The algorithm of the pathogenetic treatment of symptomatic (with biliary pain) biliary diseases with celecoxib and ursodeoxycholic acid (UDCA)

1. Treatment of gallbladder dysfunction (with biliary pain) and prophylaxis of chronic acalculous cholecystitis without biliary sludge – celecoxib – 100 mg 2 times per day – 5-7 days, next UDCA – 750 mg 1 time before going to bed – 14 days. Effectiveness of this treatment is 95% and a prolongation of remission period up to 18-24 months.
2. Treatment of chronic acalculous cholecystitis without biliary sludge (with biliary pain) and prophylaxis of chronic acalculous cholecystitis with biliary sludge, duodenogastric reflux, antral atrophic (bile-acid-dependent) gastritis and chronic biliary pancreatitis – celecoxib – 100 mg 2 times per day – 5-7 days, next UDCA – 750 mg 1 time before going to bed – 30 days. Effectiveness of this treatment is 95% and a prolongation of remission period up to 18-24 months.
3. Treatment of chronic acalculous cholecystitis with biliary sludge (with biliary pain) and prophylaxis of chronic calculous cholecystitis, duodenogastric reflux, antral atrophic (bile-acid-dependent) gastritis and chronic biliary pancreatitis (fig. 1 a, b, c, d; fig. 2, 3, 4, 5) – celecoxib – 100 mg 2 times per day – 5-7 days, next UDCA – 750 mg 1 time before going to bed – 2 months. Effectiveness of this treatment is 95%, the reduction of biliary pain and dyspeptic syndrome was revealed already on 4.1±0.2 day, the thickness of gallbladder wall was significantly decreased from 4.5±0.2 mm up to 2.4±0.2 mm and the biliary sludge was disappeared completely, the restoration of excretion function of liver and recovery of ejection fraction of gallbladder to 60% were marked, and a prolongation of remission period was up to 19.3±2.1 months.
4. Treatment of chronic calculous cholecystitis (with biliary pain) and prophylaxis of acute calculous cholecystitis, duodenogastric reflux, antral atrophic (bile-acid-dependent) gastritis and chronic biliary pancreatitis – celecoxib – 100 mg 2 times per day – 5-7 days, next UDCA – 750 mg 1 time before going to bed – 3 months. Effectiveness of this treatment is 95% and a prolongation of remission period up to 18-24 months.
5. Treatment of patients after cholecystectomy (with biliary pain) (postcholecystectomy syndrome, dysfunction of Oddi's sphincter ("biliary" type or "pancreatic" type or "mixed" type) or incompetence of Oddi's sphincter) and prophylaxis of choledocholithiasis, duodenogastric reflux, antral atrophic (bile-acid-dependent) gastritis and chronic biliary pancreatitis – celecoxib – 100 mg 2 times per day – 5-7 days, next UDCA – 750 mg 1 time before going to bed – 2 months. Effectiveness of this treatment is 95% and a prolongation of remission period up to 18-24 months.
6. Treatment of duodenogastric reflux and antral atrophic (bile-acid-dependent) gastritis (with biliary pain) (incompetence of Oddi's sphincter) – celecoxib – 100 mg 2 times per day – 5 days, next UDCA – 750 mg 1 time before going to bed – 14 days. Estimated effectiveness of this treatment is 90-95% and a prolongation of remission period up to 18-24 months.
7. Treatment of chronic biliary (bile-acid-dependent) pancreatitis (with biliary pain) (dysfunction of Oddi's sphincter – "pancreatic" type or "mixed" type) – celecoxib – 100 mg 2 times per day – 7-10 days, next UDCA – 750 mg 1 time before going to bed – 30 days. Estimated effectiveness of this treatment is 90-95% and a prolongation of remission period up to 18-24 months.

The pathogenetic correction of metabolic and morpho-functional disturbances in the gallbladder and liver in patients with gallbladder dysfunction helps decrease the risk of appearance of the chronic acalculous cholecystitis without biliary sludge, in patients with chronic acalculous cholecystitis without biliary sludge helps decrease the risk of appearance of the chronic acalculous cholecystitis with biliary sludge, in patients with chronic acalculous cholecystitis with biliary sludge helps decrease the risk of appearance of the chronic calculous cholecystitis (fig. 1 a, b, c, d; fig. 2, 3, 4, 5), in patients with chronic calculous cholecystitis helps decrease the risk of appearance of the acute calculous cholecystitis, in patients after cholecystectomy helps decrease the risk of appearance of the choledocholithiasis.

