

## A Study of Exocrine Pancreatic Function by Pancreatic Function Diagnostant (PFD) on Cancer of Pancreas and Biliary Tract\*

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### ABSTRACT

Since 1976, the authors administered the test meal PFD to patients mainly with pancreatic diseases in order to know the changes in the exocrine function of the remaining part of the pancreas. In the present study, investigation was made on the usefulness of PFD in the cases undergoing surgery for pancreatic and biliary cancers, according to the sites of cancers. Urinary PABA in 6-hour urine showed low levels in the cases of pancreatic head cancers and ampullary cancers, and their excretion patterns showed a delayed excretion type in the cases other than extrapancreatic biliary cancers. In the resectable cases, the 6-hour urine level of PABA was significantly improved within 12 months of surgery compared with that before surgery ( $p < 0.01$ ). Their excretion patterns showed the high peak levels in 2 hours and decreased sharply thereafter. When the PFD is administered out, it seems to be useful for the analysis of the excretion patterns as well as 6-hour urine levels in order to predict the conditions the pancreas duct and the recovery of the pancreatic exocrine function.

### INTRODUCTION

It is very useful, in many aspects, to know the pancreas functions before and after surgical operations because the disease in the bile duct and the pancreas are often complicated with the impairment of the functions of the pancreas as well as those of the liver. The pancreozymin-secretin test (PS test)<sup>3)</sup> has so far been believed to be the most reliable way to examine the activity of the pancreas exocrine function. However, since this test utilizes the cannulation method requiring complicated techniques, the test has been carried out mainly before operations. A synthetic peptide, N-benzoyl-L-tyrosyl-para-amino-benzoic acid (BTPABA), described first by Imondi et al.<sup>2)</sup> in 1971 has been widely used as a pancreatic

function diagnostant (PFD). Although there still remain some problems to be solved, the PFD can easily be applied to patients even after operations. Since 1976, the authors<sup>4)</sup> have carried out trials on the PFD mainly in the cases of pancreatic diseases. Descriptions are made in the present papers on the PFD for the cases with surgical operations for pancreatic and biliary cancers.

### MATERIALS AND METHODS

The sites of cancers in our cases were classified according to the criteria for the management of pancreatic and biliary cancers. For convenience' sake, cancers in the lower bile duct described in the criteria for management of pancreatic and biliary cancers were defined as intrapancreatic biliary cancer and those in

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**Table 1.** Cases of performed PFD

Portion	Resectable case	Unresectable case	Total
Extrapancreatic biliary cancer	0	3	3
Intrapancreatic biliary cancer	6	0	6
Ampullary cancer	15	0	15
Pancreas head cancer	5	7	12
Pancreas body cancer	0	1	1
Total	26	11	37

the middle part of the bile duct as extrapancreatic biliary cancers. Table 1 shows the number of cases with and without resection at each site.

Operations employed in most cases without resection were a bypass method for the reduction of yellowness. In all resectable cases, the pancreatic head and duodenum (PD) were resected.

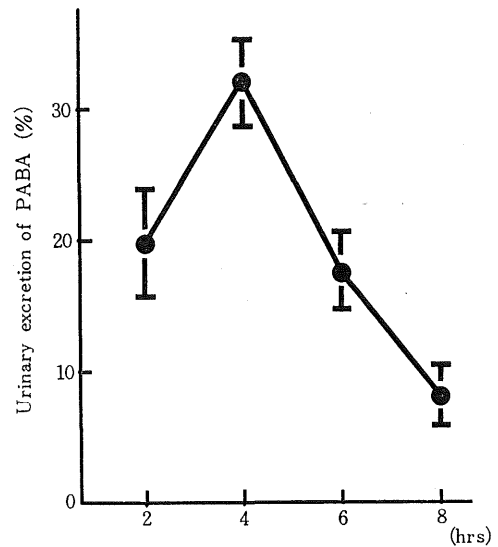
In the cases undergoing the PFD, administrations of digestive enzyme preparations were discontinued three days before the test, and ham and egg was given as breakfast (containing about 30 g of proteins) on the test day. After urination, the PFD test solution of two ampules (corresponding to 339 mg of PABA) was given, allowing the intake of water or tea of 200 ml or more. Urine was collected every two hours up to 8 hours after administration of the test solution. Urine PABA was determined using the modified Smith method designed after the Bratton-Marshall or DACA method.

