

Causal factors

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Gallstones can be divided into three main types: cholesterol, pigment (brown/black) and mixed stones. In the USA and Europe, 80% of gallstones are cholesterol or mixed stones, whereas in parts of Asia 80% are pigment stones. Cholesterol or mixed stones contain 50–99% pure cholesterol plus an admixture of calcium salts, bile acids, bile pigments and phospholipids. Cholesterol is insoluble in water and is secreted from the canalicular membrane in phospholipid vesicles. Whether cholesterol remains in solution depends on the type and relative concentrations of phospholipids and bile acids in the bile. When bile is supersaturated with cholesterol and/or bile acid concentrations are low, unstable unilamellar phospholipid vesicles form, from which cholesterol crystals may nucleate. Obesity, a high-calorie diet and certain medications (e.g. oral contraceptives) can increase the secretion of cholesterol, while ileal disease or resection can deplete the bile acid pool and result in lithogenic bile (Figure 71.25). Nucleation of cholesterol monohydrate crystals from multilamellar vesicles is a crucial step in gallstone formation. Abnormal emptying of the gallbladder may aid the aggregation of nucleated cholesterol crystals; thus, removing gallstones without removing the gallbladder will inevitably lead to gallstone recurrence. Pigment stones contain <30% cholesterol. Overall, 20–30% of pigment stones are black; the incidence rises with age. For reasons that are unclear, patients with cirrhosis have a higher incidence of pigment stones. Black pigment stones are composed largely of an insoluble bilirubin pigment polymer mixed with calcium phosphate and calcium bicarbonate. These stones are associated with haemolysis, as in hereditary spherocytosis and sickle cell disease. Brown pigment stones contain calcium bilirubinate, calcium palmitate and calcium stearate, as well as cholesterol. Brown stones are more common in the bile ducts and are related to bile stasis and infection secondary to deconjugatable unconjugated bilirubinate precipitates. Brown pigment stones are also associated with the presence of foreign bodies within the bile ducts, such as endoprostheses (stents) or parasites such as *Clonorchis sinensis* and *Ascaris lumbricoides*.

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