Fig. 15.1. Physiologic processes that influence plasma or serum concentrations of TLI, PLI, or TAP.

- **TLI**: Most trypsinogen is secreted in enzyme-rich pancreatic secretions into the intestine, where it is converted to trypsin, a potent digestive protease. In health, a small amount of trypsinogen escapes the pancreas and enters the blood, in which it can be measured as TLI. Also, small amounts of trypsin may be formed in the pancreas (see TAP); this trypsin may enter the blood, bind to antiproteases, and contribute to [TLI]. Plasma trypsinogen and trypsin are degraded in the kidneys and by the mononuclear phagocyte system.

- **TAP**: In health, small amounts of trypsinogen are cleaved to form trypsin and TAP within the pancreas; this TAP enters the plasma (probably via lymph), and some of it is cleared via the kidneys and is excreted in the urine. Activation of trypsinogen to trypsin by enterokinase in the intestine also results in the formation of TAP, but this TAP is not absorbed and thus does not enter the plasma.

- **PLI**: Most pancreatic LPS is secreted in enzyme-rich pancreatic secretions into the intestine, where it catalyzes the lipolysis of dietary triglycerides. In health, a small amount of pancreatic LPS escapes the pancreas and enters the blood, in which it can be measured as PLI. The kidneys are involved in the removal of LPS from the plasma.

Fig. 15.2. Physiologic processes that influence plasma or serum concentrations of cobalamin or folate and the cellular relationship of cobalamin and folate.

- **Cobalamin**: Cobalamin (Cbl) enters the stomach via ingested foods. In the acidic environment, it binds with R protein (cobalophilin or haptocorrin; R for rapid electrophoretic migration) that is produced by the gastric mucosa. Cobalamin enters the intestine bound to R protein (R), but when it enters the alkaline environment, it detaches from R protein and binds to intrinsic factor (IF) that is secreted by the pancreatic cells (dogs and cats) and the gastric mucosa (dogs). Enteric bacteria use some of the cobalamin as it moves through the small intestine. When it reaches the ileum, the cobalamin/intrinsic factor complex binds to specific mucosal receptors involving cubam (cubilin and amnionless) and megalin, and enters enterocytes. When cobalamin enters the portal blood, it binds to transcobalamin 2 (Trans), a transport protein. From the blood, cobalamin may be used in tissues, stored in the liver, or excreted in bile.

- **Folate**: Folate is present in food (e.g., green leafy plants) in a polyglutamate form. After digestion releases it from food, the polyglutamate folate is hydrolyzed to monoglutamate folate at the brush border of the proximal small intestine. After cellular uptake, it is converted to N5-methyltetrahydrofolate (commonly called folate), which enters the blood and is transported to tissues for biochemical reactions. Enteric bacteria can also produce folate. Folate from erythrocytes lysed during sample collection can increase measured serum [folate].

- **Relationship of cobalamin and folate**: Cobalamin is a required cofactor for methionine synthase, which catalyzes the conversion of N5-methyltetrahydrofolate (the primary molecule in plasma) to tetrahydrofolate, which is then available for DNA synthesis in cells. If there is a cobalamin deficiency, the methyl group of N5-methyltetrahydrofolate is not transferred to cobalamin (methyl trapped), and thus a cellular deficiency in tetrahydrofolate occurs.