Dynamic changes in the gallbladder wall, in the gallbladder bile and in the liver in patients with symptomatic (with biliary pain) biliary diseases

Early detection and the treatment of symptomatic (with biliary pain) biliary diseases have the important clinical importance because of transformation of functional disturbances biliary system into the organic pathology – **gallbladder dysfunction → chronic acalculous cholecystitis without biliary sludge → chronic acalculous cholecystitis with biliary sludge → chronic calculous cholecystitis** (table 1).

It is a result of disturbance of colloidal stability of the gallbladder bile, of precipitation of the cholesterol monohydrate crystals and calcium bilirubinate granules, and the addition of chronic aseptic inflammation in the gallbladder wall (table 2).

Laparoscopic cholecystectomy is a "gold" standard of the treatment of chronic calculous cholecystitis.

The absence of gallbladder promotes the appearance of the functional biliary hypertension and the dilation of the common hepatic duct and common bile duct. In some patients it is accompanied with progressive deterioration of the chronic pancreatitis, with appearance of dysfunction of Oddi's sphincter, of duodeno-gastral reflux and/or of reactive hepatitis (table 3).

Possibly, the symptomatic (with biliary pain) biliary diseases are the "COX-2" associated biliary diseases. The main cause of these diseases is the excessive COX-2 expression in the smooth muscle cells and in the epithelial cells of the gallbladder and of the common hepatic duct and common bile duct.

Probably, the symptomatic (with biliary pain) biliary diseases are the diseases of the smooth muscle cells of the gallbladder wall or of the smooth muscle cells of cystic duct, of the common bile duct sphincter or of the pancreatic duct sphincter or of the sphincter of ampulla (the excessive COX-2 expression).

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Table 1

Symptomatic (with biliary pain) biliary diseases (Gallbladder)

		Control	Gallbladder hypomotility	Chronic acalculous cholecystitis	Chronic acalculous cholecystitis with biliary sludge	Chronic calculous cholecystitis	Acute calculous cholecystitis	State after cholecyst-ectomy
	Gallbladder							
1	**COX-2 expression in smooth muscle cells**	–	+	++	+++	+++	++++	
2	**PGE2 in smooth muscle cells**	–	↑	↑↑	↑↑↑	↑↑↑	↑↑↑↑	
3	**6-keto-PGF-1alpha in smooth muscle cells**	–	↑	↑↑	↑↑↑	↑↑↑	↑↑↑↑	
4	**Hypertrophy smooth muscle cells**	–	+	++	+++	+++	?	
5	**CCK receptors**	normal	↓	↓↓	↓↓↓↓	↓↓	↓	
6	**Fibrosis of muscular layer**	–	нет	+	++	++	+++	
7	**COX-2 expression in epithelial cells**	–	±	+	++++	+++	++++	
8	**PGE2 in epithelial cells**	–	–	↑	↑↑↑	↑↑↑	↑↑↑↑	
9	**6-keto-PGF-1alpha in epithelial cells**	–	–	↑	↑↑↑	↑↑↑	↑↑↑↑	
10	**Hyperplasic and hyper-trophy epithelial cells**	–	+	++	+++	+++	?	
11	**Atrophy of mucosal layer**	–	–	+	++	+++	++++	
12	**Gallbladder motility**	> 70%	< 40%	< 50%	< 50%	< 50%	< 5%	
13	**Absorption of water**	normal	↓	↓↓	↓↓↓↓	↓↓	0	
14	**Absorption of biliary cholesterol**	normal	↓	↓↓	↓↓↓↓	↓↓	0	
15	**Secretion of biliary mucin**	–	±	↑↑	↑↑↑↑	↑↑↑	↑↑↑↑	
16	**Thickness of gallbladder wall**	2 mm	2 мм	3-4 мм	3-6 мм	3-4 мм	5-10 мм	
17	**Biliary pain**	–	+	++	+++	+++	++++	
18	**Degree of inflammation**	–	±	+	+++	+++	++++	
19	**“Active” passage of he-patic bile**	> 70%	< 40%	< 50%	< 50%	< 50%	< 0%	
20	**“Passive” passage of hepatic bile**	> 70%	< 40%	< 50%	< 30%	< 50%	< 0%	

