# PHYSIOLOGY

## THE ROLE OF GASTRIC AND DUODENAL INTEROCEPTORS IN BLOOD AMYLASE CHANGES

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(Received February 2, 1956. Submitted by Full Member of the Acad. Med. Sci. USSR S. E. Severin)

Changes in the activity of blood amylase are considered in clinical practice to be of great diagnostic significance in acute pancreatitis. At the same time, however, the physiological mechanism of blood amylase changes is still not clear.

Our previous investigations [5, 6, 7] have shown that changes in the activity of blood amylase may be of a reflex nature and are closely linked with digestive processes. In connection with this it was necessary to elucidate the role of interoceptors in the gastro-intestinal tract in the reflex changes of blood amylase following the intake of food, and to attempt to establish the possible sources from which amylase could enter the blood stream.

### EXPERIMENTAL

In order to solve this problem extensive experiments were staged on dogs with gastric and duodenal fistulas and externalized pancreatic duct (I. P. Pavlov's technique). In some cases the accessory pancreatic duct was preserved, in others - cut. Dogs with intestinal fistulas (Thiry's technique) and gall bladder fistulas were also used. Stimulation of the mechanoreceptors was effected by inflation of a rubber balloon in the stomach up to 30 and 60 mm of mercury, the air content in the balloon being 250 and 500 cc, and in the duodenum up to 30 mm of mercury, the air content being 100 and 250 cc. Stimulation of the chemoreceptors was carried out by the introduction of 100 and 200 ml of 0.25 and 0.5% hydrochloric acid and 50 ml of fat into the stomach, and 50 ml of fat into the duodenum. The activity of blood amylase was determined by the Engelhardt-Gerchuk method. Since the blood amylase activity in dogs is 10-20 times higher than in man, 4 times less blood was added to the reaction mixture, i.e. 0.06 ml blood was diluted to 6.0 ml and 0.5 ml of the solution was taken for the determination. In cases of a steep rise of amylase activity in the blood of dogs the reaction mixture was diluted after incubation at 37° for 2 hours. Controls were set up to correspond to the dilution. The amylase activity of the intestinal juice and saliva was similarly determined. In bile it was determined in the same way as in human blood.

In the pancreatic juice amylase activity was determined as follows: to 30 ml of 2% starch solution previously heated to 37° was added 0.1 ml of pancreatic juice diluted with physiological solution 1:10. The starch solution was prepared with phosphate buffer (pH = 6.5). Samples of 0.1 ml in 10 ml distilled water were withdrawn after 30 minutes incubation at 37°. 4 ml 0.005 N $K_3Fe(CN)_6$ was added immediately and sugar was then estimated by the Hagedorn-Jensen method. The remaining reaction mixture was tested for starch as a control for the presence of starch or dextrins. At the commencement of a series of experiments the most suitable concentration of starch and time of incubation were usually determined.

## RESULTS

Stimulation of the gastric and duodenal mechanoreceptors for 30 minutes (the balloon being inflated up to 30 mm of mercury) led to increased blood amylase activity 15-45 minutes after cessation of stimulation (Fig. 1).

Analogous data were obtained on introduction of 100 ml 0.25% hydrochloric acid (Fig. 2, 1) and 50-100 ml fat (Fig. 2, 2) into the stomach, and of 50 ml fat into the duodenum (Fig. 2, 3).

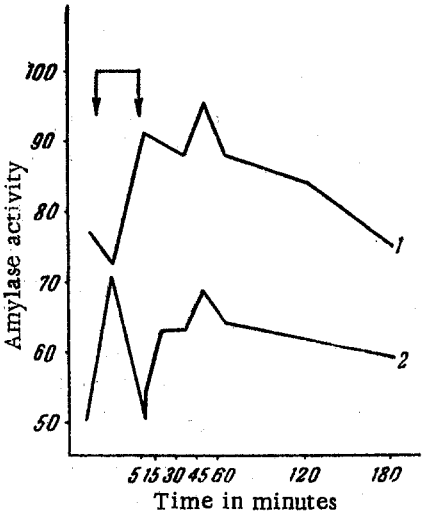


Fig. 1. Changes in blood amylase activity in dogs. A) Time in minutes; B) amylase activity. 1) After mechanical stimulation of the stomach- 2) after mechanical stimulation of duodenum. Amylase activity - in milligrams of sugar, split off by 1 ml blood. Arrows indicate time of stimulation.

