Hiroshima Journal of Medical Sciences
Vol.36, No.4, 367~375, December, 1987
HIJM 36-50

Urinary and Serum Bile Acids in Bile Peritonitis

Makoto TAKAHASHI, Mitsuo HARADA, Kazuo INAGAKI,
Naotaka AKIMOTO, Hiroyuki TAMURA, Kiyoshi MATSUNO,
Yorinobu MAEDA and Susumu FURUYASHIKI
Department of Surgery, Chugoku Rosai Hospital, Kure, Hiroshima 737-01, Japan
(Received August 21, 1987)

Key words: Hypercholanuria, Hypercholanemia, Urinary bile acids, Serum bile acids, Bile peritonitis

ABSTRACT

Serum or urinary bile acids were determined in bile peritonitis with emphasis on peritoneal bile acid absorption. Bile peritonitis patients consisted of each two patients with insidious type, and acute or dramatic type, of bile peritonitis. All of them exhibited elevation in bile acid concentrations of 95.3, 37.0 mg/liter urine in the former, and of 87.6, 12.8 mg/liter serum in the latter. This finding implies that intraperitoneal bile acids were absorbed through the peritoneum into the blood resulting in hypercholanemia and hypercholanuria, in bile peritonitis. Early diagnosis of bile peritonitis is sometimes difficult because there are fewer signs of peritoneal irritation. Therefore our data indicate that enzymatic determination for serum bile acids is effective for early detection of bile peritonitis and thus the fatal outcome in insidious type of bile peritonitis can be avoided.

Although normal man excretes small amounts of bile acids into urine, the concentration of bile acids in peripheral blood increases in certain conditions such as intrahepatic cholestasis and hepatocellular damage, resulting in spillover of serum bile acids into urine[1,2,3,7].

Most of bile peritonitis belong to acute, dramatic type as bile peritonitis has been said to be associated with intense clinical symptoms. However we have found that there exists insidious type of bile peritonitis which is difficult to diagnose early and develops in intraperitoneal infection at the time diagnosed definitely, resulting in poor prognosis.

On the other hand, diffuse peritonitis secondary to perforated duodenal ulcer exhibits remarkable symptoms of peritoneal irritation in spite of the intraperitoneal existence of bile component as in bile peritonitis, so that early diagnosis is easy.

In the present paper, the measurement of urinary and serum bile acids has been employed in the peritonitis with emphasis on peritoneal bile acid absorption. Moreover urinary bile acids were determined in some diseases which are encountered by the practicing surgeon.

MATERIALS AND METHODS

Gas Chromatographic Analysis for Urinary and Serum Bile Acids

Analytical procedure was based on the method of Makino[8], with modifications (Fig. 1). After 50 ml of urine or 5 ml of serum was passed through a Sep-pak cartridge (Waters Associates,

Address for correspondence and reprint requests:
Makoto Takahashi, M.D.,
Department of Surgery, Chugoku Rosai Hospital 1477, Hiro-machi, Kure City, Hiroshima 737-01, Japan.
Telephone: 0823-72-7171, Japan