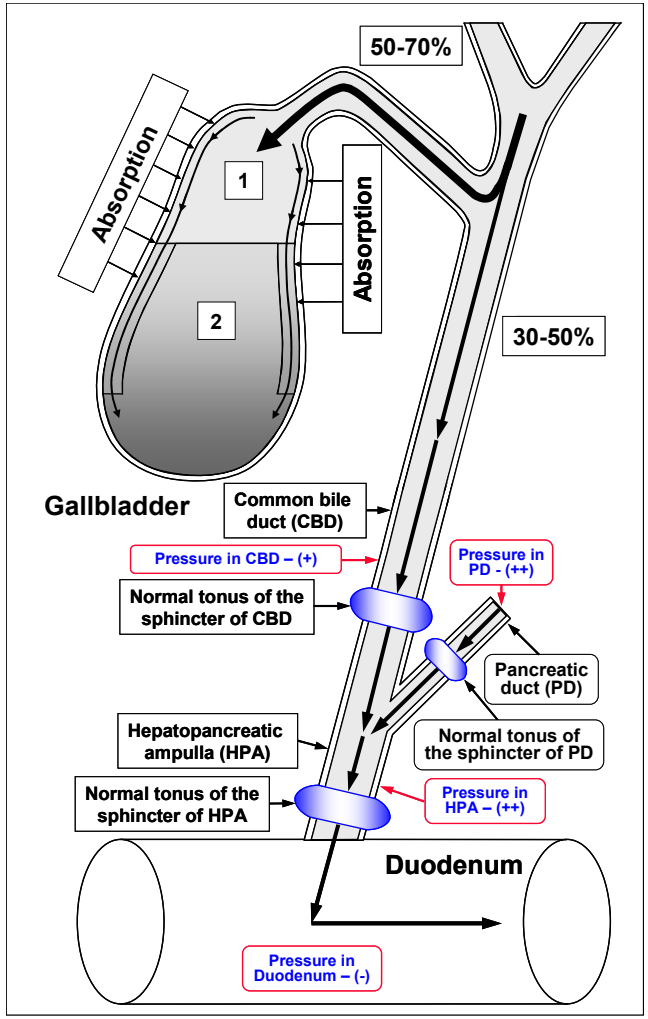

Fig. 1. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen **in control** (normal motility of the sphincter of common bile duct, sphincter of pancreatic duct and sphincter of hepatopancreatic ampulla).
1 = unconcentrated hepatic bile (uncon HB);
2 = normal concentrated gallbladder bile (GB).

