"On the Adaptation of the Pancreas to different Food-stuffs." Preliminary Communication. By F. A. BAINBRIDGE, M.B., M.R.C.P. Communicated by Professor E. H. STARLING, F.R.S. Received May 25,—Read May 28, 1903.

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It has been found by Walther and other observers that the chemical composition of pancreatic juice varies in response to the stimulus of different food-stuffs; a fatty diet, for example, led to the secretion of a larger amount of steapsin in the pancreatic juice than did a diet devoid of fat.

Further, Weinland showed that whereas the pancreatic juice of adult dogs normally contained no lactase, the juice of dogs fed for some days on milk contained lactase in large amount.

My experiments have been made in the hope of determining, firstly, whether the pancreas does adapt itself to different food-stuffs, and secondly, by what means this adaptation takes place.

Method.—Milk was chosen as a convenient food, which could readily be added to or excluded from the diet; and the enzyme studied was *lactase*, which converts lactose into galactose and dextrose. Dogs were fed on milk, sometimes with the addition of pure lactose, for periods varying from 12—60 days. Then the animals were anæsthetised with morphia and A.C.E. mixture, and the pancreatic juice obtained by means of secretin.

A certain quantity of pure lactose was weighed, and made up to a known volume. Part of this was estimated at once by Pavy's method; to another part pancreatic juice was added, and the mixture incubated at 37° for 18—48 hours, chloroform or toluol being also added to prevent bacterial action; a control experiment was also made.

The solution was then acidified with acetic acid, boiled for several minutes, filtered, made up to a known volume, and estimated by Pavy's method. In each experiment the same solution of Pavy's fluid was employed for estimating the pure lactose, and the solution after incubation, so as to exclude any error due to varying strengths of the Pavy's solution; moreover, the conditions as regards the duration of the boiling of the sugar solutions during estimation, the rate at which the Pavy's fluid was added, and other details were kept as far as possible constant in every experiment. With these precautions, Pavy's method was found to be extremely accurate, and it has the advantage that the reducing power of inverted lactose is very much larger than that of pure lactose. Almost invariably 50 c.c. Pavy's solution were titrated at each observation, and the sugar solutions used for the estimation had a concentration of about 0·5 per cent.

The extracts of intestinal mucous membrane were made by scraping the gut after washing away all food débris; the gut was ground up with sand, and extracted with chloroform-water, lactose solution, or tap-water. The extracts were then filtered through muslin, and either injected at once, or kept in an ice-chest until they were required.

Results.—The samples of lactose, galactose, and dextrose which I used, had the following reducing powers on Pavy's solution, taking dextrose as 100.

Pure lactose	52·0
Lactose inverted with hydrochloric acid ...	88·5
Pure dextrose	100·0
Pure galactose	87·4

The theoretical value of inverted lactose is therefore 93·7, but I never succeeded in obtaining this figure by even prolonged boiling of lactose with acid.

I. The pancreatic juice was first examined in dogs kept for some days in the laboratory, and fed on biscuits only. In such dogs no lactose was ever found. The following protocol illustrates a typical experiment:—

Experiment I. Dog fed on biscuits only for 2 weeks—

The dog was anæsthetised with morphia and A.C.E. mixture, and pancreatic juice collected by means of secretin.

Pure lactose solution, strength 3·640 per cent.

(*a.*) 25 c.c. pure lactose solution, diluted to 200 c.c. and titrated.

10·2 c.c. = 50 c.c. Pavy's solution.

(*b.*) 25 c.c. lactose solution
2 c.c. pancreatic juice } Incubated at 37° for 72 hours.
Few drops $CHCl_3$.....

Neutralised with acetic acid, boiled, filtered, and made up to 200 c.c.

10·4 c.c. = 50 c.c. Pavy's solution.

II. *Dogs fed on milk.*—When dogs were fed on milk, to which lactose was added in some cases, their pancreatic juice invariably contained lactase, and an inversion of lactose, varying from 12—30 per cent., occurred in different cases. A table of the different experiments and a protocol of one of them illustrates this point:—

TABLE I.—Figures representing the number of c.c. which reduced 50 c.c. Pavy's solution.

Experiment.	Pure Lactose.	Lactose + Juice (Milk-fed dog).	Degree of Inversion.
	C.c.	C.c.	Per cent.
I	11·1	10·53	16·3
II	14·5	12·6	31·6
III	8·6	7·8	22·6
IV	9·65	9·05	15·0
V	9·4	8·8	15·4

Experiment II.—Dog fed on milk only for 26 days.