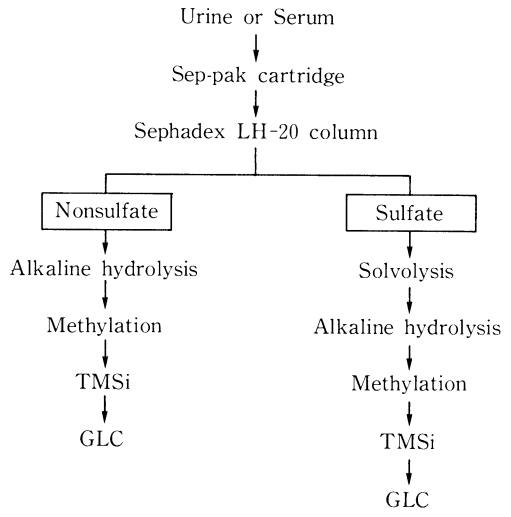


Fig. 1. Analytical procedure for serum and urinary bile acids

Milford, MA, U.S.A.), the bile acid fraction was obtained by eluting the cartridge with methanol, and was passed through a Sephadex LH-20 column (particle size: 25—100 μm, Pharmacia Fine Chemicals, Uppsala, Sweden) resulting in a group separation of the nonsulfated by methanol-chloroform (1:1, v/v) and sulfated fractions by methanol. The sulfated fraction was solvolyzed with HCl and subjected to alkaline hydrolysis, the unsulfated fraction was hydrolyzed without prior solvolysis. The bile acids, after extraction, were analyzed by gas-liquid chromatography (GLC) as methyl ester-trimethyl-silyl ether derivatives.

For the glc analyses, 5-cholestane (Sigma Chemical Co., St. Louis, MO, U.S.A.) was used as the internal standard. All data were obtained with a Shimadzu GC-7A chromatograph employing 3% 0V-17 and 2% Poly-I 110 columns. Measurements of peak areas were accomplished with a Shimadzu C-RIA chromatopac adjusted to record retention time in minutes. Unknown glc peak was analyzed by glc-ms (Shimadzu GCMS 7000 mass spectrometer) and was finally identified.

Enzymatic Analysis for Serum Total Bile Acids

Serum total bile acids were determined by an enzymatic assay using 3α-hydroxysteroid dehydrogenase (Enzabile, Daiichi Pure Chemicals, Tokyo, Japan) in a few patients.

Patients

Urinary or serum bile acids were determined in 29 patients who were admitted to the Department of Surgery, Chugoku Rosai Hospital since January 1982. The patients were divided into seven groups, as follows:

Group A: 6 normal subjects (control group).
Group B: 4 patients with disturbed renal function having serum BUN levels greater than 50 mg/dl.
Group C: 4 patients with cirrhosis of the liver.
Group D: 2 patients with hepatomas but without cirrhosis.
Group E: 3 patients with extensive liver metastases secondary to gastric cancer.
Group F: 6 patients with diffuse peritonitis secondary to perforated duodenal ulcer.
Group G: 4 patients with generalized bile peritonitis; 2 patients with insidious type (cases I, II), and 2 patients with dramatic type (cases III, IV), of bile peritonitis.

All the patients of group F presented with a sudden onset of abdominal pain, and were operated upon within twenty four hours from the onset. They had moderate amounts (500 to 1000 ml) of bile-colored fluid in the peritoneal cavity at surgery. Preoperative urinary bile acids were analyzed in this group. The patients had normal liver function tests and normal renal function preoperatively.

Clinical Course of Patients with Bile Peritonitis

Case I: A 78 yr old female with colicky epigastralgia was diagnosed as having gallstones by ultrasonic examination. As serum bilirubin level gradually elevated up to 6.2 mg/dl, PTC (percutaneous transhepatic cholangiography) was carried out using a fine needle for precise visualization of the biliary trees. However the procedure failed because there was no appreciable dilatation of the intrahepatic bile ducts. Thereafter she had an uneventful clinical course with no fever, no signs of peritoneal irritation, and remission of the jaundice, except for gradual abdominal distension.

Nevertheless, on the 9th day after PTC, she suddenly fell into shock and an emergency

laparotomy was carried out. Turbid, brown bile (1200 ml) was aspirated from the peritoneal cavity, and the patient was diagnosed as having Mirizzi's syndrome. Very careful inspection confirmed intraperitoneal bile leakage from the liver surface which had been punctured with the needle during PTC. Cholecystectomy and peritoneal drainage were carried out.

On the 5th postoperative day discharge from the drains became clear, but bile discharge resumed from the 6th postoperative day. Bile leakage finally stopped on the 12th day after surgery. Unfortunately, in spite of ICU management, the patient died of pneumonia and renal failure on the second week postoperatively.

In this patient, 24 hr urine samples were taken for urinary bile acid determination on days 1, 2, 3, 4, 7, 9 and 10 after surgery. Acinetobacter lowoffii was detected in a bacterial culture of the peritoneal fluid aspirated during the operation.

