As described in the previous paper, gallstones can form in the gallbladder when the concentration of biliary cholesterol increases. If one or more stones blocks the cystic duct and prevents proper release of bile into the duodenum, an individual may feel severe pain as a result of the increased pressure in the gallbladder. The formation of gallstones is especially common among obese individuals. Cholecystectomy is a common surgical procedure to remove the gallbladder in patients with symptomatic gallstones. This procedure is often performed laparoscopically to reduce the number and size of incisions, the risk of infection, and overall recovery time. While the gallbladder is not essential for digestion and absorption to occur, its removal causes several short and long term physiological changes in the GI tract.

**Topic #1: Obesity and the Risk of Gallstones**

Obesity is a significant risk factor for developing gallstones. In a large study of 90,302 women, those with BMI over 32 kg/m² were six times more likely to suffer from symptomatic gallstones than women with a normal BMI less than 24. Women with BMI over 45 were seven times more likely to have gallstones. The risk of gallstone disease increases with BMI. While the exact reason behind the increased risk of gallstones in obese patients is not fully understood, several mechanisms are likely to be involved.

One mechanism is the hypersecretion of cholesterol into bile in obese individuals. Cholesterol-saturated bile leads to gallstone formation in non-obese individuals as well, but the obese are more likely to secrete excessive cholesterol into their bile because it is common to have altered lipid levels in obesity. Because their bile is more saturated with cholesterol, the likelihood of gallstone formation in the gallbladder greatly increases. Impaired contractility of the gallbladder is also involved in the pathogenesis of gallstones in obesity. Many obese individuals experience insulin resistance, which increases serum insulin levels. Hyperinsulinemia has been shown to interfere with cholecystokinin (CCK) action at the gallbladder. Normally, CCK binds to receptors on gallbladder muscle cells to begin contraction and emptying of bile from the gallbladder. Excessive insulin interferes with CCK action at the receptor level, which leads to impaired contraction. A review of several studies by Petroni discovered that obese individuals have larger gallbladder volume between meals due to poor gallbladder contractility after a meal. Incomplete emptying of
the gallbladder increases the time that cholesterol-saturated bile is stored in the gallbladder, an ideal environment for stone formation.

**Topic #2: Short and Long Term Physiological Changes after Cholecystectomy**

Laparoscopic surgery, while minimally invasive, is still a traumatic experience for the body. Several researchers have studied the body’s immediate response to cholecystectomy, including hormone release, immune response, and changes in serum mineral concentrations. In response surgical incisions in the skin, the hypothalamus secretes corticotropin releasing hormone (CRH), which signals the anterior pituitary to release adrenocorticotropic hormone (ACTH). ACTH signals the adrenal cortex to release cortisol, the body’s primary stress hormone. Chambrier *et al* reports that cortisol levels remain high up to three days after surgery. Several hours after the start of surgery, white blood cells secrete interleukins (a cytokine), which initiate an immune response to the trauma. These changes are all part of the body’s stress response to surgery. Iron, copper, and zinc concentrations also change during and shortly after cholecystectomy as a part of the acute-phase response to the surgery. According to Fraser *et al*, serum iron levels and transferrin saturation drop after cholecystectomy in an effort to prevent the growth of bacteria that may enter the bloodstream during surgery. Serum zinc levels increase after surgery, but steadily return to normal several days after the procedure. Zinc has been shown to be a component in the repair of tissue damage. Cells release zinc into the bloodstream after the laparoscopic incisions to help heal the damaged tissues. Copper levels decrease after incision, but for unknown reasons. During the healing process, hormone, immune, and mineral levels return to normal.

These short-term physiological changes are coupled with several long-term changes to the physiology of the biliary and gastrointestinal systems after cholecystectomy. Normally, the gallbladder plays a key role in the concentration of bile through secondary active transport of sodium and chloride ions out of the gallbladder. Water follows these solutes out of the lumen, which concentrates the remaining bile. In the absence of a gallbladder, bile is not concentrated or stored. As the liver produces bile, it is released at a slow but continuous rate into the small intestine. Cholecystectomy patients often cannot tolerate high fat meals. Without sufficient bile to emulsify the fat in the intestine, the
excess fat remains undigested and can lead to diarrhea and discomfort as it passes through the body.

Gallstones are thought to form as a result of the hypersecretion of cholesterol or low concentrations of bile acid salts in bile. After cholecystectomy in non-obese patients, bile returns to normal proportions of cholesterol and bile acids. A study by Shaffer and Small analyzed a group of cholecystectomy patients and found that the improved bile composition after surgery was a result of faster secretion of bile acid salts, which reduces the previously high concentration of cholesterol in the bile. Without the storage time in the gallbladder, bile acids are recycled, circulated, and deposited into new bile more quickly. Shaffer and Small observed that the cycling rate doubles after cholecystectomy.

One of the most common side effects of the surgery is postcholecystectomy diarrhea (PCD). Many patients who undergo cholecystectomy experience altered frequency and form of bowel movements, especially PCD. The mechanism behind the altered bowel movements is thought to be bile acid malabsorption in the intestine. After cholecystectomy, bile acids continuously circulate through the liver and intestine, instead of being stored in the gallbladder for up to several hours. The increased rate of bile acid flow allows some of the acids to enter the large intestine. The acids increase the osmolarity of the material in the colon, which draws water into the colon and results in diarrhea. According to Sauter et al, up to 50% of patients who undergo cholecystectomy experience some form of diarrhea, but the condition generally resolves completely after several weeks as the body adjusts to the removal of the gallbladder.

In conclusion, cholecystectomy is a common procedure to remove the gallbladder in patients who suffer from gallstones. During and immediately after the surgery, the body responds to the stress by altering hormone, white blood cell, and mineral levels to protect the body from trauma. Long-term physiological changes after the surgery include intolerance of high fat meals, diarrhea, and a return to normal ratios of cholesterol and bile acid salts in the patient’s bile. The risk of gallstones, and subsequent need for cholecystectomy, is increased in obese individuals. Obesity results in excessive secretion of cholesterol into bile, poor gallbladder contraction due to impaired CCK action, and increased gallbladder volume between meals. All of these mechanisms increase the likelihood that cholesterol-rich bile will remain in the gallbladder and form stones.
References