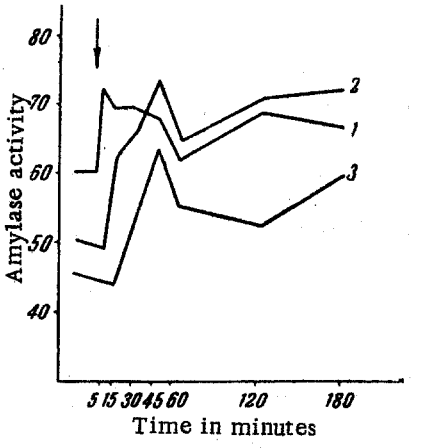


Fig. 2. Changes in blood amylase activity in dogs. A) Time in minutes; B) amylase activity. 1) After introduction of 100 ml 0.25% hydrochloric acid into the stomach; 2) after introduction of 50 ml fat into the stomach; 3) after introduction of 50 ml fat into the duodenum. Amylase activity in milligrams sugar, split off by 1 ml blood. Arrow indicates time of test substance.

An increase in the blood amylase activity after stimulation of gastric and duodenal mechano - and chemoreceptors occurred at exactly the intervals which usually correspond to the complex reflex phase of pancreatic juice secretion.

Of particular interest is the reflex increase in blood amylase activity following the introduction of fat into the stomach and the duodenum. It was noted in our previous investigations that the greatest increase in blood amylase activity in man and dogs was observed after the intake of food which consisted predominantly of fat.

Fat, as well as hydrochloric acid, was considered by I. P. Pavlov [8] to be an independent pancreatic stimulant, and it has been shown [2, 3] that fat acts directly on the secretory process without the participation of hydrochloric acid. Experiments carried out by B. P. Babkin [1], A. V. Tonkikh [9], and others have shown that a reflex mechanism is involved in the stimulating action of fat.

Thus it can be readily taken that a neuro-reflex mechanism is involved in those changes of blood amylase activity which arise under the action of fat.

Excessive stimulation of gastric chemoreceptors (introduction of 200 ml of 0.5% hydrochloric acid) may lead to a steeper rise in blood amylase activity (Fig. 3, 1); in dogs concurrent general restlessness and vomiting are not infrequently observed. An equally great increase in blood amylase activity is observed with excessive

stimulation of gastric mechanoreceptors (inflation of balloon to 60 mm of mercury, with an air content of 500 cc).

It is known from the work of I. T. Kurtsin [4] that excessive stimulation of gastric mechanoreceptors may lead to decreased secretion of pancreatic juice. Apparently, conditions are created on excessive stimulation of gastric mechano- and chemoreceptors which lead to spasm of the pancreatic ducts, as the result of which amylase begins to enter the blood with enhanced intensity. This hypothesis is strengthened by the data of Anrep [10, 11], and Korovitzky [12]. These authors demonstrated that the inhibitory effect of vagus stimulation on pancreatic secretion is associated with an increase in the volume of the pancreas due to engorgement resulting from contraction of the pancreatic ducts.

In fact, an increase in blood amylase activity, similar to that seen on constriction of the pancreatic duct after food intake (Fig. 3, 2), is observed on excessive stimulation of gastric chemo- and mechano receptors.

The increased blood amylase activity in dogs observed on artificial constriction of the pancreatic duct following food injestion indicates that amylase can enter the blood stream directly from the pancreas.

This is also confirmed by blood analyses performed after various operations on the digestive organs in dogs (Table 1).

It can be seen from Table 1 that blood amylase activity in dogs rises steeply after externalization of the pancreatic duct, both when the accessory pancreatic duct is cut and when it is left intact. It must be noted that the high level of blood amylase activity persists over precisely that period of time when no secretion of pancreatic juice occurs through the externalized duct.

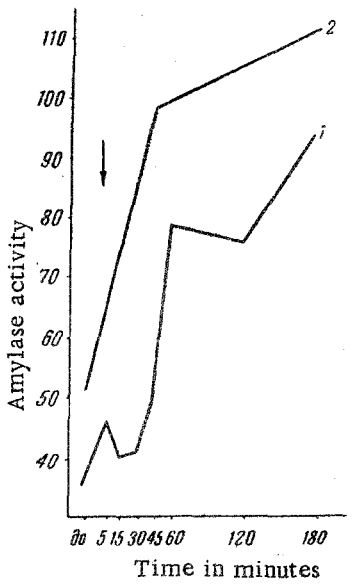


Fig. 3. Change of blood amylase activity in dogs. A) Time in minutes; B) amylase activity. 1) After introduction into the stomach of 200 ml 0.5% hydrochloric acid. Arrow indicates end of administration of acid- 2) during constriction of pancreatic duct after ingestion of food. Arrow indicates end of meal and constriction of duct. Activity of amylase in milligrams sugar, split off by 1 ml blood.