Case II: Conservative therapy had been carried out to a 51 yr old male, who suffered from right hemiparesis and motor aphasia secondary to obstruction of the left middle cerebral artery. Although the motor aphasia made it difficult to evaluate his condition, he seemed to have abdominal pain on the 5th day prior to the emergency laparotomy. Thereafter he had an uneventful course without fever tachycardia. However he had no bowel movement with gradual abdominal distension, and suddenly fell into preshock with anuria.

Physical examination disclosed minimal signs of peritoneal irritation and abdominal paracentesis was performed with a diagnosis of generalized bile peritonitis, leading in an emergency laparotomy. During the operation 600 ml of turbid light-brown bile was aspirated from the peritoneal cavity. Careful inspection confirmed perforation of the cholecystolithiasis, and cholecystectomy with peritoneal drainage was completed surgically. Postoperatively, abdominal signs were free from symptoms with the exceptions of pneumonia and intractable diarrhea.

In this patient an 8 hr urine sample was obtained just prior to surgery, and 24 hr urine samples were obtained on days 1, 2, 3, 6, 7, 8 and 17 after surgery for determination of urinary bile acids. Enterococcus faecalis was demonstrated in a bacterial culture of the peritoneal fluid aspirated during the operation.

Cases III and IV: These two patients had distinct symptoms of peritoneal irritation following the onset of bile leakage. Case III (a 71 yr old man) had received cholecystectomy with choledochal T-tube drainage for cholecysto- and choledocho-lithiasis. However, removal of the T-tube on the 3rd postoperative week caused intraperitoneal bile leakage, and an emergency laparotomy was performed in 24 hr following the leakage. Choledochal and peritoneal drainage was carried out as an operative procedure. 250 ml of dark-yellow bile was aspirated from the peritoneal cavity during the operation. In this patient, serum bile acids just prior to surgery were analyzed by gas-chromatographic and enzymatic methods. Case IV (a 55 yr old man) was a bile peritonitis patient secondary to perforated cholecystolithiasis, and was operated upon in 7 hr after the onset. Following the aspiration of 100 ml of bile-colored intraperitoneal fluid, cholecystectomy with peritoneal drainage was carried out. In this patient, serum total bile acids were determined prior to the operation, on days 3, 5 and 7 after surgery, using enzymatic method. Both patients showed normal liver function tests throughout the study, and rapidly returned to healthy conditions postoperatively. Bacterial cultures of the intraperitoneal fluids aspirated during the operation demonstrated the presence of Escherichia coli, Enterococcus faecalis in case III, and Enterobacter amnigenes, Enterococcus faecalis in case IV, respectively.

RESULTS

Table 1 shows the bile acid data for all groups of patients. The concentration and daily excretion of bile acids were 0.64 ± 0.66 mg/liter urine and 0.66 ± 0.66 mg/day in the normal subjects of group A. Significant elevations of urinary bile acids were found in groups C and E compared with the controls [11.75 ± 6.41 mg/liter urine ($P < 0.05$) and 10.20 ± 6.88 mg/day ($P < 0.05$) for group C; 20.71 ± 10.25 mg/liter urine ($P < 0.05$) for group E].

The concentration of urinary bile acids in group F were similar to that of the controls (0.98 ± 0.95 mg/liter urine). In contrast, all of the patients with bile peritonitis showed elevated concentration of bile acids in biological samples.

