Enterokinase		Alkaline phosphatase	
	mean value	limits of variation	mean value	limits of variation
3435	901	600—1 680	156	83—337
3434	1 019	400—1 500	241	100—450
3742	934	250—1 870	87	25—187

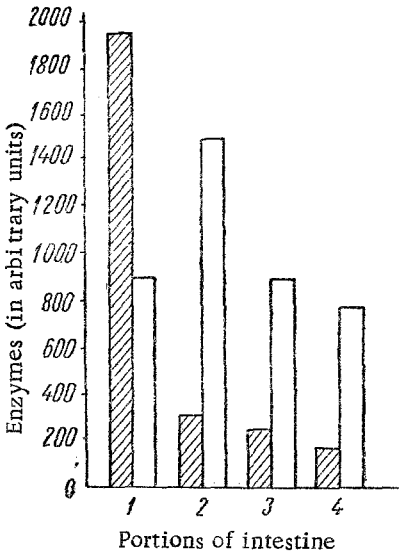

Fig. 2. Enzyme content in the villi of the intestinal mucosa of the small intestine (mean values from thirteen monkeys). 1) Duodenum; 2) initial portion of jejunum; 3) middle of small intestine; 4) end of small intestine. Shaded columns – enterokinase, White columns – alkaline phosphatase.

On comparing the results shown in Tables 3 and 4 it can be seen that the increased secretion of juice caused by mechanical stimulation is associated with a reduction of enzymatic activity. However, this reduction is only relative, because the total amount of enzymes secreted with or without mechanical stimulation is the same. This fact shows that the amount of enzymes liberated during periodic secretion, or in response to mechanical stimulation over a different period, has a constant value. This relationship has been observed previously on dogs and in man by other authors.

In order to determine the site at which the enzymes are elaborated in the small intestine we killed thirteen adult Chinese monkeys, and measured the amounts of enterokinase and alkaline phosphatase in different parts of the small intestine.

Figure 2 shows that the highest concentration of enterokinase was in the duodenal mucosa; it falls sharply in the first portion of the jejunum and is still smaller towards the end of the small intestine. Alkaline phosphatase is more or less evenly distributed along the length of the small intestine, but there is a slightly greater amount in the upper portion of the jejunum.

In general, then, secretion of intestinal juice and intestinal enzymes from an isolated portion of monkey intestine occurs in the same sort of way as has been demonstrated in experiments on dogs, and as determined from observations on man [9].

However, certain special features have been observed which distinguish the secretion of monkey enzymes from those recorded from dogs. The first difference concerns the activity of the enzymes. A comparison of the activities of enterokinase and alkaline phosphatase obtained by the same methods from dogs, monkeys and man reveals the following features. In dogs the enterokinase activity measured in certain arbitrary units is less by several tens of times than that of alkaline phosphatase [1, 5, 6], whereas in monkeys (our own observations) and in man [4], on the contrary it is 3-6 times higher.

We carried out parallel experiments with and without treatment of monkey intestinal juice with self-activated trypsin; no difference was found. The same thing is true of human intestinal juice [4]. These observations show that kinasogen (the precursor of enterokinase in the intestinal juice) may be very rapidly converted into enterokinase by the very small amounts of trypsin and proteinase present in the intestinal lumen. G. K. Shlygin [8] has indicated the possibility of interaction between kinasogen and proteinases.

Therefore the intestinal juice of monkeys shows the usual general characteristics. In addition there are several features in which it resembles the juice of man rather than of dog. Therefore, the monkey may usefully be used for many experiments on the small intestine as a model close to man.

SUMMARY

Experiments were carried out on four adult female macaque monkeys from which the anterior portion of the jejunum was isolated by the Thiry method. It was found that the intestinal secretion of monkeys followed the well known general pattern. When the animal was fasting, and when no mechanical stimulation was applied,intestinal juice was secreted periodically. No secretion occurred in response to local mechanical stimulation and it secreted continuously. The amount of secretion was brought about through an increase in the portion. The greater the solid portion the more active were the enzymes. The enzymatic properties of monkey intestinal juice bear a closer resemblance to human than to canine juice.

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