## RESULTS

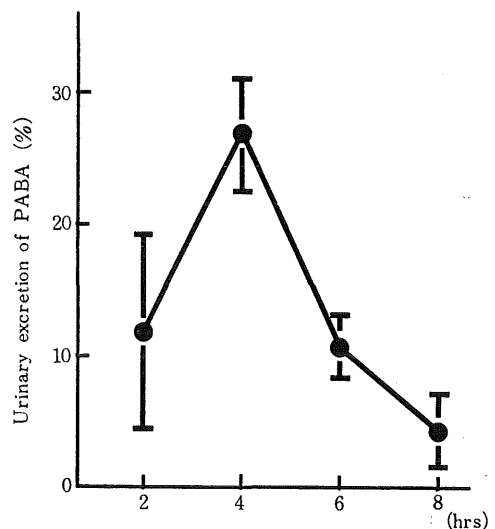
Urinary PABA in 6-hour urine was  $71.9 \pm 2.9\%$  (mean  $\pm$  S. D.) in seven normal subjects. As shown in Fig. 1, the urinary excretion of PABA reached the peak level in 4 hours and then decreased gradually.

PABA levels in six-hour urine before operation were  $48.3 \pm 11.6\%$  for extrapancreatic biliary cancer ( $n=3$ ),  $60.9 \pm 19.9\%$  for intrapancreatic biliary cancer ( $n=4$ ),  $24.0 \pm 12.3\%$  for ampullary cancer ( $n=7$ ),  $29.3 \pm 12.4\%$  for pancreatic head cancer ( $n=10$ ) and  $49.9\%$  for pancreatic body cancer ( $n=1$ ). Their excretion patterns are shown in Fig. 2 to Fig. 5.

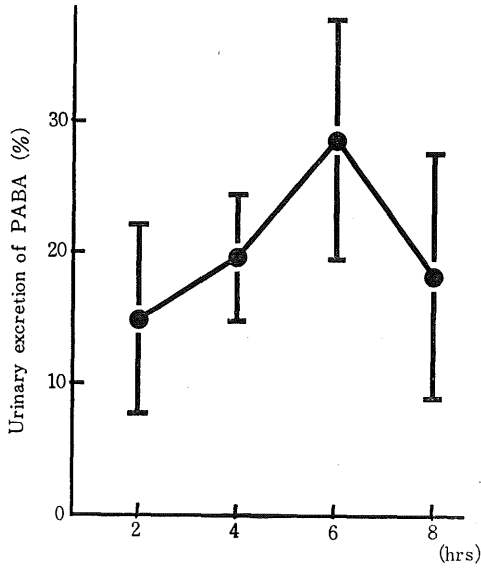
PABA excretion in six-hour urine before operation was  $36.2 \pm 13.3\%$  ( $n=11$ ) in cases without resection. PABA levels in six-hour



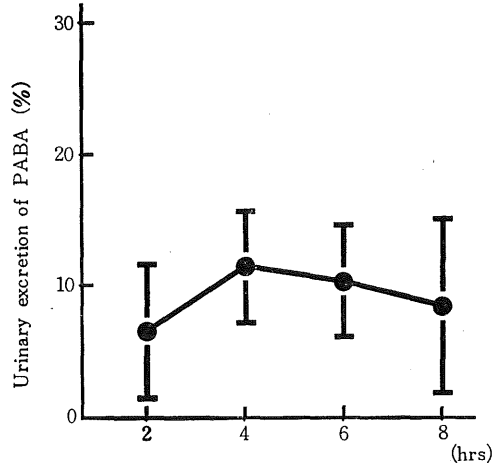
**Fig. 1.** Urinary PABA excretion in 7 normal subjects



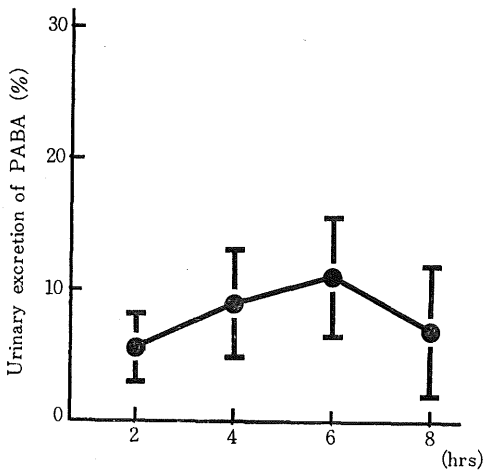
**Fig. 2.** Pattern of urinary PABA excretion in 3 patients with extrapancreatic biliary cancer before operation



