HYPERCHOLANEMIA

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HYPERCHOLANEMIA: RELEVANT FACTS

- bile acids are synthesized in liver from cholesterol
- bile acids are converted to their salt form by a liver conjugating enzyme (**BAAT**)
- bile salts are secreted to the gall bladder for storage via the bile duct
- leakage of bile salts from the bile duct to the plasma is prevented by a barrier (tight junction) that includes tight junction protein 2 (**TJP2**) (Fig. 1)
- hypercholanemia, excess bile acids in the blood, can be caused by a **deficiency of TJP2** (Fig 1) or **deficiency of BAAT** (Fig 2)
- bile salts assist in fat digestion and absorption and in the absorption of fat-soluble vitamins (D, E, K) by the intestine and in their absence patients have **deficiency of these vitamins** and fatty diarrhea (**steatorrhea**) (Fig. 3)
- symptoms can be treated by oral administration of a bile salt (**ursodeoxycholic acid**)

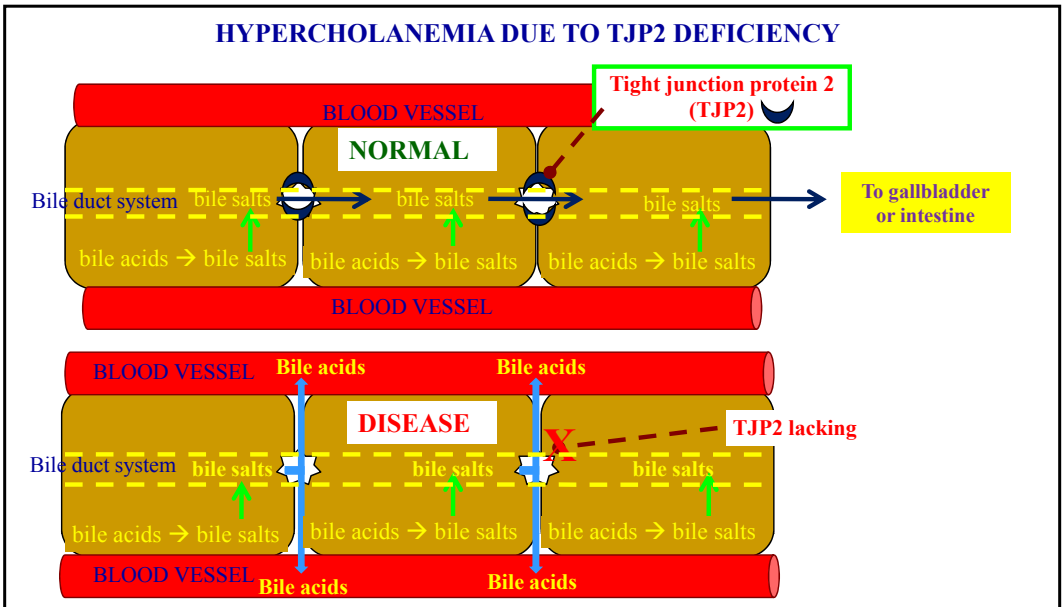

Figure 1. Liver cells make bile acids that are then conjugated to form bile salts. Bile salts are secreted into the bile duct system for delivery to the gall bladder and intestine. Leakage of bile salts from the bile duct system to the blood is prevented by tight junctions (tight junction protein 2) at the membrane interface (top). In this form of **hypercholanemia**, the tight junction protein 2 is deficient **(X)** allowing bile salts to leak into the blood rather than be transported to the gall bladder and liver. The lack of bile salts in the intestine affect absorption of fats and fat-soluble vitamins (see Fig. 3).