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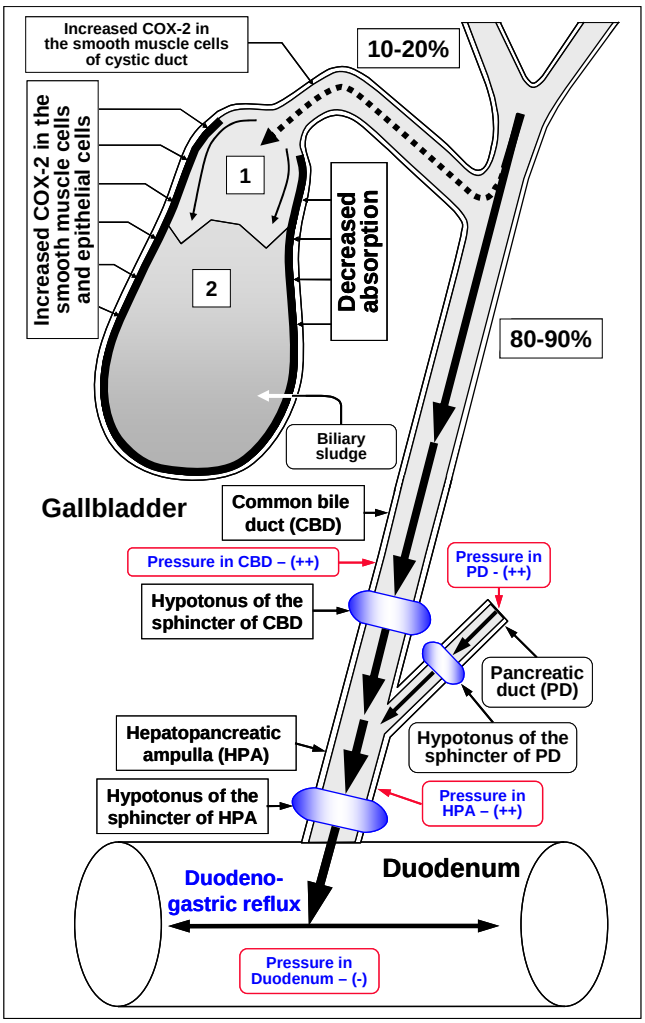
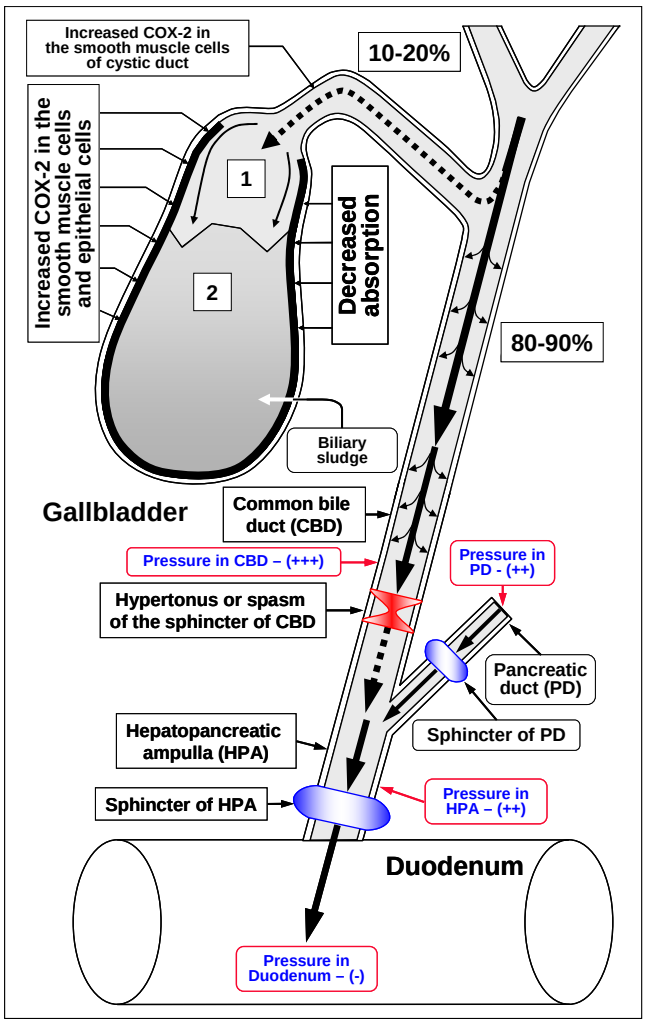