Table 1. Bile acid data in various diseases[a]

Group	Diagnosis (number of patients)			magnitude of jaundice	Concentration of bile acids[b] (mg/liter sample)	Daily excretion of urinary bile acids (mg/day)
A	Normal (6)			(−)	0.64 ± 0.66	0.66 ± 0.66
B	Renal insufficiency (4)			(−)	1.22 ± 0.93	2.86 ± 2.90
C	Liver cirrhosis (4)			(−)~(+)	11.75 ± 6.41[c]	10.20 ± 6.88[c]
D	Hepatocellular carcinoma without liver cirrhosis (2)			(+)	7.37 ± 2.33	4.76 ± 2.02
E	Extensive hepatic metastasis of gastric cancer (3)			(++)	20.71 ± 10.25[c]	17.87 ± 10.26
F	Diffuse peritonitis due to perforated duodenal ulcer (6)			(−)	0.98 ± 0.95	
G	Bile peritonitis (4)	Case I	Insidious type	(−)	95.3	219.2
		Case II		(−)	37.0	
		Case III	Dramatic type	(−)	87.6	
		Case IV		(−)	12.8	

[a]Values are given as mean ± SD except for group G.
[b]All the data show the concentration of urinary bile acids (mg/liter urine) except for cases III and IV. Cases III and IV show the concentration of serum total bile acids (mg/liter serum)
[c]$P < 0.05$ compared to group A.

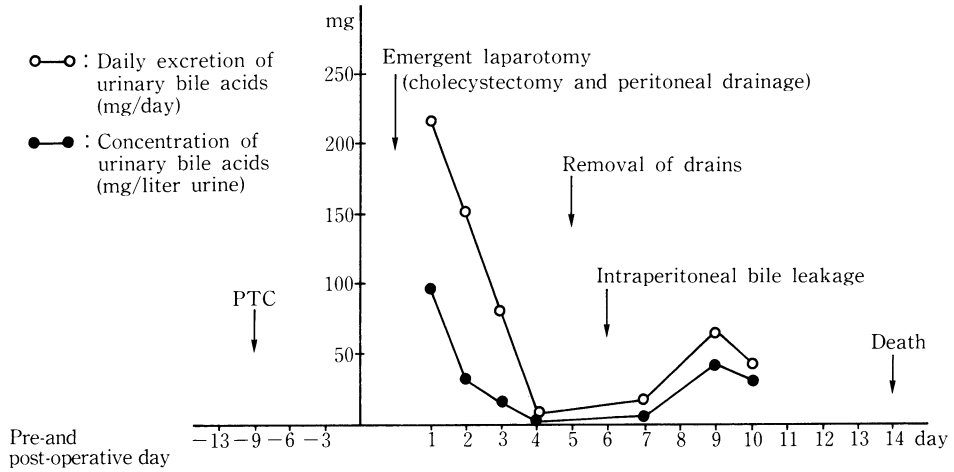
Table 2. Postoperative change of urinary bile acids in case I

Postoperative day		1		2		3		4		7		9		10	
Nonsulfate or sulfate[a]		NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S
Bile acid composition[a] (mg/liter urine)	CA	40.0	—	13.0	—	8.7	—	0.4	—	4.5	—	8.5	16.2	8.4	6.0
	CDCA	6.1	—	—	—	5.8	—	0.1	—	—	—	—	12.3	1.3	10.9
	UDCA	16.3	—	9.3	—	—	—	0.6	—	—	—	—	—	1.1	—
	DCA	—	—	—	—	—	—	—	—	—	—	0.4	2.0	—	0.9
	LCA	—	—	—	—	—	—	—	—	—	—	—	2.8	—	3.0
	7-K DCA[b]	32.9	—	9.4	—	1.7	—	—	—	—	—	—	—	—	—
Concentration of urinary bile acids (mg/liter urine)		95.3		31.7		16.2		1.1		4.5		42.2		31.6	
Percentage of sulfated bile acids (%)		0		0		0		0		0		7.9		66	
Urine volume (ml)		2300		4800		5000		4060		3745		1550		1370	
Daily excretion of urinary bile acids (mg/day)		219.2		152.2		81.0		4.5		16.9		65.4		43.3	

[a]Abbreviations: NS = nonsulfated bile acids; S = sulfated bile acids; CA = cholic acid; CDCA = chenodeoxycholic acid; UDCA = ursodeoxycholic acid; DCA = deoxycholic acid; LCA = lithocholic acid; 7—K DCA = 7—keto deoxycholic acid.
[b]7—keto deoxycholic acid was finally identified by glc—ms.