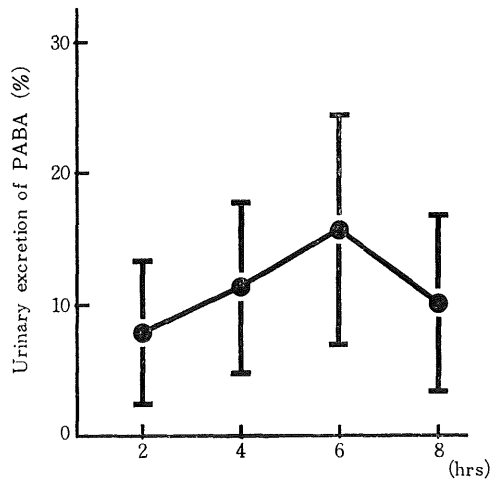
**Fig. 3.** Pattern of urinary PABA excretion in 4 patients with intrapancreatic biliary cancer before operation



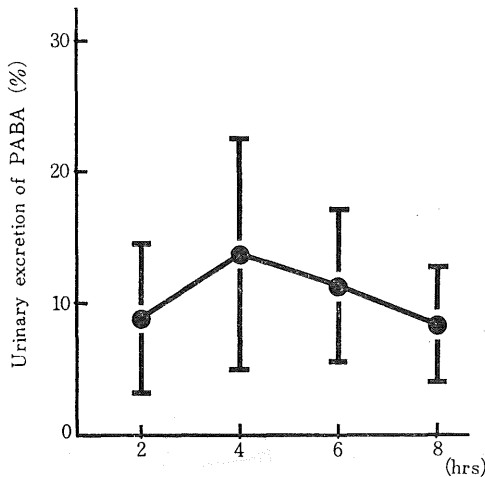
**Fig. 5.** Pattern of urinary PABA excretion in 10 patients with pancreas head cancer before operation



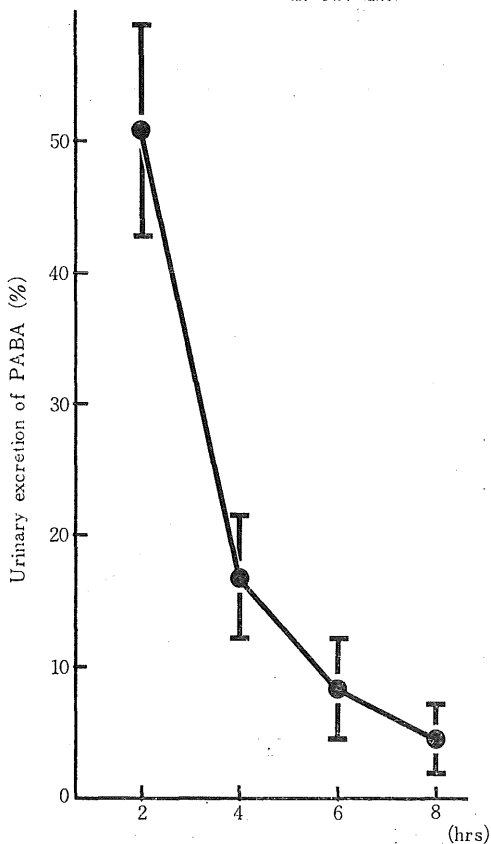
**Fig. 4.** Pattern of urinary PABA excretion in 7 patients with ampullary cancer before operation



**Fig. 6.** Pattern of urinary PABA excretion in 15 patients before pancreaticoduodenectomy



**Fig. 7.** Pattern of urinary PABA excretion in 23 patients within two months after pancreaticoduodenectomy



**Fig. 8.** Pattern of urinary PABA excretion in 6 patients over one year after pancreaticoduodenectomy

urine were  $35.0 \pm 24.0\%$  before operation ( $n=15$ ),  $32.8 \pm 23.1\%$  within 2 months after operation ( $n=23$ ) and  $74.0 \pm 6.2\%$  after one year of the surgery ( $n=6$ ) in resected cases. There were significant differences in excretion patterns ( $p < 0.01$ ) before operation and after one year of the surgery, as well as within 2 months and after one year of the surgery. Excretion patterns are shown in Fig. 6 to Fig. 8.