Patients with chronic acalculous cholecystitis with biliary sludge, sphincter of Oddi hypomotility and duodenogastric reflux **before treatment**

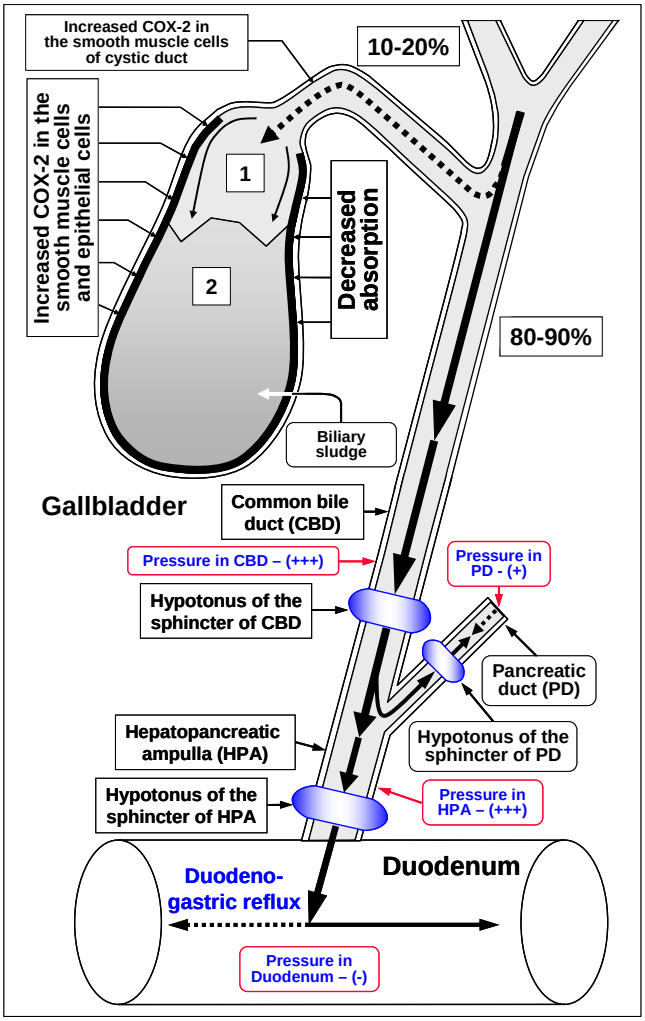
Fig. 1a. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen in patients with chronic acalculous cholecystitis with biliary sludge, sphincter of Oddi hypomotility (hypomotility of the sphincter of common bile duct, sphincter of pancreatic duct and sphincter of hepatopancreatic ampulla) and duodenogastric reflux before treatment with celecoxib and UDCA.
1 = unconcentrated hepatic bile;
2 = low concentrated gallbladder bile.



Patients with chronic acalculous cholecystitis with biliary sludge and biliary type III of sphincter of Oddi dysfunction **before treatment**