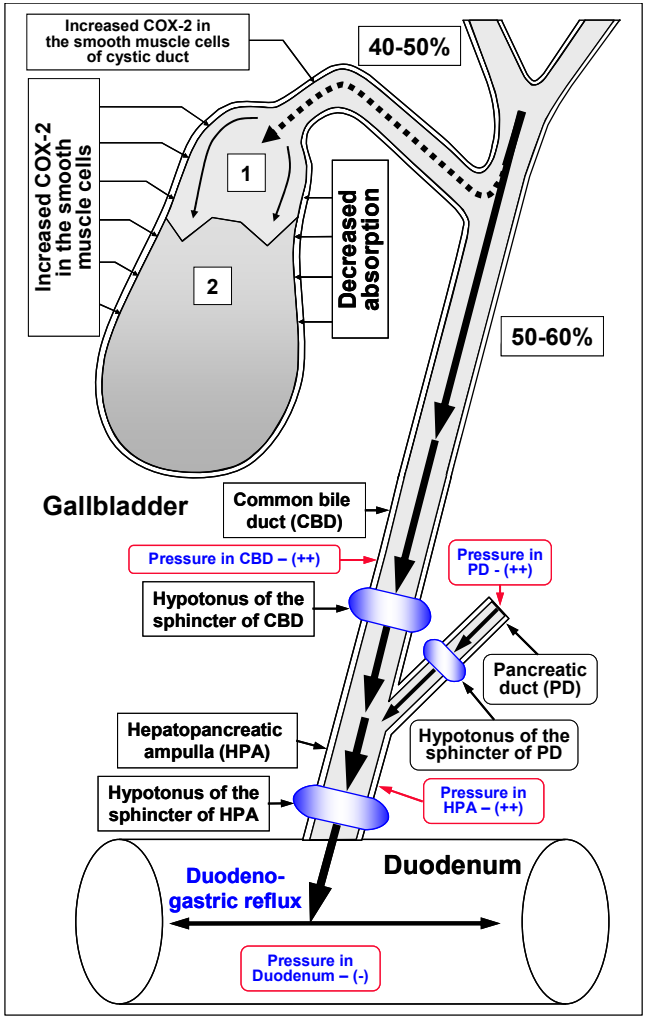

Fig. 2. Passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with gallbladder dysfunction, sphincter of Oddi hypomotility** (hypomotility of the sphincter of common bile duct, sphincter of pancreatic duct and sphincter of hepatopancreatic ampulla) and **duodeno-gastric reflux.** **1** = unconcentrated HB;
2 = low concentrated GB (low con GB).

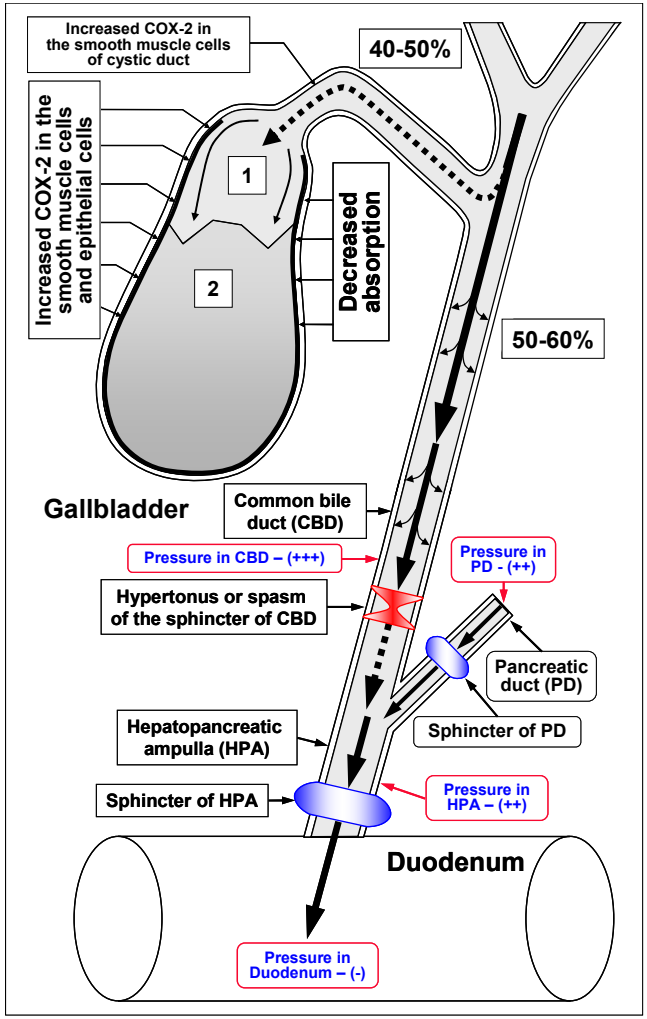

Fig. 3. Passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with chronic acalculous cholecystitis without biliary sludge and hypertonus (spasm) of the sphincter of common bile duct** (biliary type III of sphincter of Oddi dysfunction).
1 = unconcentrated hepatic bile (uncon HB);
2 = low concentrated gallbladder bile (GB).