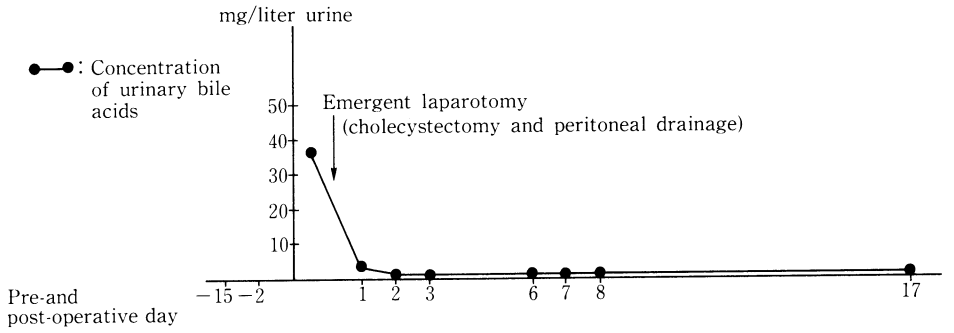
Bile Acid Data in Patients with Generalized Bile Peritonitis

Case I: Daily changes of the concentration and excretion of urinary bile acids after surgery are shown in Table 2. Throughout this study the urinary bile acids exhibited their highest elevation on the first postoperative day (95.3 mg/liter and 219.2 mg/day) and all of the bile acids were in the nonsulfated form. Bile acid levels gradually decreased consistent with successful course of the abdominal condition and returned to normal on the 4th day, postoperatively (1.1 mg/liter urine and 4.5 mg/day). An unknown peak found in the GLC pattern of the urinary bile acids on



Serum direct bilirubin(0.1-0.4mg/dl)[a]	4.2 6.2 3.7 3.0	1.1 0.8	2.2 1.9 1.4	0.2
GOT(5-35mU/ml)[a]	121 132 65 45	37 44	39 45 23	20
GPT(0-30mU/ml)[a]	109 90 69 43	17 17	36 44 29	5
Urinary bilirubin(−)[a]		± − − − −	− + − −	

Fig. 2. Clinical course, and changes of urinary bile acids, liver function and urinary bilirubin in case I.
[a]Parenthesis shows normal values.



Serum direct bilirubin(0.1-0.4mg/dl)	0.3 0.2	0.6	0.3	0.2	0.3
GOT (5-35mU/ml)	45 62	56	20	24	129
GPT (0-30mU/ml)	52 103	91	33	34	262
Urinary bilirubin	−	−	−	−	

Fig. 3. Clinical course, and changes of urinary bile acids, liver function and urinary bilirubin in case II.

days 1, 2 and 3 after surgery was confirmed as 7-ketodeoxycholic acid by glc-ms. This bile acid was present in relatively large amounts on those days.

Figure 2 shows changes of the urinary bile acid concentrations together with changes of the patient's clinical course, liver function and urinary bilirubin. Urinary bilirubin was negative except for (±) on day 1 and (+) on day 9 after the operation. SGOT and SGPT values were almost within normal limits after the operation, although they were slightly elevated before surgery. Serum direct bilirubin levels gradually decreased after PTC and slightly increased postoperatively. Renal function was normal on the days that urinary bile acids were determined.

Case II: Table 3 shows the results of urinary bile acids in pre- and post-operations in case II. In accordance with smooth postoperative course in the abdomen, urinary bile acids rapidly decreased on the 1st postoperative day (3.2 mg/liter urine) and remained to be normal thereafter, whereas they were remarkably elevated