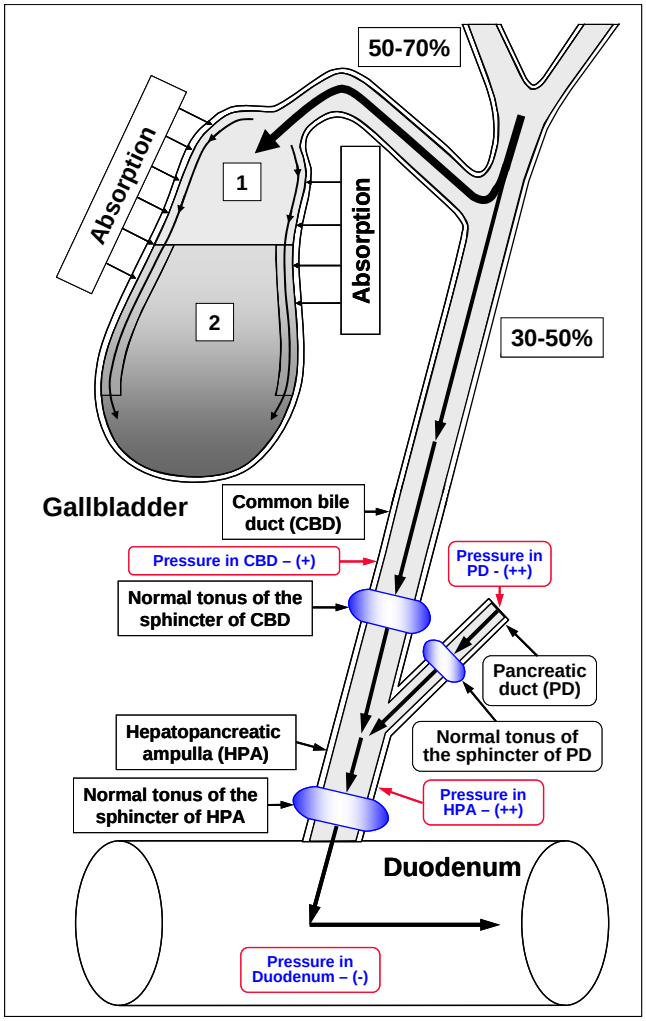
Fig. 1b. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen in patients with chronic acalculous cholecystitis with biliary sludge and hypertonus (spasm) of the sphincter of common bile duct (biliary type III of sphincter of Oddi dysfunction) before treatment with celecoxib and UDCA. The increase of COX-2 activity in the smooth muscle cells of the sphincter of common bile duct may be accompanied by hypertonus (spasm) formation.

This algorithm of pathogenetic treatment will help diminish the duration of disease period and the quantity of patients with biliary diseases by 30-40%. Also, the remission period will be increased up to 18-24 months. Celecoxib may be replaced by COX-2 inhibitors such as Rofecoxib or Valdecoxib or Etoricoxib.



Patients with chronic acalculous cholecystitis with biliary sludge, and sphincter of Oddi hypomotility with biliopancreatic reflux (chronic biliary pancreatitis) **before treatment**

Fig. 1c. Passive passage of hepatic bile into the gallbladder and passive 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 hepatopancreatic ampulla) with choledocho-pancreatic reflux before treatment with celecoxib and UDCA.



Patients with chronic acalculous cholecystitis with biliary sludge **after treatment with celecoxib and UDCA**

Fig. 1d. Passive passage of hepatic bile into the gallbladder and passive passage of hepatic bile and pancreatic juice into the duodenum lumen in patients with chronic acalculous cholecystitis with biliary sludge (normal motility of the sphincter of common bile duct, sphincter of pancreatic duct and sphincter of hepatopancreatic ampulla) after treatment with celecoxib and UDCA.

1 = hepatic bile; **2** = gallbladder bile.

The conducted pathogenetic treatment of patients with chronic acalculous cholecystitis with biliary sludge promotes more effective controlling of biliary pain and inflammation in gallbladder wall, the restoration of excretion function of liver and recovery of ejection fraction of gallbladder, the restoration of the portal blood flow and the decrease of serum total cholesterol concentration.

The pathogenetic treatment must include the celecoxib and UDCA.