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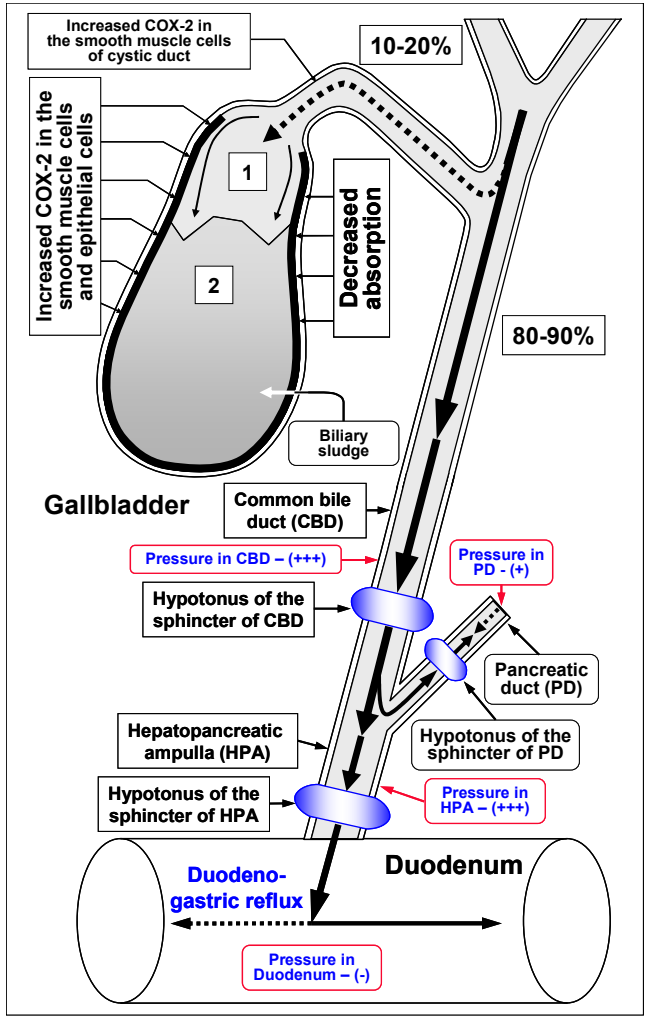

Fig. 4. Passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with chronic acalculous cholecystitis with biliary sludge and sphincter of Oddi hypomotility** (hypomotility of the sphincter of common bile duct, sphincter of pancreatic duct and sphincter of hepatopan-creatic ampulla) **with biliopancreatic reflux.** **1** = uncon HB; **2** = low concentrated GB.

