ON THE UNIFORMITY OF THE PANCREATIC MECHANISM IN VERTEBRATA.

By W. M. BAYLISS and E. H. STARLING. (Nine Figures in Text.)

(*From the Physiological Laboratory, University College.*)

In a previous paper[1] we pointed out that the secretion of pancreatic juice, which ensues on the introduction of acid into the duodenum or jejunum, is due, not to a reflex but to the production, under the influence of the acid, of a substance (secretin) in the epithelial cells of the mucous membrane. This substance is at once absorbed into the blood vessels and carried by the blood to the pancreas, where it acts as a specific stimulus of the pancreatic cells. Since the appearance of this paper our results have been confirmed by a number of observers[2], and Wertheimer[3] has succeeded in demonstrating the presence of secretin in the blood flowing from a loop of intestine into which acid has been introduced. If, as we think is the case, the secretion of pancreatic juice is normally evoked by a similar mechanism as by the entry of the acid chyme into the duodenum, we should expect to find that in all vertebrate animals pancreatic secretion would be brought about in the same way, since in all the food is first subjected to an acid digestion in the stomach, and the need of a pancreatic secretion arises only as the acid products of digestion pass from the stomach into the first part of the intestine. Moreover the few chemical characteristics of secretin with which we are acquainted point to this substance being of definite chemical composition and not a labile proteid or allied body, which might be specific for every variety of animal.

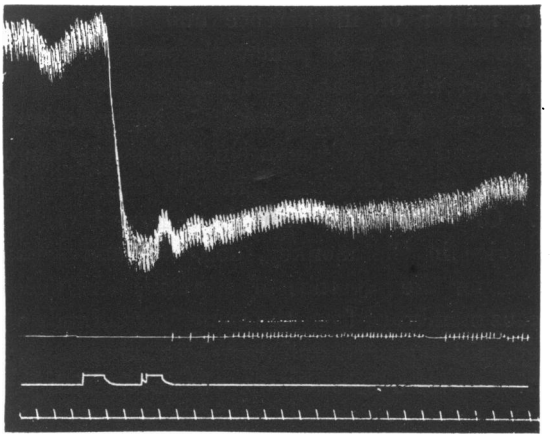
[1] This *Journal*, XXVIII. p. 325. 1902.

[2] Camus and Gley, *C. R. de la Soc. de Biol.* LIV. p. 448, 1902; Camus, *Journ. de Physiol. et de Path. gén.* No. 6, Nov. 1902; Borissow and Walther, *Verhandl. d. Section f. Anat. &c., Versammlung nordischer Naturforscher.* Helsingfors, 1902; Délezenne, various communications in *C. R. Soc. de Biol.* 1902; Stassano, *C. R. Soc. de Biol.*, May 1902.

[3] *C. R. Soc. de Biol.*, May 1902, p. 475, and *Journ. de Phys. et Path. gén.* 1902, p. 1069.

We have sought to decide the question as to the identity of the mechanism in two different ways:

1. In a number of animals we have examined the effects of injecting acid extracts of the mucous membrane of the upper part of the small intestine on the pancreatic secretion, having previously introduced a cannula into the pancreatic duct.



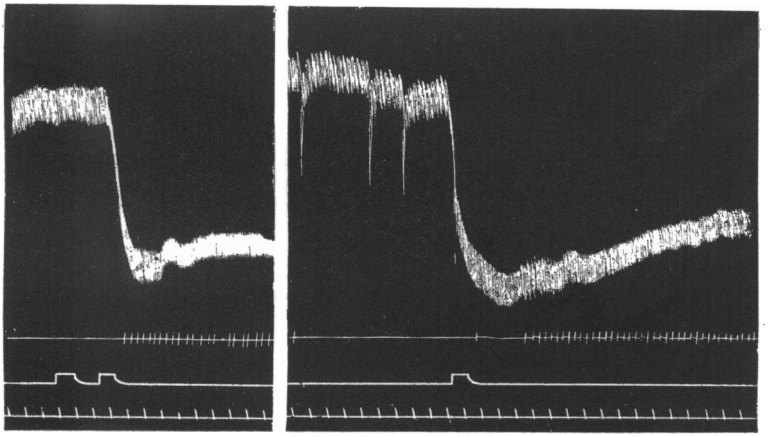


Fig. 1. Pancreatic secretion in dog. Effect of injecting 5 c.c. of acid decoction of rabbit's duodenum. Blood-pressure zero 25 mm. below signal.