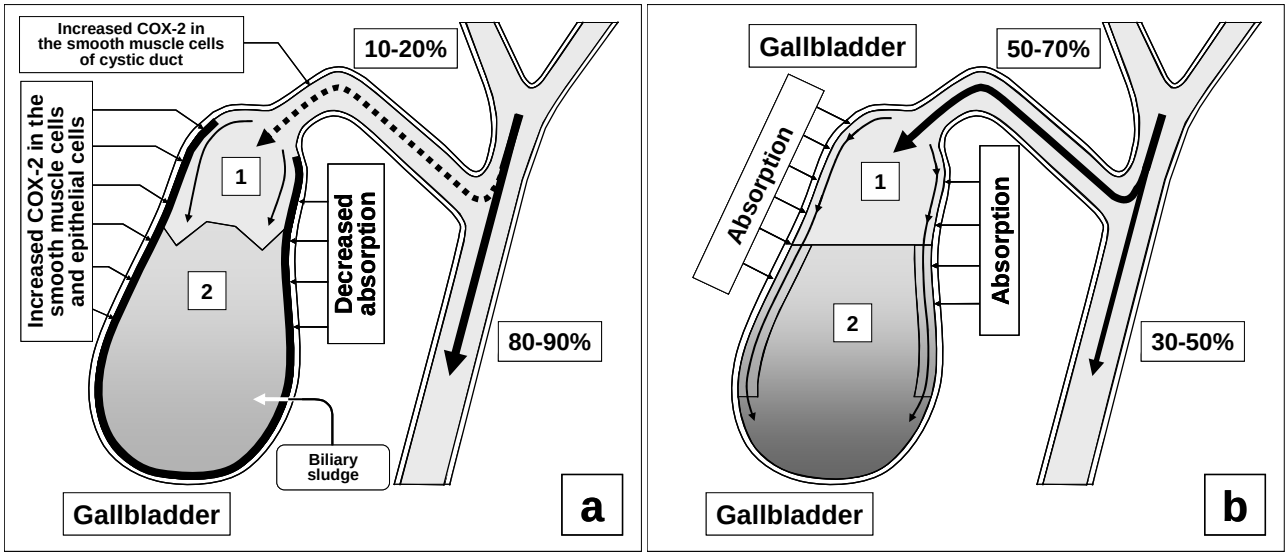


Fig. 2. "Passive" passage of hepatic bile into the gallbladder and into the duodenum in patients with chronic acalculous cholecystitis with biliary sludge before (a) and after (b) treatment with celecoxib and UDCA. **1** = hepatic bile; **2** = gallbladder bile.

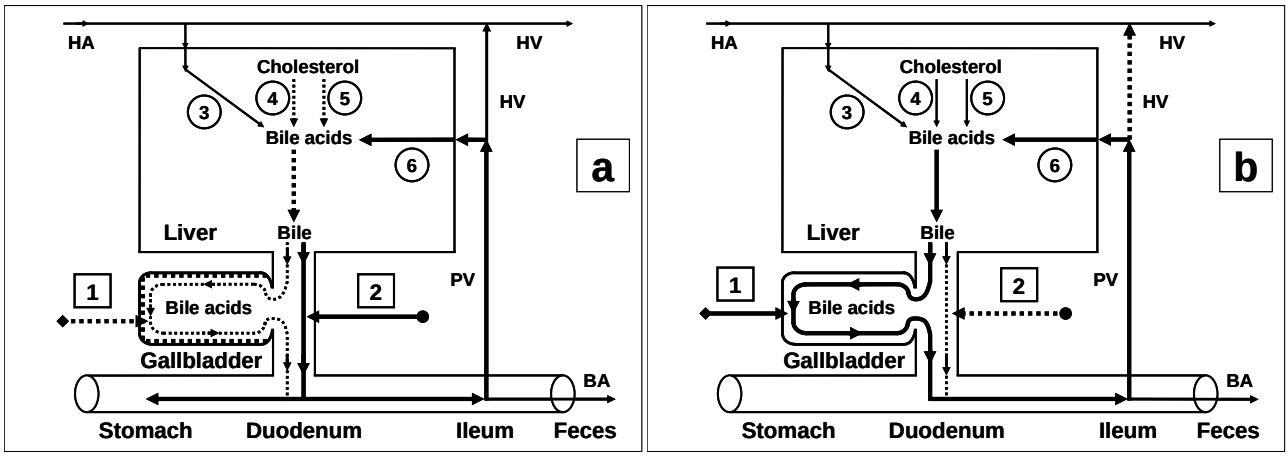


Fig. 3. Enterohepatic circulation of bile acids in patients with chronic acalculous cholecystitis with biliary sludge before (a) and after (b) treatment with celecoxib and UDCA.
1 = gallbladder-dependent enterohepatic circulation of bile acids; **2** = gallbladder-independent enterohepatic circulation 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.