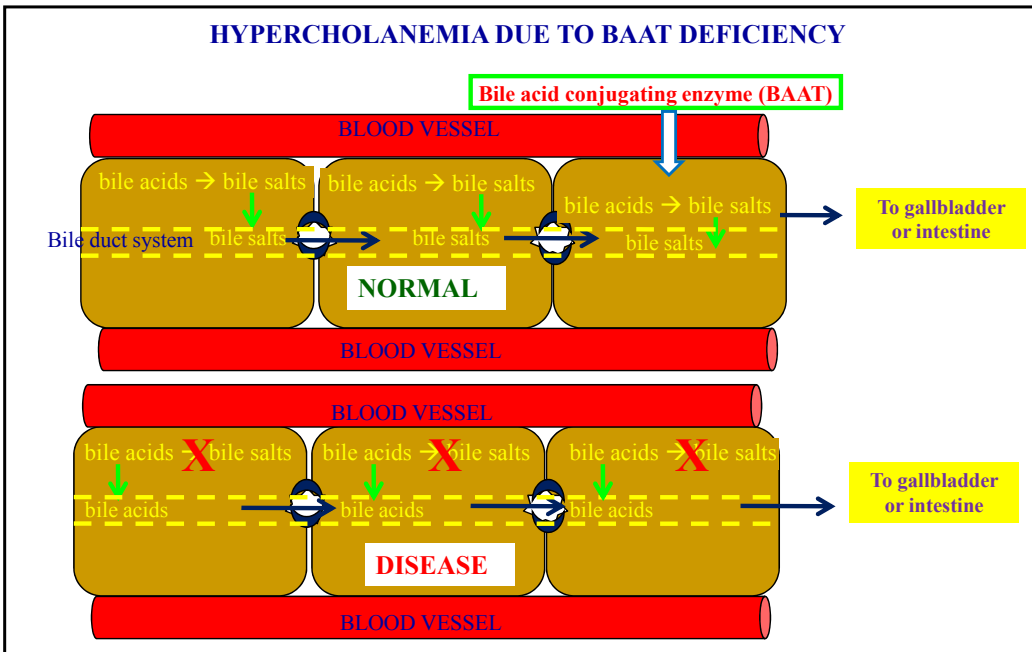

Figure 2. Liver cells make bile acids that are then conjugated to form bile salts by the bile acid conjugating enzyme (BAAT). Bile salts are secreted into the bile duct system for delivery to the gall bladder and intestine (top). In this form of **hypercholanemia**, the bile acid conjugating enzyme is deficient **(X)**. Consequently bile acids rather than bile salts are transported to the gall bladder and liver. Because bile acids are ineffective for the intestinal absorption of fats and fat-soluble vitamins, they are excreted in the stool (see Fig. 3).

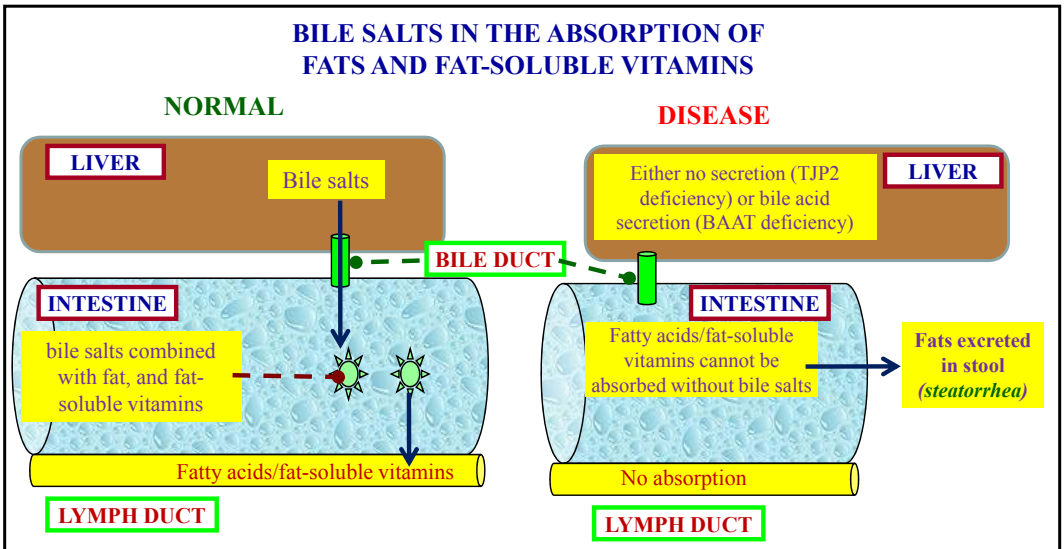

Figure 3. Bile salts are required for the solubilization and absorption of fats and fat-soluble vitamins (e.g., D and K). With **hypercholanemia - TJP2 deficiency** no bile salts are secreted (Fig 1) and with **hypercholanemia - BAAT deficiency** only bile acids are secreted (Fig 2) to the intestine. In both instances, the lack of bile salts in the intestine means that fatty acids cannot be absorbed. Instead fats are excreted in the stool causing fatty diarrhea (**steatorrhea**). Fat-soluble vitamins also cannot be absorbed. Vitamin K is essential for the blood clotting cascade so in **hypercholanemia** abnormal bleeding can occur. Vitamin D is essential for promoting calcium absorption by the intestine or reabsorption by the kidney. Hence deficiency of vitamin D in **hypercholanemia** leads to calcium deficiency in bones of children (**rickets**).