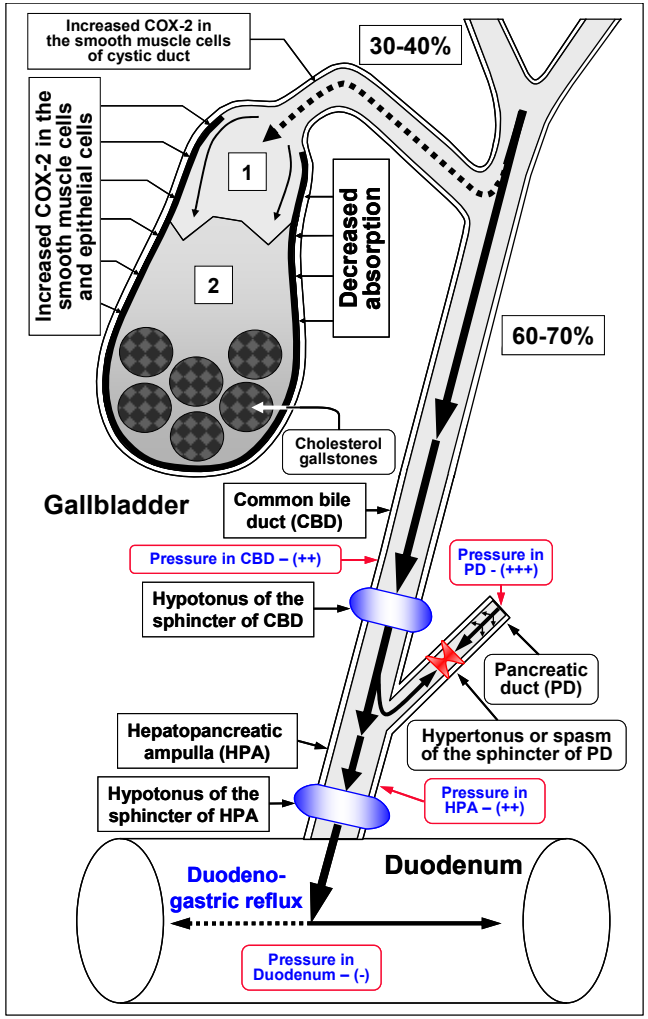

Fig. 5. Passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients with chronic calculous cholecystitis and pancreatic type III of sphincter of Oddi dysfunction** (hypomotility of the sphincter of common bile duct and sphincter of hepatopancreatic ampulla, hypertonus (spasm) of the sphincter of pancreatic duct). **1** = uncon HB; **2** = low concentrated GB.

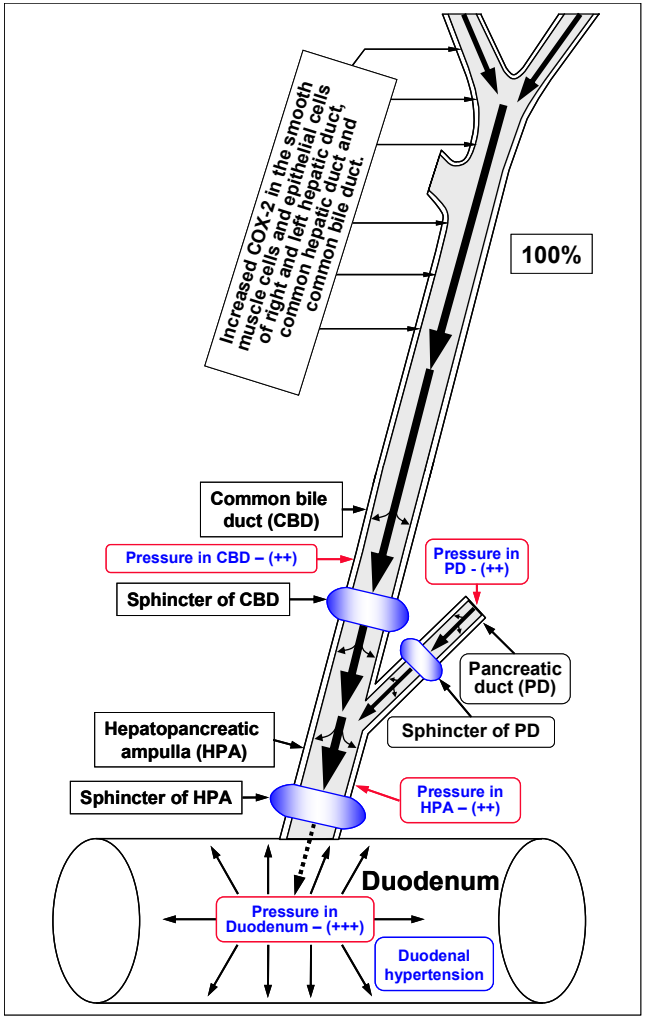

Fig. 6. Passage of hepatic bile and pancreatic juice into the duodenum lumen **in patients after cholecystectomy (postcholecystectomy syndrome) and duodenal hypertension** (the increase of intraluminal pressure in the duodenum – small intestinal bacterial overgrowth syndrome). **1** = low concentrated hepatic bile; **2** = low concentrated hepatic bile in common bile duct.

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Table 2.

Symptomatic (with biliary pain) biliary diseases (Gallbladder bile)

