

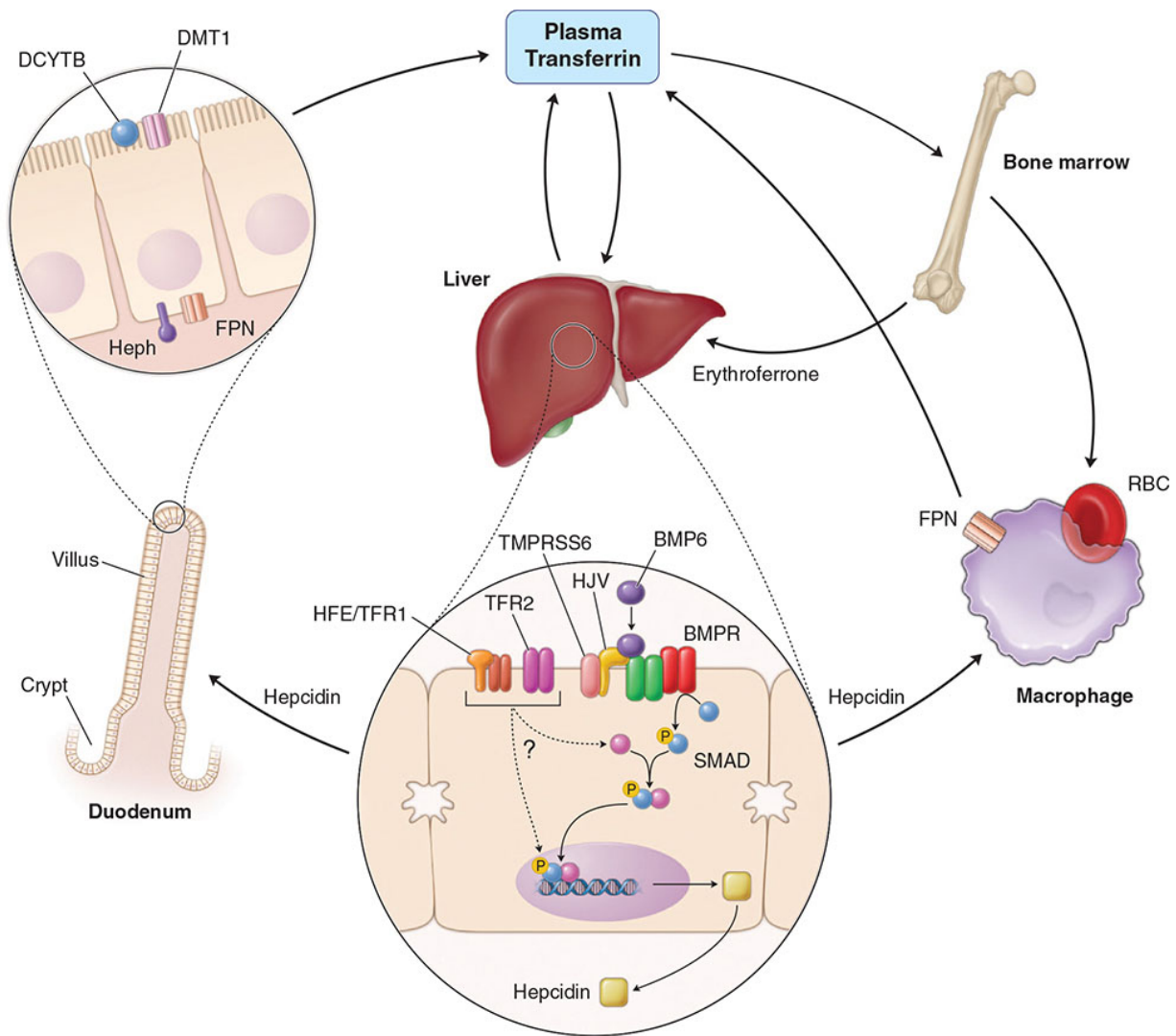


FIGURE 414-1 Pathways of normal iron homeostasis. Dietary inorganic iron traverses the brush border membrane of duodenal enterocytes via divalent metal-ion transporter 1 (DMT1) after reduction of ferric (Fe^{3+}) iron to the ferrous (Fe^{2+}) state by intestinal ferrireductases such as duodenal cytochrome B (DCYTB). Iron then moves from the enterocyte to the circulation via a process requiring the basolateral iron exporter ferroportin (FPN) and the iron oxidase hephaestin (Heph). In the circulation, iron binds to plasma transferrin and is thereby distributed to sites of iron utilization and storage. Much of the diferric transferrin supplies iron to immature erythrocyte cells in the bone marrow for hemoglobin synthesis. At the end of their life, senescent red blood cells (RBCs) are phagocytosed by macrophages, and iron is returned to the circulation after export through ferroportin. The liver-derived peptide hepcidin represses basolateral iron transport in the gut as well as iron released from macrophages and other cells and serves as a central regulator of body-iron traffic. At least two separate signals regulate hepcidin production in response to changes in body-iron requirements. The first