

# PBC: Mechanism of Disease

## What do we currently know?

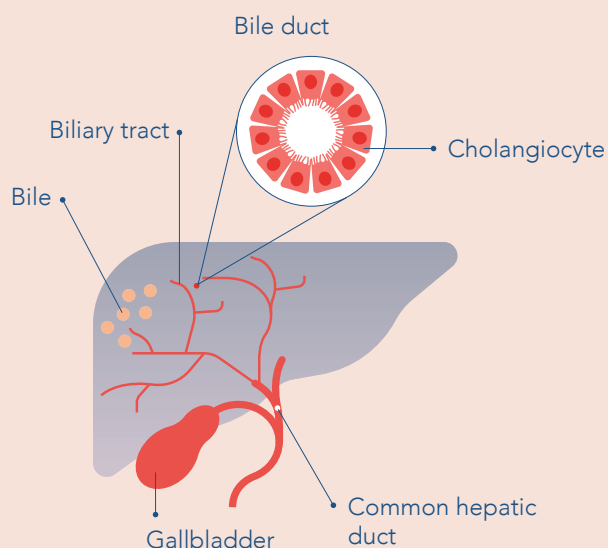
Primary biliary cholangitis (PBC) is a **cholestatic liver disease**<sup>1</sup>

In PBC, the **gradual destruction of bile ducts** causes cholestasis (reduced flow of bile from the liver)<sup>1,2</sup>



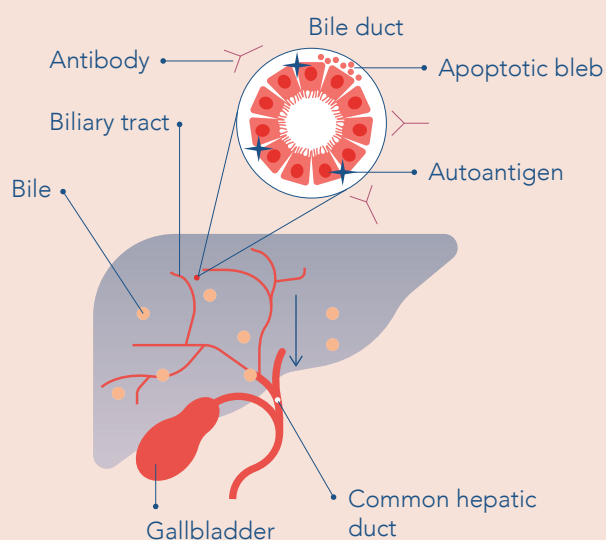
Cholestasis leads to **inflammation in the liver and damage to hepatocytes and cholangiocytes**<sup>2</sup>

Bile is produced by hepatocytes, and then modified by cholangiocytes lining the bile ducts<sup>3,4</sup>



**Under normal circumstances, bile is transported to the gallbladder via the biliary tract**<sup>3,4</sup>

- Around 50% of bile is stored in the gallbladder<sup>4</sup>; the rest enters the small intestine where it **aids digestion** and **helps to remove waste products** from the body<sup>3,4</sup>



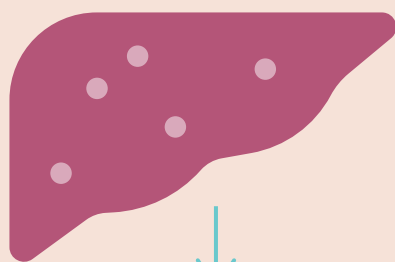
**In PBC, a T-cell-mediated immune response leads to the apoptosis of cholangiocytes and inappropriate expression of autoantigens**<sup>5,6</sup>

- This promotes further immune attack and bile duct damage<sup>5</sup>
- Over time, the bile ducts are destroyed and cholestasis occurs<sup>2</sup>

1. Appanna G, Kallis Y. Clinical Medicine 2020;20:513–6; 2. Santiago P et al. Ther Adv Gastroenterol 2018;11:1–15; 3. Hundt M et al. Physiology, Bile Secretion. [Updated 2022 Sep 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022; 4. Johns Hopkins Medicine: Biliary System Anatomy and Functions. Available at: [www.hopkinsmedicine.org/health/conditions-and-diseases/biliary-system-anatomy-and-functions](http://www.hopkinsmedicine.org/health/conditions-and-diseases/biliary-system-anatomy-and-functions). Last accessed May 2024; 5. Li H et al. Biomed Pharmacother 2021;140:111754; 6. Lleo A et al. Hepatology 2009;49:871–879.

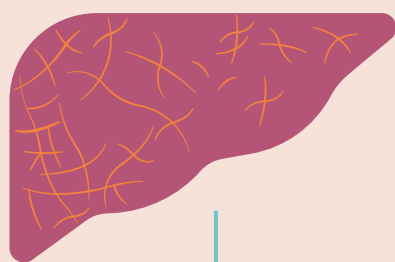
# Natural History of Untreated Primary Biliary Cholangitis (PBC)<sup>1</sup>

Cholestasis<sup>1,2</sup>



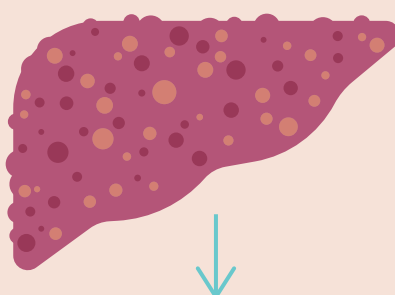
- Impairment of bile formation and/or flow<sup>2</sup>

Fibrosis<sup>1</sup>



- Formation of an abnormally large amount of scar tissue in the liver due to chronic damage<sup>3</sup>
- Precursor to cirrhosis<sup>4</sup>

Cirrhosis<sup>1</sup>



- Final stage of many chronic liver diseases<sup>4</sup>
- Pathological characteristics include degeneration and necrosis of hepatocytes, replacement of liver tissue with fibrotic scar tissue, and loss of liver function<sup>4</sup>

**Liver transplantation or  
premature death**

- Ultimately, PBC can lead to liver failure and patients may require liver transplantation<sup>5</sup>

1. Galoosian A et al. J Clin Transl Hepatol 2020;8:49–60; 2. Jungst C and Lammert F. Dig Dis 2013;31:152–154; 3. Ahmad A and Ahmad R. Saudi J Gastroenterol 2012;18:155–167; 4. Zhou W et al. World J Gastroenterol 2014;20:7312–7324; 5. Lammers W et al. Ann Hepatol 2014;13:316–326.