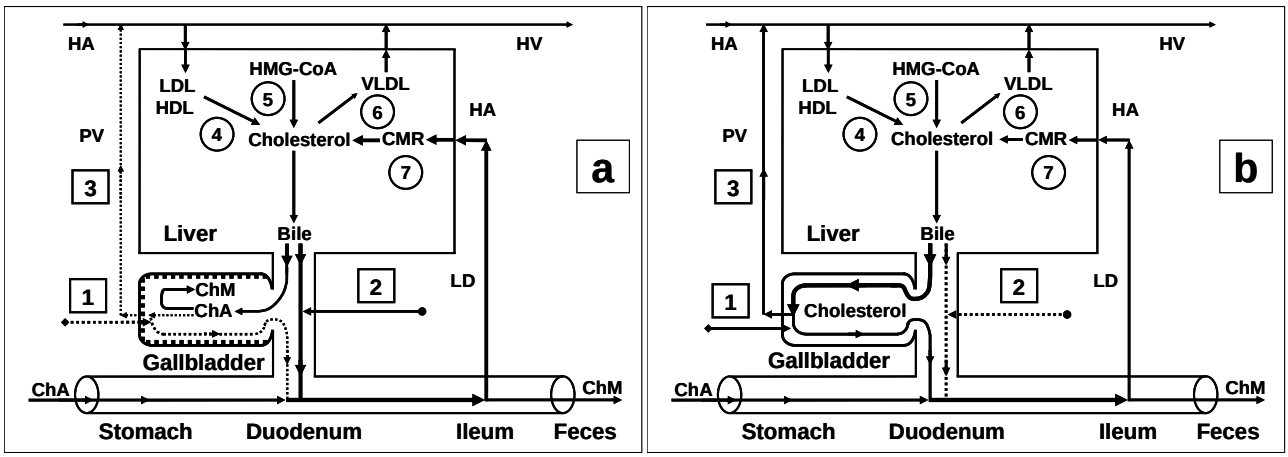


Fig. 4. Exchange of cholesterol in patients in patients with chronic acalculous cholecystitis with biliary sludge before (a) and after (b) treatment with celecoxib and UDCA.
1 = gallbladder-dependent output of biliary cholesterol; **2** = gallbladder-independent output of biliary cholesterol; **3** = gallbladder-hepatic circulation of biliary cholesterol; **4** = hydrolysis of cholesterol esters entered the hepatocytes with HDL and LDL; **5** = synthesis of cholesterol; **6** = synthesis of cholesterol esters for VLDL; **7** = hydrolysis of cholesterol esters entered the hepatocytes with CMR.
ChA = cholesterol anhydrous; **ChM** = cholesterol monohydrate; **HA** = hepatic artery; **HV** = hepatic vein; **PV** = portal vein; **LD** = lymphatic duct.

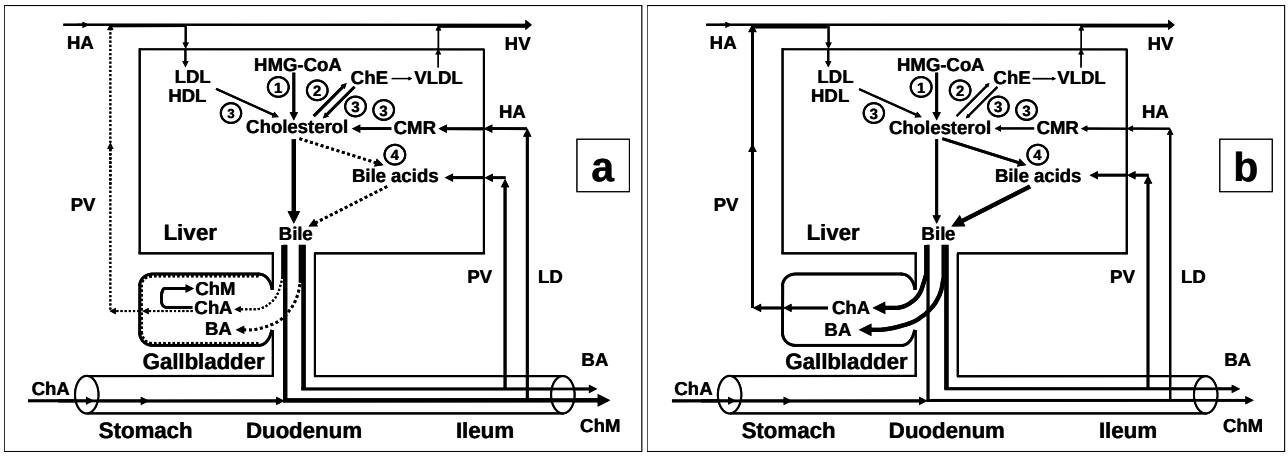


Fig. 5. Exchange of cholesterol and bile acids in patients with chronic acalculous cholecystitis with biliary sludge before (a) and after (b) treatment with celecoxib and UDCA.
1 = synthesis of cholesterol; **2** = synthesis of cholesterol esters for VLDL; **3** = hydrolysis of cholesterol esters entered 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.

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