PROSECRETIN IN RELATION TO DIABETES MELLITUS

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The treatment of diabetes mellitus with secretin is based primarily upon the assumption that the normal stimulus to pancreatic secretion—secretin—is deficient or absent, owing to the lack of prosecretin in the intestinal mucous membrane of diabetic patients. With a view to ascertaining whether this assumption was justifiable, Beddard and I examined the duodenum of several cases of diabetes. Our observations, which were recorded in a former paper, showed that prosecretin was absent, or almost absent, from the duodenal mucous membrane of five out of six cases of diabetes. It seemed desirable to examine a larger number of cases before attempting an explanation of the facts, and the observations made on several other diabetic patients are here described.

METHODS

The duodenum and upper part of the small intestine were obtained from the diabetic patients as soon as possible after death; the mucous membrane was scraped off, and an acid extract made, as described by Bayliss and Starling. The activity of the extract was tested by intravenous injection into cats anaesthetised with chloroform and ether, and having a cannula in the pancreatic duct. In each experiment the activity of the extract was compared with that obtained by injecting secretin prepared from normal animals, or from non-diabetic patients. The blood pressure was usually recorded, and the depressor effect observed.

RESULTS

Previous observations have shewn that prosecretin is always present in the intestinal mucous membrane of non-diabetic patients. The following are the results yielded by the diabetic cases.

Case	Sex, age, and cause of death	Clinical duration of disease	Interval between death and preparation of extract	Flow of pancreatic juice produced by extract
I.	Boy, aged 17: diabetic coma	1 year	24 hours	Very scanty flow
II.	Man, aged 21: diabetes and phthisis	About 18 months	12 hours	Fair flow
III.	Man, aged 53: diabetic gangrene	—	8 hours	Good flow
IV.	Man, aged 45: diabetic coma	18 months	30 hours	Fair flow
V.	Woman, aged 42: diabetic coma	5 months	24 hours	Good flow

Case I.—A boy, aged 17, was admitted to St. Bartholomew's Hospital, October 3rd, 1906, for diabetes. Sugar was first observed in his urine in November, 1905.

On admission the patient was very wasted, his urine contained abundance of sugar (300 grammes for twenty-four hours) but no diacetic acid. Two days later he became comatose, and 'air-hunger' was noticed; death occurred early on October 6th.

Post mortem: The pancreas appeared to be normal; the other viscera showed no noteworthy alterations.

The duodenal mucous membrane was obtained and extracted twenty-four hours after death. The extract was injected into a cat anaesthetised with chloroform and ether, and a scanty flow of pancreatic juice was produced.

Case II.—A man, aged 21, was admitted to Guy's Hospital in May, 1906, for thirst and wasting. These symptoms had been noticed for about a year.

On admission, the patient was extremely wasted; his urine contained much sugar, and gave an intense reaction with ferric chloride. He remained in hospital for some months, during which the daily output of sugar varied from 200 to 300 grammes. Death took place on October 9th, 1906, from acute tuberculosis.

The *post mortem* examination was made twelve hours after death. Both lungs showed extensive acute tuberculosis. The pancreas was normal both macroscopically and microscopically.

An extract of the duodenal mucous membrane was tested on a cat anaesthetised with chloroform and ether, and a fair flow of pancreatic juice resulted.

Case III.—A man, aged 53, was admitted to hospital on September 15th, 1906, for gangrene of the right foot.

On admission, his urine was found to contain much sugar. On October 3rd, the right leg was amputated above the knee; death occurred on October 9th, 1906.

Post mortem : The aorta was atheromatous, the heart wall fatty, the kidneys and liver large, but not definitely fibrosed; the pancreas was tough and fibrous.

The duodenal mucous membrane was obtained and tested eight hours after death; the extract, when injected into a cat anaesthetised with chloroform and ether, produced a good flow of pancreatic juice.

Case IV.—A man, aged 45, was admitted to Guy's Hospital in March, 1906, for thirst, polyuria and wasting; he had been losing weight for nearly a year.

On admission, the patient was found to be very wasted; his breath smelt strongly of acetone; his urine contained acetone, diacetic acid, and a moderate quantity of sugar. During his stay in the hospital he passed daily from 70 to 100 grammes of sugar; on one occasion he showed signs of incipient coma. He was treated with secretin by the mouth, but it had no effect on his output of sugar.

Some months later he died, outside the hospital, from diabetic coma. The intestinal mucous membrane was obtained thirty hours later, and an extract was at once made and examined; when injected into a cat it produced a fair flow of pancreatic juice.

Case V.—A woman, aged 42, began to suffer from pruritus and thirst in October, 1906, and in November, sugar and diacetic acid were found in her urine.

She was admitted to the Metropolitan Hospital, under the care of Dr. Langdon Brown, on February 8th, 1907, and placed on a moderately restricted diet. Two days later she became drowsy, and 'air-hunger' was noticed; she soon became completely comatose, and died on February 11th.

The duodenal mucous membrane was obtained twenty-four hours after death. A boiled acid extract, injected into a cat, yielded a good flow of pancreatic juice.

The following protocol shows the amount of pancreatic juice secreted as a result of injecting the various duodenal extracts. As far as could be judged by their depressant action on the blood-pressure, the extracts (with the exception of the cat's secretin) were approximately of the same concentration.

The first four observations were made on the same cat, and are, therefore, more strictly comparable than the last two observations.

Injection				Blood-pressure			Flow of pancreatic juice	
5 c.c.	Extract from normal cat	...	...	140	fell to	65 mm. Hg	...	1.6 c.c. juice
10 c.c.	" " Case I	...	...	140	"	90 "	...	1 drop
10 c.c.	" " Case II	...	...	130	"	75 "	...	0.4 c.c. juice
10 c.c.	" " Case III	...	...	145	"	65 "	...	1.0 c.c.
10 c.c.	" " Case IV	...	...	120	"	50 "	...	0.5 c.c.
10 c.c.	" " Case V	...	...	—			...	1.6 c.c.
5 c.c.	" " Non-diabetic case			120	fell to	60 mm. Hg	...	0.75 c.c.

I am indebted to Professor Starling for permitting me to publish, in a footnote, the particulars of two other cases of diabetes; in each case an acid extract of the duodenal mucous membrane contained secretin.

NOTE.—*Case I.*—Diabetes and phthisis. *Post mortem*: The pancreas was microscopically normal. An acid extract of the mucous membrane contained abundance of secretin.

Case II.—A diabetic patient, operated on for an ischio-rectal abscess, died three days later from diabetic coma.

Post mortem: The pancreas was large and fibrous; sections showed degeneration of the alveoli—the cells being small and free from granules—rather like a pancreas after ligation of the duct. The duodenal extract contained secretin.

CONCLUSIONS

In all the cases of diabetes described above, a boiled acid extract of the duodenal mucous membrane contained secretin ; with one exception, the activity of the extracts was almost or quite as great as that of extracts from the duodenum of non-diabetic patients.

These cases, taken together with those previously recorded by Beddard and myself, show that prosecretin is more often present than absent in diabetes, and it may be doubted whether the absence of prosecretin has any causal relation to diabetes. It is quite possible, of course, that, as Moore suggests, prosecretin is deficient in *some* diabetic patients during life. But this suggestion is not supported by the clinical observations of Dakin, of Foster, and of Beddard and myself ; and the rapid *post mortem* degeneration which diabetic tissues often undergo might well account for the failure to find prosecretin *after death* in certain cases.

I wish to express my indebtedness to Dr. Beddard, Dr. Andrewes, and Dr. Langdon Brown for their kindness in supplying me with *post mortem* materials and with notes of the cases.

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