

CHOLESTASIS: FAMILIAL INTRAHEPATIC TYPE 1

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CHOLESTASIS, FAMILIAL INTRAHEPATIC TYPE 1

- bile salts are required for the digestion of dietary fats
- bile acids are synthesized by the liver and then converted to bile salts for secretion via the bile duct to the gall bladder where they are concentrated
- progressive familial intrahepatic cholestasis falls into three categories:
 - ✓ type 1 disorder: defective bile salt ATP-binding cassette transporter (ATP8B1 gene)
 - ✓ type 2 disorder: defective bile salt export pump (ABCB11 gene)
 - ✓ type 3 disorder: multidrug resistance protein (ABCB4 gene)
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SECRETION OF BILE SALTS FROM LIVER CELLS

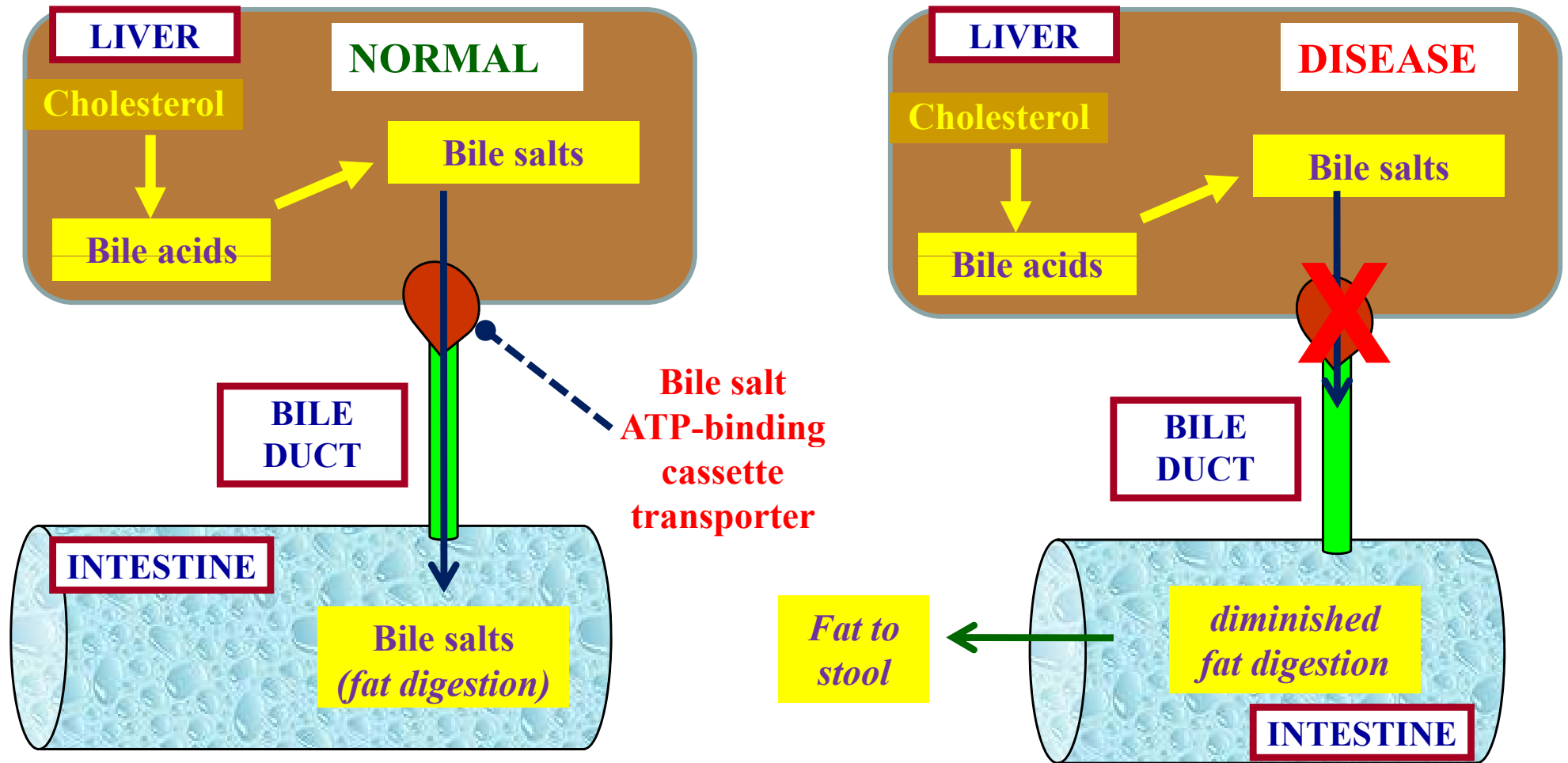


Figure 1. Cholesterol is processed in liver cells to bile acids and then to bile salts. The bile salts are released into the bile duct, in part, via the **bile salt ATP-binding cassette transporter**. In the intestine, bile salts are used in the digestion of fats. In **progressive intrahepatic cholestasis**, the **bile salt ATP-binding cassette transporter** is defective (**X**). Hence there is not sufficient bile salts in the intestine for fat digestion leading to **loose, fatty, foul smelling stools (steatorrhea)**. This malabsorption of fats leads to **malnutrition** and hence **delayed growth**. Consequences that lead to other symptoms are depicted in Figure 2.