		Control	Gallbladder hypomotility	Chronic acalculous cholecystitis	Chronic acalculous cholecystitis with biliary sludge	Chronic calculous cholecystitis	Acute calculous cholecystitis	State after cholecyst-ectomy
	Gallbladder bile							
1	**CSI**	**<1.0**	**≥ 1.0**	**≥ 1.25**	**≥ 1.50**	**≥ 1.25**	**≥ 1.25**	
2	**Calcium bilirubinate granules**	–	±	++	++++	+++	++++	
3	**Cholesterol monohydrate crystals**	–	±	++	++++	+++	++++	
4	**Biliary mucin**	–	± soluble	++ soluble	++++ polymerization	+++ polymerization	++++ polymerization	
5	**Biliary sludge**	–	±	±	+++	++	++++	
6	**Concentration of choles-terol in gallbladder bile**	**normal**	↑	↑↑	↑↑↑	↑↑↑	↑↑↑↑	
7	**Concentration of bile salts in gallbladder bile**	**normal**	↓	↓↓	↓↓↓↓	↓↓	↓↓	
8	**Gallbladder storage ca-pacity of bile acid pool size**	**> 70%**	**< 40%**	**< 50%**	**< 50%**	**< 50%**	**?**	

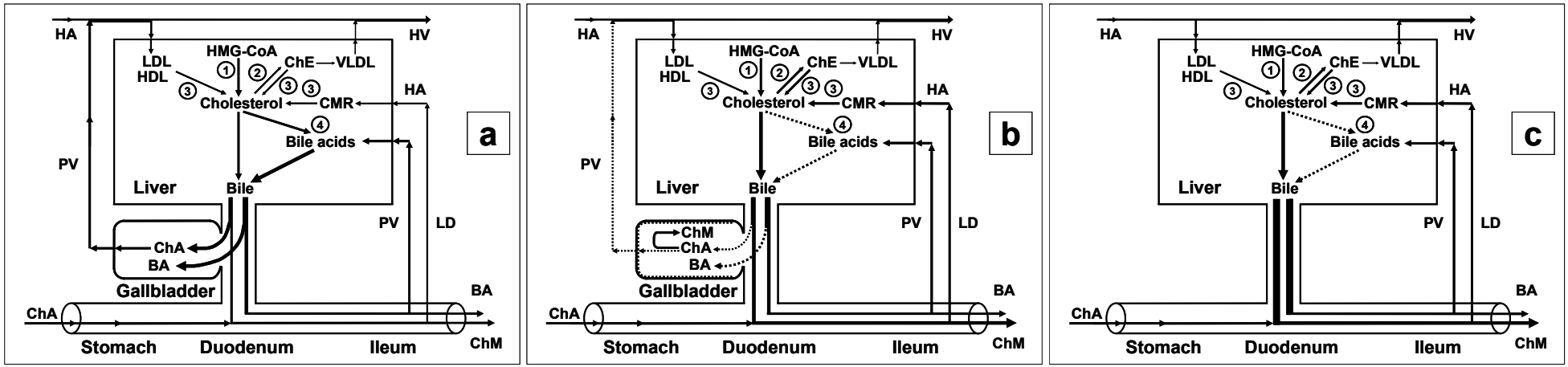

Fig. 7. Exchange of cholesterol and bile acids: **(a)** in control; **(b)** in patients with chronic acalculous cholecystitis or chronic calculous cholecystitis; **(c)** in patients after cholecystectomy. **1** = synthesis of cholesterol; **2** = synthesis of cholesterol esters for VLDL; **3** = hydrolysis of cholesterol esters entered the hepatocytes with HDL and LDL, and hydrolysis of cholesterol esters entered the hepatocytes with CMR; **4** = synthesis of bile acids. **ChE** = cholesterol esters; **ChA** = cholesterol anhydrous; **ChM** = cholesterol monohydrate; **BA** = bile acids; **HA** = hepatic artery; **HV** = hepatic vein; **PV** = portal vein; **LD** = lymphatic duct.