Fig. 2. Same experiment. Effect of injecting 5 c.c. of secretin solution from monkey. Blood-pressure zero 36 mm. below signal.

Fig. 3. Same experiment. Effect of injecting 5 c.c. of secretin solution obtained from a boy's intestines (post-mortem). Blood-pressure zero 28 mm. below signal. In these and all other tracings the time-marker indicates 10 second intervals.

2. In those animals in whom we could not conveniently examine the secretion of pancreatic juice we confined ourselves to extracting the mucous membrane of the upper part of the intestine with acid, and testing this extract on the dog or other animal for the presence of secretin. We felt that we were justified in assuming the identity of the pancreatic mechanism in these animals with that in the dog, when we found that the animal from which the preparation was derived was a matter of indifference and that a secretin solution, which would produce a flow of pancreatic secretion in the dog, would also produce a flow in the cat, rabbit, monkey, or frog.

We have so far as possible examined representatives of all the vertebrate classes, and need only mention very shortly the distinguishing features of the pancreatic mechanism in each case.

Mammals. Of this class of animals we have investigated the flow of pancreatic juice in the monkey, dog, cat, and rabbit. We have moreover tested, for the presence of secretin, acid decoctions of the intestinal mucous membrane from the same four animals as well as from man, ox, sheep, pig, squirrel, and new-born kitten. From all these animals an active secretin solution was obtained which produced a flow

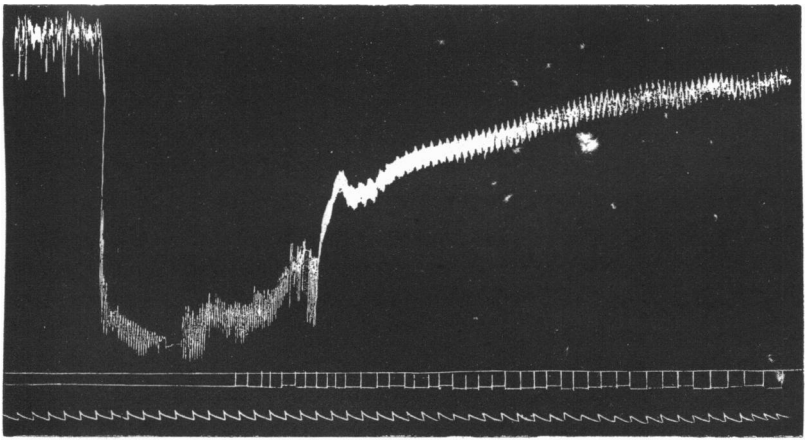


Fig. 4. Pancreatic secretion of cat. Effect of injecting 5 c.c. of secretin solution from dog's gut. Blood-pressure zero raised 15 mm.

of juice in any of the above four animals. In all cases the acid decoction of mucous membrane contains also a depressor substance, although the extent of the depressor effect varies in different animals. In the cat

the depressor effect was even more marked than in the case of the dog, and was often associated with vagus inhibition of the heart.

On the other hand in the monkey and rabbit, the two herbivorous animals we experimented on, the depression of blood-pressure was very much less marked than in the dog and cat. In fact, on several occasions in the monkey a distinct rise of pressure was observed to accompany the secretory effect of the injection.

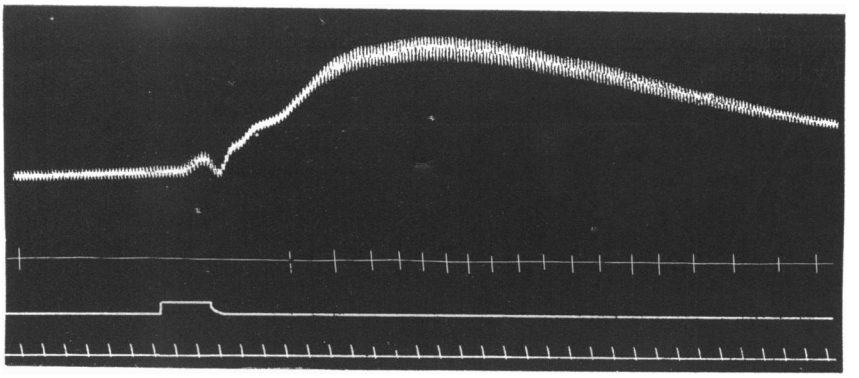


Fig. 5. Pancreatic secretion in monkey. Injection of secretin from human intestine. Blood-pressure zero 23 mm. below time-marker.