Anæsthetised with morphia and HCl mixture; pancreatic juice collected.

Pure lactose solution = 5·167 per cent.

(*a.*) 20 c.c. pure lactose solution made up to 200 c.c.

9·4 c.c. = 50 c.c. Pavy's solution

(*b.*) 20 c.c. lactose solution
5 c.c. pancreatic juice
Few drops $CHCl_3$..... } Incubated at 37° for 24 hours.

Neutralised, boiled several minutes, filtered, made up to 200 c.c.

8·8 c.c. = 50 c.c. Pavy's solution.

These experiments indicate that when dogs are fed on milk, the pancreas secretes a ferment—lactase—which is capable of inverting milk-sugar, although in dogs *not* fed on milk no such ferment is present in pancreatic juice. It appears, therefore, that the pancreas does adapt itself to different food-stuffs by modifying the composition of its secretion, at any rate as regards the enzymes.

It is believed by Pawlow and others that this adaptation is carried out entirely by a nervous mechanism, and that a given food reflexly excites the pancreas to secrete a juice specially adapted for the digestion of that particular food-stuff. The same view has been adopted by Weinland, as regards the lactase of the pancreas. In the light of Professor Starling's work on "Secretin," however, it seemed much more probable that the adaptation was due to a chemical stimulus.

Since lactase is normally present in the intestinal mucous membrane of adult dogs and is increased in amount by a milk diet, it seemed possible that lactase entered the blood stream from the intestine and was picked out by the pancreas and secreted. But the blood of a milk-fed dog was found to have no inverting action on lactose, nor did intravenous injections of extract of the mucous membrane of the intestines of biscuit-fed dogs cause any secretion of lactase in the

pancreatic juice. Consequently, the lactase of the pancreas is not taken up as such from the blood, but must be formed by the pancreas itself.

Weinland's observation that lactose injected subcutaneously did not cause the formation of lactase by the pancreas, led to the inference that the intestinal mucous membrane must be concerned in the production of lactase. I therefore made secretin from a milk-fed dog and injected it into a biscuit-fed dog, but the pancreatic juice of the latter contained no lactase. Then the intestinal mucous membrane of a biscuit-fed dog was ground up with sand and a strong solution of lactose. After standing for some hours, the fluid was filtered off and injected into a second biscuit-fed dog. Ordinary secretin was also injected and the pancreatic juice collected; it contained no lactase.

The influence of lactase injected into the gut during life was then investigated. A strong solution of lactose was injected into the intestine of a biscuit-fed dog, and after $1\frac{1}{2}$ hours, secretin was injected, and the pancreatic juice collected and examined; no lactase was present.

The intestinal mucous membrane of this dog was extracted with sand and water, filtered and injected intravenously into a second dog (also biscuit-fed). After waiting $1\frac{1}{2}$ hours, the pancreatic juice was collected and examined; slight inversion occurred, so that the pancreas had secreted some lactase.

Then the intestinal mucous membrane of a kitten fed only on milk was extracted and intravenously injected into a dog; after two hours the pancreatic juice was collected and found to contain lactase, as the following figures show:—

Pure lactose	8·8 c.c.	= 50 c.c. Pavy's solution.
Lactose and pancreatic juice of dog injected with extract of kitten's gut.....	8·0 ,,	

Inversion of 22 per cent. of the lactose.

A modification of this method was subcutaneously to inject into biscuit-fed dogs a $CHCl_3$ water extract of intestinal mucous membrane of kittens or of milk-fed dogs. Two injections were made on successive days, and on the third day the pancreatic juice was collected and examined. In all these cases lactase was produced, as shown by the following table:—

TABLE II.—Figures representing the number of c.c. which reduced 50 c.c. Pavy's solution.

Experiment.	Pure Lactose.	Lactose + Juice.	Degree of Inversion.
	C.c.	C.c.	Per cent.
I	7·4	6·8	19
II	7·8	7·5	9·3
III	7·05	6·75	10
IV	7·95	7·65*	9
V	8·8	8·0	22

* Control, 8·0 c.c.

As far as they go, these experiments show that the intestinal mucous membrane of milk-fed animals, injected into dogs not fed on milk, causes the pancreas to secrete lactase, whereas lactose or extracts of mucous membrane injected separately have no such action. In the present stage of this investigation no complete explanation of these results can be offered. But it seems probable that as a result of the action of the intestinal mucous membrane on lactose, some chemical substance is formed, which passes by the blood-stream to the pancreas, where it stimulates the latter to manufacture a specific enzyme —lactase.

REFERENCES.

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