Increased blood amylase activity in dogs deprived of the entry of pancreatic juice into the intestine (externalized main duct, sectioned accessory duct) can only be explained by the direct penetration of amylase from the pancreas into the blood.

At present there is no evidence to suggest that amylolytic enzymes are produced in other organs and tissues (in dogs) in quantities as large as those in the pancreas.

Analysis of the digestive juices in dogs has revealed that only pancreatic juice possesses high amylolytic activity (Table 2).

On the basis of data contained in Table 2 it may be supposed that marked changes in blood amylase activity in dogs cannot be explained by the appearance of amylase from digestive juices other than the pancreatic.

Thus it is possible to conclude that reflex mechanisms are very important in changes of blood amylase activity.

The facts presented indicate the role of gastric and duodenal interoceptors in the complex reflex regulation of blood amylase and allow the deduction that reflex increase of blood amylase activity is closely related to the function of the pancreas.

The data obtained also permit an approach to the discovery of the physiologic mechanism of the changes of blood amylase activity in pancreatic disorders, which is important for diagnosis and elucidation of the pathogenesis of pancreatitis.

TABLE 1

Changes of Blood Amylase Activity in Dogs Following Various Operations

| No. of Dog | Nature of Operation | Amylase Activity in mg Sugar Split Off by 1 ml Blood | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | before operation | days after operation | | | | | | | | | | | | | |
| | | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 14 | 16 | 18 |
| 1 | Fistula of gall-bladder and intestine Thiry's technique | 33 | | 38 | 42 | | | | 34 | | | 47 | | | | | |
| 2 | Fistula of gall-bladder and externalization of bile duct | 57 | | 52 | 45 | | 40 | | | | | | | | 47 | | |
| 3 | " " " " | 31 | 38 | 23 | 32 | 32 | | | | | | | | | | | |
| 4 | " " " " | 46 | 50 | 48 | | | 44 | | | 40 | | | | | | | |
| 5 | Intestinal fistula, Thiry's technique | 40 | 44 | 51 | | | | 37 | | | | 42 | | | | 53 | |
| 6 | " " " | 38 | | 40 | | 39 | | | | 42 | | | | | | | |
| 7 | " " " | 33 | 38 | | 41 | | 37 | | | | 40 | | | 44 | | | 47 |
| 8 | Duodenal fistula and gastric fistula . . . . . | 30 | | 35 | 27 | | 41 | | | | | | | 34 | | | |
| 9 | " " " " | 41 | 47 | 43 | | 50 | | 36 | | | 42 | 49 | | | 39 | | |
| 10 | Gastric fistula . . . . . | 40 | 36 | 39 | 42 | | | | | | | | | | | | |
| 11 | Coagulation of the premotor area of cerebral cortex . . | 35 | | 44 | 37 | | 47 | | | | | | | | | | |
| 12 | Externalization of the pancreatic duct . . . . . | 38 | 449 | 508 | 312 | | 298 | 168 | 147 | | | 79 | | 70 | 56 | 62 | 49 |
| 13 | " " | 47 | 258 | | 382 | | 199 | | 93 | | 64 | | 68 | | 78 | | 76 |
| 14 | " " | 34 | 156 | | 247 | | 189 | | | | 95 | | | | | 39 | |
| 15 | " " | 49 | 93 | | 170 | | | | | | 58 | | | | 39 | | |
| 16 | Externalization of the pancreatic duct with ligature of the accessory duct | 41 | 334 | | 336 | | 478 | 644 | 630 | | 418 | 234 | | 189 | 134 | | 159 |
| 17 | " " " " | 43 | 289 | | 457 | | 320 | | | | 161 | | | | 47 | | |
| 18 | " " " " | 47 | 96 | 163 | 103 | 54 | | | 106 | | 204 | | | 94 | | 64 | |
| 19 | " " " " | 40 | 157 | 297 | 395 | 249 | | 79 | | | | | | | 74 | | |
| 20 | Externalization of pancreatic duct and duodenal fistula | 33 | 161 | 216 | 213 | 180 | | 115 | 92 | 110 | | | | | | | 45 |
| 21 | " " " " | 37 | 89 | | 258 | | 116 | | 85 | | | | | | 43 | | |

TABLE 2

Amylase Activity in Digestive Juices and Blood in Dogs

| Name of Fluid | Amylase Activity in mg Sugar Split off by 1 ml |
|---|---|
| Pancreatic juice | 4,000-20,000 |
| Intestinal juice | 10-50 |
| Bile | 3-15 |
| Saliva | 0-50 |
| Blood | 30-60 |

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* In Russian.