Although it is at present difficult to express quantitatively differences between the pancreatic activities of various animals, we have acquired the impression that in the carnivora the pancreas is much more active and the intestinal extract richer in secretin than in herbivorous animals, such as the rabbit or sheep. In the rabbit we found in every case a slight spontaneous secretion, as has been already described by other authors. On injecting secretin the rate of flow was quickened three or four times.

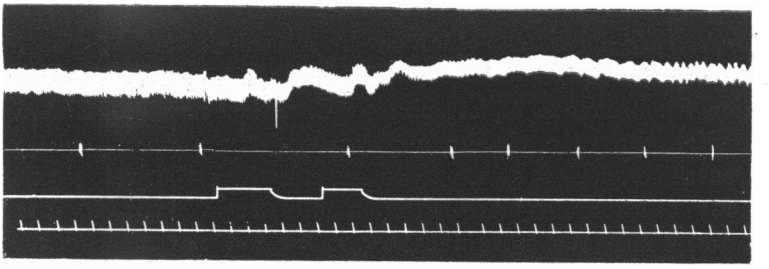


Fig. 6. Pancreatic secretion in rabbit. Effect of injecting 10 c.c. secretin solution from dog's gut. Blood-pressure zero 38 mm. below signal.

If another dose were now given no further effect was produced, the only influence being to prolong the maximal effect already existing in consequence of the first injection.

In view of the possibility that some therapeutic use might be made of secretin, we have investigated the action of this substance when injected subcutaneously or into a serous cavity. In Fig. 7 we see that 10 min. after the intrapleural injection of 12 c.c. of secretin a slow flow of pancreatic juice was still going on, though the effect is insignificant when compared with that produced immediately afterwards by less than half the dose administered intravenously.

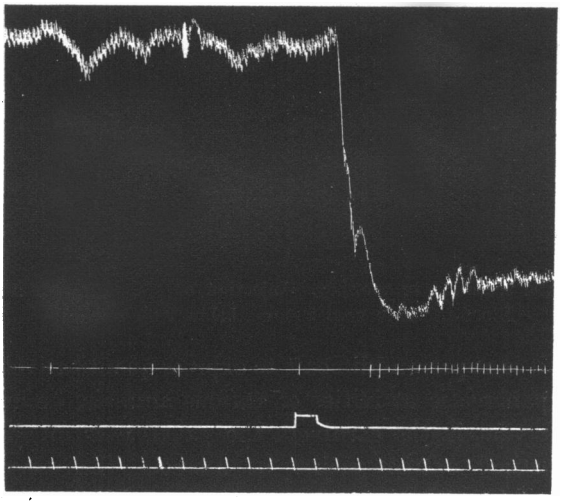


Fig. 7. Pancreatic secretion in dog, 10 minutes after injection of 12 c.c. secretin solution into pleural cavity, by which a slow continuous secretion was set up (about 1 drop a minute). At the point marked by the signal 5 c.c. of the same solution was injected intravenously, and produced a large flow of juice.

Birds. We have made only one experiment on the pancreatic secretion in the bird, choosing for this purpose the goose. The goose in question was in process of fattening for Christmas and was in a state of active digestion. On placing a cannula in the duct of one of its two pancreases, a slow spontaneous secretion was obtained, which was distinctly quickened by the injection of secretin prepared from the dog's intestine. We were inclined to ascribe the absence of any greater effect to the stuffing process which the bird had undergone, especially as the intestinal mucous membrane of the goose or fowl

yields a secretin solution which when tested on the dog or cat is little if at all inferior to that obtained from the intestine of the cat.