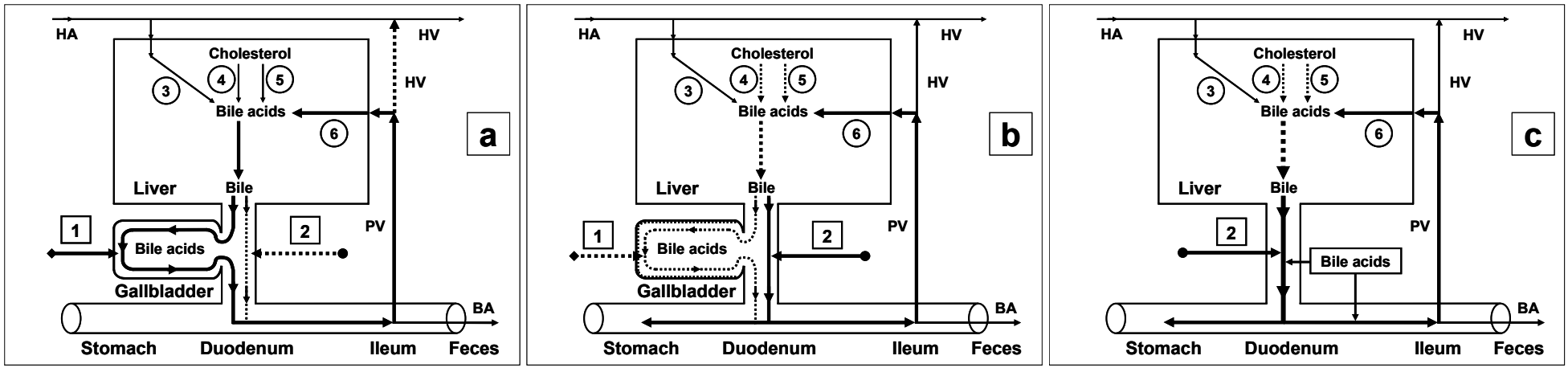

Fig. 8. Enterohepatic circulation of bile acids: **(a)** in control; **(b)** in patients with chronic acalculous cholecystitis or chronic calculous cholecystitis; **(c)** in patients after cholecystectomy. **1** = Gallbladder-dependent enterohepatic circulation of bile acids; **2** = gallbladder-independent enterohepatic circulation of bile acids; **3** = bile acids entering the liver through the hepatic artery; **4** = synthesis of cholic acid: cholesterol-7α-hydroxylase; **5** = synthesis of chenodeoxycholic acid: cholesterol-27-hydroxylase; **6** = bile acids entering the liver through the portal vein. **BA** = bile acids; **HA** = hepatic artery; **HV** = hepatic vein; **PV** = portal vein.

Table 3

Symptomatic (with biliary pain) biliary diseases (Liver)

		Control	Gallbladder hypomotility	Chronic acalculous cholecystitis	Chronic acalculous cholecystitis with biliary sludge	Chronic calculous cholecystitis	Acute calculous cholecystitis	State after cholecyst-ectomy
	Liver							
1	**Biliary cholesterol secre-tion**	**normal**	±	++	++++	+++	?	+++
2	**Hepatic bile volume**	**normal**	↓	↓↓	↓↓↓	↓↓↓	?	↓↓↓↓
3	**Bile acids concentration in liver tissue**	**normal**	±	++	++++	+++	?	++++
4	**Degree of chronic "bland" intrahepatic cho-lestasis**	–	±	++	++++	+++	?	++++
5	**Enterohepatic circulation of bile acids**	–	↑	↑↑	↑↑↑	↑↑↑	?	↑↑↑↑
6	**Gallbladder-independent enterohepatic circulation of bile acids**	–	↑	↑↑	↑↑↑	↑↑↑	?	↑↑↑↑
7	**Total pool size of bile acids**	**normal**	↓	↓↓	↓↓↓↓	↓↓↓	?	↓↓↓↓
8	**Absorption of bile salts in ileum**	**normal**	↓	↓↓	↓↓↓↓	↓↓↓	?	↓↓↓↓
9	**Bile acids concentration in portal vein**	**normal**	±	++	++++	++++	?	++++
10	**Gallbladder-independent enterohepatic circulation of biliary cholesterol**	**normal**	↑	↑↑	↑↑↑	↑↑↑	?	↑↑↑↑
11	**Absorption of biliary cholesterol in ileum**	**normal**	↑	↑↑	↑↑↑	↑↑↑	?	↑↑↑↑
12	**Gallbladder-independent enterohepatic circulation of biliary bilirubin**	**normal**	↑	↑↑	↑↑↑	↑↑↑	?	↑↑↑↑