Table 3. Pre- and post-operative change of urinary bile acids in case II

Postoperative day		Before operation		1		2		3		6		7		8		17	
Nonsulfate or sulfate[a]		NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S	NS	S
Bile acid composition[a] (mg/liter urine)	CA	15.4	2.0	2.4	0.3	—	—	—	—	—	—	—	—	—	—	—	—
	CDCA	9.8	4.2	—	0.5	—	—	—	—	—	—	—	—	—	—	—	—
	7β-CA[b]	5.6	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Concentration of urinary bile acids (mg/liter urine)		37.0		3.2		trace		trace		trace		trace		trace		trace	
Percentage of sulfated bile acids (%)		17		25													
Urine volume (ml)		150 for 8 hr		2280		1800		3890		2600		2500		2800		2600	
Daily excretion of urinary bile acids (mg/day)		5.6/8 hr		7.2		trace		trace		trace		trace		trace		trace	

[a]Abbreviations: NS = nonsulfated bile acids; S = sulfated bile acids; CA = cholic acid; CDCA = chenodeoxycholic acid; 7β—CA = 7β—cholic acid

[b]7β—cholic acid was tentatively identified from relative retention time on GLC with 3% 0V—17 and 2% Poly-I 110.

Table 4. Serum bile acids prior to surgery in case III

Analytical method		GLC method		Enzymatic method
Nonsulfate or sulfate		NS	S	
Bile acid composition (mg/liter serum)	CA	41.5	5.6	
	CDCA	25.9	14.6	
Percentage of sulfated bile scids (%)		23		
Concentration of serum bile acids (mg/liter serum)		87.6		80.0

in the preoperative state (37.0 mg/liter urine). Urinary bile acids, liver function, urinary bilirubin and clinical course are shown in Fig. 3. Peritoneal fluid aspirated during the operation contained 3.96 mg/ml bile acid (a total of 2.376 g).

Cases III and IV: In case III, a remarkable elevation (87.6 mg/liter) in serum bile acids was found preoperatively. Table 4 shows analytical results by gas-chromatographic and enzymatic methods. There was a good coincidence in results between these two different analytical methods. In case IV, serum total bile acids successfully decreased on the 3rd, 5th postoperative days (4.5, 5.7 mg/liter) and returned to normal on day 7 postoperatively (2.2 mg/liter), whereas they were elevated in the preoperative state (12.8 mg/liter).

DISCUSSION

Three factors are the determinants of serum bile acid concentration[10]: 1) Intestinal absorption 2) Hepatic elimination and 3) Renal excretion of bile acids. Bile acid concentrations in peripheral blood are determined by interrelation of these factors. The hepatic clearance of bile acids is achieved by an efficient active transport system located in the sinusoidal plasma membrance of the hepatocytes. Therefore, diminished hepatic clearance of bile acids due to hepatocellular damage and/or portal-systemic shunting secondary to hepatitis or liver cirrhosis causes an increase in bile acid concentration of the peripheral blood. Renal clearance of bile acids is negligibly small under normal conditions, but increases when the bile acid concentration of peripheral blood becomes to be elevated. Polar

bile acids, such as cholic acid are excreted in the nonsulfated form, while less polar bile acids, such as lithocholic acid are sulfated. Our data are consistent with this mechanism since they show significant elevations of urinary bile acids in patients with cirrhosis of the liver and extensive hepatic metastases of gastric cancer.

So far it has been asserted that the symptoms of bile peritonitis are severe and that the prognosis is poor. However, the two patients of case I and II with bile peritonitis reported in the present paper had insidious clinical manifestations without evident signs of peritoneal irritation. They only manifested gradual abdominal distension. This type of bile peritonitis causes the greatest diagnostic problem. They are good examples of delayed diagnosis, in spite of the intraperitoneal existence of bile for five to nine days, because the diagnosis was made only when the patients fell into shock and an emergency laparotomy had to be carried out. At early stage of bile leakage they are considered to have no intraperitoneal bacterial infection, but the delayed diagnosis led them to the infection resulting in clinically serious condition. Therefore it could be better to call the early stage of these patients as bile ascites rather than as bile peritonitis. In retrospect, remission of the intrahepatic cholestasis secondary to intraperitoneal bile leakage in case I resulted in diminished concentrations of serum direct bilirubin (6.2 mg/dl on the day of PTC and 3.0 mg/dl just prior to surgery).