ADDITIONAL CONSEQUENCES OF CHOLESTASIS

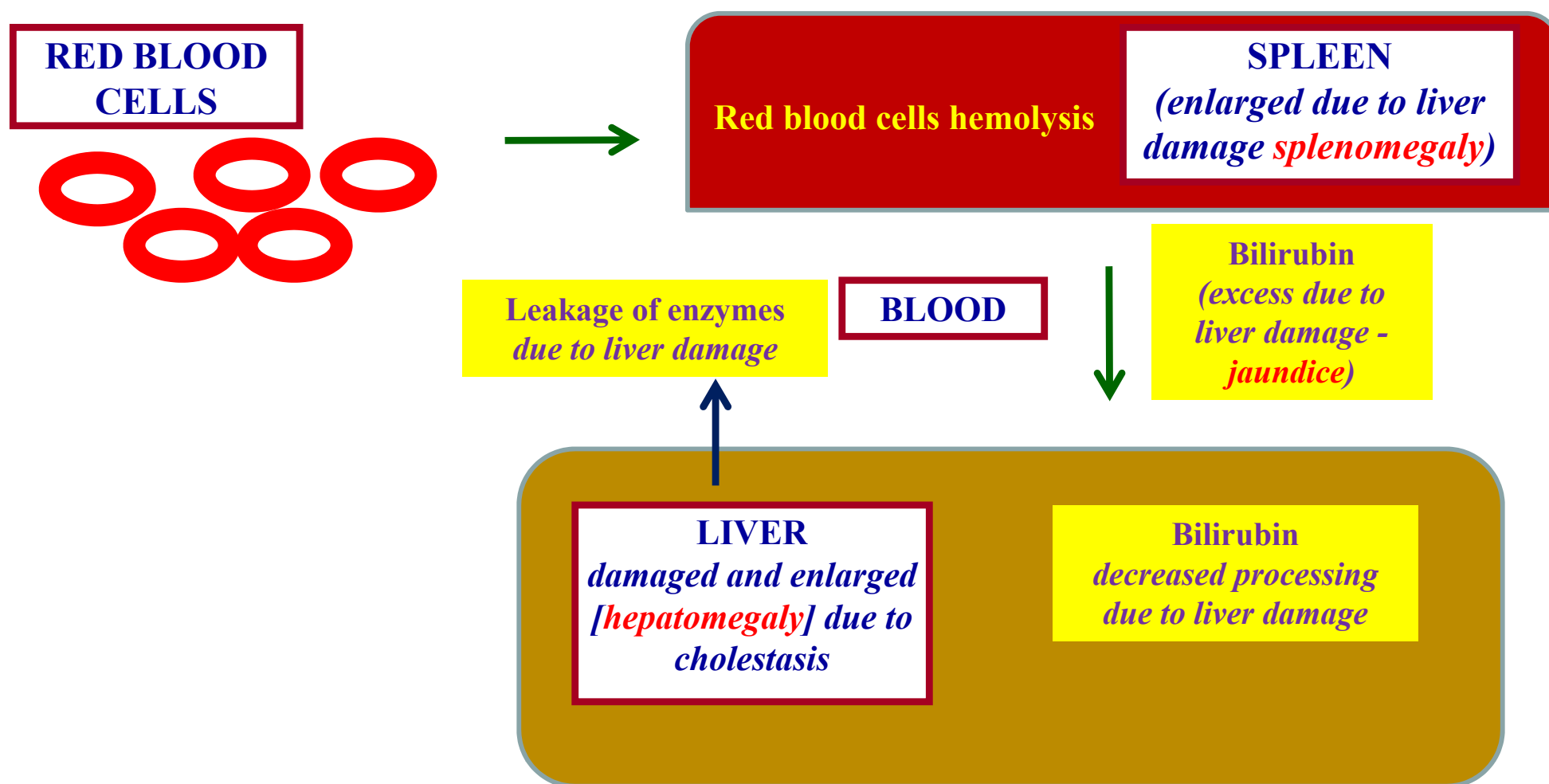


Figure 2. Red blood cell destruction by the spleen leads to production of small amounts of bilirubin, which is then processed and excreted by the liver. The failure of the liver to secrete bile acids leads to liver damage that causes bilirubin to accumulate in the blood resulting in yellowing of skin and sclera of the eyes (**jaundice**). Damage to the liver causes enlargement of this organ (**hepatomegaly**) as well as the spleen (**splenomegaly**). The only treatment is to transplant the liver to restore functional bile acid secretion.