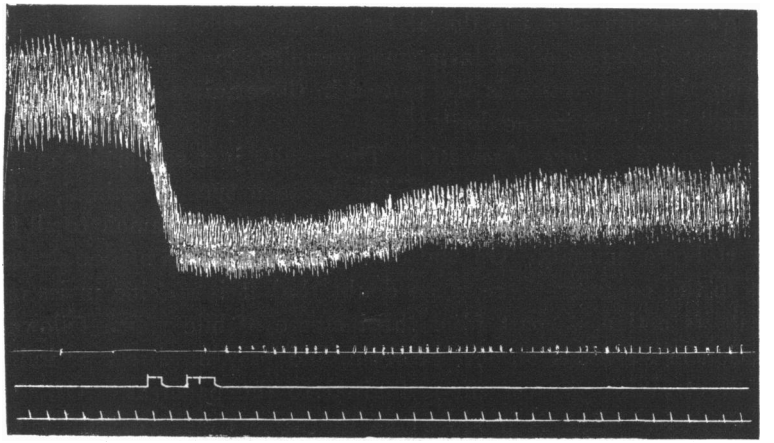


Fig. 8. Pancreatic secretion in dog. Effect of injecting intravenously 15 c.c. of a secretin solution prepared from the intestine of the fowl.

Other classes of vertebrates. Acid decoctions of the mucous membrane of the upper part of the intestines were made in the case of the following animals: tortoise (reptilia), frog (amphibia), salmon (teleostean fish), dogfish and skate (elasmobranchs). In each case the decoction

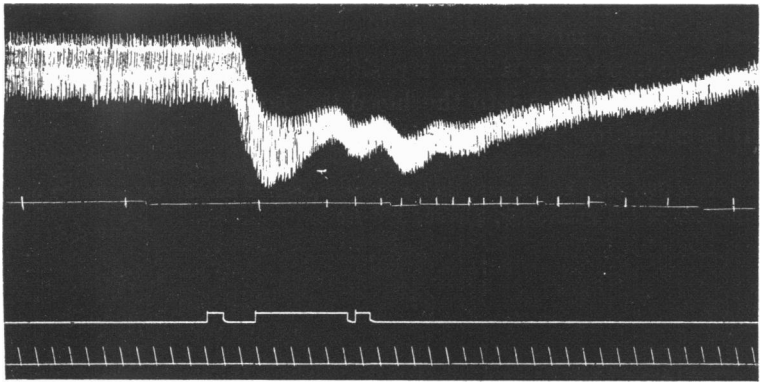


Fig. 9. Pancreatic secretion in dog. Effect of injecting 5 c.c. of secretin solution obtained from the intestines of the dogfish.

was found to contain secretin when tested on the dog. In Fig. 9 we reproduce the record of an experiment in which the acid decoction of

the dogfish intestines was injected intravenously into a dog. It will be seen that a typical though slight secretin effect is produced.

In the case of the frog and toad Mr Dale has found that injection of dog's secretin into the dorsal lymph-sac causes within 24 hours a complete discharge of all zymogen granules from the pancreas, thus showing that a secretion is also caused in these animals by a mechanism identical with that in the dog[1].

The specific nature of secretin. The results just set forth show that the pancreatic secretin is not specific for each type of animal, but is a simple substance of definite chemical constitution common to all types of vertebrate animals. On the other hand, in spite of certain assertions to the contrary, there is no doubt that it is specific in its origin and in its action. Apart from the increase of bile which follows the injection of solutions of pure secretin, and may be direct or indirect, the direct action of secretin is limited to the pancreas. Of course, if a depressor effect is produced at the same time, we shall get the usual effects of anæmia of the medullary centres, amongst which salivation may be mentioned. This secretion of saliva is not observed however if the nerves to the glands be previously divided.

Secretin is obtained by extracting the mucous membrane of the upper part of the small intestine with acid. From no other part of the body can secretin be obtained by a similar or any mode of procedure. We have tried in this way mucous membrane of all other parts of the alimentary canal, the salivary glands, the liver, spleen, pancreas, kidneys, and tongue. We must therefore conclude that pro-secretin exists only in that situation where it is in a position to be acted upon by the acid chyme and to discharge into the blood the body which shall act as the timely stimulus of the pancreatic cells.

[1] Camus (*loc. cit.*) has shown that a secretin, active on the dog, can be obtained from the cat, rabbit, guinea-pig, pigeon, and frog.