Hitherto there have been very few reports about bile peritonitis. The pathogenesis of the symptoms and signs seen in intraperitoneal biliary extravasations has remained to be unsolved. Cohn[4] showed in dog experiments that the severity of the bile peritonitis was dependent upon the presence of bacterial infection rather than simply the presence of bile. Makino reported in the Japanese literature that bile peritonitis was associated with few signs of peritoneal irritation making early diagnosis difficult[6]. Mizumoto likewise reported in the Japanese literature that intraperitoneal bile leakage without infection did not cause distinct signs of peritoneal irritation[9]. Moreover, Kune described in his book that early diagnosis of bile peritonitis was difficult in some cases because the clinical picture of the intraperitoneal bile extravasation was mild in symptoms and slow in development[5]. Likewise, we have opinion that a number of cases show insidious clinical manifestations, although the majority of patients have dramatic clinical presentation as cases III and IV, in bile peritonitis.

Our data showed the elevation of serum or urinary bile acids in all the patients with generalized bile peritonitis. Especially in case I, the concentration and daily excretion of urinary bile acids were 95.3 mg/liter urine and 219.2 mg/day, on the first postoperative day. Since in normal man the daily synthesis of bile acids is 0.5 g, it is easily understandable that we are dealing with considerable amounts of these compounds. This postoperative hypercholanuria is explained as follows: Preoperatively, intraperitoneal bile acids had been absorbed through the peritoneum into the blood stream and then excreted in the bile via hepatic clearance (interruption of the enterohepatic circulation and development of a peritoneo-hepatic circulation). However, excess serum bile acids, i.e. amounts exceeding hepatic clearance capability were excreted into the urine. Postoperatively, the bile acids that had accumulated inside the body continued to be excreted into the urine in large amounts. 7-Ketodeoxycholic acid was identified in urine, and may be the result of intraperitoneal bacterial metabolism. The absence of deoxycholic acid in the urine samples obtained in a few days postoperatively may be ascribed to the long-term interruption of the enterohepatic circulation. On the fourth day after surgery the output of urinary bile acids returned to normal in accord with the absence of abdominal symptoms. However, resumption of the intraperitoneal bile leakage on the 6th day postoperatively caused an elevated output of urinary bile acids on days 7, 9 and 10 after the operation. This reflects the peritoneal absorption of bile acids. Case II had the same pathologic condition as in case I. In this case, preoperative renal function was impaired as evidenced particularly by an anuric condition for 4 hr before surgery. Therefore, if the urinary bile acid analysis had been carried out when perforation of the gallbladder was not accompanied by impaired renal function, even more elevated bile acid concentrations might have been observed. Similarly, preoperative elevation of serum bile acids in cases III and IV also reflects

the peritoneal absorption of the biliary bile acids leaked intraperitoneally.

Diffuse peritonitis secondary to duodenal perforation is also pathologic condition having bile component intraperitoneally, as in bile peritonitis. This has symptoms of peritoneal irritation of such severity that practicing surgeons should not find it difficult to arrive at the correct diagnosis. In this study, all the patients with perforated duodenal ulcer had moderate amount of fluids contaning bile in the peritoneal cavity at surgery. However, the concentration of urinary bile acids was not elevated in those patients (0.98 mg/liter urine), and was almost similar to that of normals. Three factors are conceivable which account for the lower levels of urinary bile acids in the patients with perforated duodenal ulcer. First, is the fact that these patients presented with a sudden onset of abdominal pain were operated upon within a day after the onset. This results in the bile contamination of the peritoneum residing in the peritoneal cavity for a relatively short time. Second, the concentration of the bile in perforated duodenal ulcer patients would be expected to be lower because of the simultaneous presence of gastric and pancreatic juice. Third, this disease might cause an early impairment of peritoneal absorbing ability because duodenal perforation leads to intraperitoneal leakage of duodenal juice containing bile, pancreatic and gastric secretions with strong digestive power. This factor may be important because the two patients (cases III and IV) with dramatic type of bile peritonitis exhibited preoperative elevation in serum bile acids despite an emergency laparotomy carried out within 24 hr after the onset.