## DISCUSSION

It has been widely accepted that the PS test is one of the most excellent methods for the determination of pancreatic exocrine functions. However, the PS test requires cannulation and is not actually performed after operation because of technical difficulties. For this reason, the function of the remaining part of the pancreas before and after pancreatic surgery has remained largely unclarified, though it has been attracting much attention among the researchers.

In 1971, Imondi et al.<sup>2)</sup> reported on a new pancreatic exocrine function test (PFD) using BTPABA. Its principle was based on the urine excretion of BTPABA which is specifically decomposed by chymotrypsin in the pancreatic juice, absorbed from the intestinal mucosa and undergoes conjugation in the liver. Therefore, the measurement of urine PABA represents the indirect chymotrypsin activity in the pancreas. Unlike the PS test, this method does not require cannulation and is very simple. It is therefore acceptable by patients and can be performed even after the surgery.

The correlation between the PFD and PS test was described in details in terms of various factors<sup>1)</sup>. It is reported that the high correlation between the PFD and PS test is obtained with the increase in the severity of pancreatic impairments. As the PFD provides insufficient evidence for the establishment of diagnosis in patients with a mild pancreatic impairment, the combination with the PS test is desirable. The PFD shows no zero point after the total resection of the pancreas. There still remain problems especially in the cases of hepatic, renal or digestive impairments.

The authors have conducted the test meal PFD giving ham and egg as a load meal in patients mainly pancreatic diseases in order to know the exocrine of the remaining part of the pancreas before and after pancreatic

surgery. Because of different aspects of physiopathology, chronic pancreatitis is not handled similarly as in the cases of pancreatic head cancer by the test of the remaining pancreatic exocrine function. As chronic pancreatitis was previously reported<sup>9)</sup>, the present study describes only periampullary carcinoma.

The result of each site of cancer before operation was compared. The six-hour urine excretion level was low in ampullary cancer and pancreatic head cancer, which might possibly compress and obstruct the main pancreatic duct. The apparent peak level was not observed in the excretion patterns. The peak level was lower (10 to 15%) than the normal peak level (about 30%). This indicates the severe obstruction of the main pancreatic duct. The six-hour urine excretion level was slightly lower in extrapancreatic biliary cancer than in normal subjects, but showed the similar pattern. The excretion pattern observed in intrapancreatic biliary cancer was in the mid way between that of the extrapancreatic biliary cancer and of ampullary cancer. It is reasonably necessary to take consideration of the progress of cancers, and it cannot draw conclusions only from the present results. However, it seems to be clear that the opening state of the pancreatic duct exerts influence on the PFD.

Then, the changes in the extrapancreatic secretion were studied before and after operation in PD cases. The prognosis of PD cases was observed and there were often the cases which required no administration of digestive enzymes, showing the constant body weight and improvement in digestive symptoms such as diarrhea, after one year of the surgery. Accordingly, we administered the PFD within two months of the surgery or after one year of the surgery when the patients showed stabilized conditions. There was no significant difference in 6-hour urine excretion levels, comparing patterns before operation and within two months of the surgery. However, there were significant differences between the states before operation and after one year of the surgery, or between within two months of the surgery and after one year of the surgery. The cases of a delayed excretion before surgery showed characteristic patterns; their peak level was attained at an early stage within two months after the surgery, and high peak level was attained after two

hours and then decreased sharply in the cases after one year of the surgery. Examination on these changes in the pattern revealed following four points; i) improvement in exopancreatic secretion, ii) maintenance of the opening of the anastomotic pancreatic duct and the success of pancreatic drainage, iii) changes in dynamics of digestive hormones due to the resection of the gastric vestibular region, duodenum and upper jejunum or digestive reconstruction, and iv) vagotomy and changes in innervation due to lymphoidectomy.

If pancreatic exocrine secretion after operation is predicted based on the preoperative PFD test, it will give us useful information about the selection of operative procedures. At present, it is difficult to know the changes in post-operative pancreatic exocrine functions before the surgery is performed. However, operable pancreatic head cancer shows a short suffering period compared with chronic pancreatitis, which accompanies minor secondary pancreatic disorders. Thus, the improvement in the pancreatic exocrine function is expected after the operation.

In the test on pancreatic exocrine function using the PFD, it is useful to analyze excretion patterns as well as PABA levels in 6-hour urine which may provide information on the opening conditions of the pancreatic duct.

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