Extravasation of bile into the peritoneal cavity is an uncommon condition, and the majority of such patients present with acute, dramatic clinical manifestations leading to early diagnosis. However, clinicians should not forget a fewer patients with insidious (subacute or chronic) type of bile peritonitis because its early diagnosis is difficult. The delay in making the diagnosis finally allows an intraperitoneal bacterial infection causing to sudden shock and poor prognosis. In this study, all of the patients with bile peritonitis exhibited elevation in serum or urinary bile acids. This implies that enzymatic assay for serum bile acids aids as a good cue in early detection of intraperitoneal bile extravasation. As bile peritonitis is strongly suspected of when serum bile acids are elevated, abdominal computerized tomographic scans, abdominal ultrasonic examination, or abdominal paracentesis should be performed for the confirmation of intraperitoneal fluids. And thus fatal outcome in insidious type of bile peritonitis would be prevented.

Moreover, although elevation in serum and urinary bile acids has been discussed in relation to hepatocellular damage and jaundice so far, the present study shows that bile peritonitis is an interesting pathologic condition producing hypercholanuria and hypercholanemia without relation to such hepatic factors.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. T. Hoshita, Institute of Pharmaceutical Sciences, Hiroshima University School of Medicine, and Dr. E. H. Mosbach and Dr. L. D. Dillon, Department of Surgery, Beth Israel Medical Center, New York, for their valuable advice and criticism.

REFERENCES

1. **Almé, B., Bremmelgaard, A., Sjövall, J. and Thomassen, P.** 1977. Analysis of metabolic profiles of bile acids in urine using a lipophilic anion exchanger and computerized gas liquid chromatography-mass spectrometry. J. Lipid Res. **18**: 339—362.
2. **Arborgh, B., Eklund, A., Norman, A. and Strandvik, B.** 1980. Urinary bile acid excretion in correlation to liver histopathology in cystic fibrosis. Scan. J. Gastroenterol. **15**: 73—80.
3. **Bremmelgaard, A. and Sjövall, J.** 1979. Bile acid profiles in urine of patients with liver disease. Eur. J. Clin. Invest. **9**: 341—348.
4. **Cohn, I. Jr., Cotlar, A.M., Atik, M., Lumpkin, W.M., Hudson, T.L. and Wernette, G.J.** 1960. Bile peritonitis. Ann. Surg. **152**: 827—835.
5. **Kune, G.A.** 1972. Current practice of biliary surgery. Chapter 10: Biliary peritonitis, p. 323—332. Little, Brown.
6. **Makino, E., Mieno, K., Sato, M., Hirooka, Y., Aoki, K. and Yo, K.** 1974. Differential diagnosis of acute peritonitis. Operation (Japan) **28**: 133—138.
7. **Makino, I., Hashimoto, H., Shinozaki, K., Yoshino, K. and Nakagawa, S.** 1975. Sulfated and nonsulfated bile acids in urine, serum and bile of patients with hepatobiliary diseases. Gastroenterology **68**: 545—553.
8. **Makino, I., Shinozaki, K., Nakagawa, S. and**

Mashimo, K. 1974. Measurement of sulfated and nonsulfated bile acids in human serum and urine. J. Lipid Res. **15**: 132—138.

9. **Mizumoto, R., Sudo M., Kasai, Y. and Miyazaki, I.** 1984. Trauma of the liver, gallbladder, pancreas and spleen. Kan-Tan-Sui (Japan) **8**: 219—235.

10. **Paumgartner, G., Mannes, G.A. and Stellaard, F.** 1983. Serum bile acids and bile acid tolerance tests in liver disease. p. 217—222. *In* L. Barbara, R.H. Dowling, A.F. Hoffmann and E. Roda (ed.), Bile acids in gastroenterology. Lancaster: MTP Press.