PYRUVATE KINASE DEFICIENCY
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- **glycolysis** is a pathway in all cells that metabolizes glucose to pyruvate and produces limited amounts of usable energy as ATP, without dependence on oxygen (Figure 1)
- ATP drives a variety of processes in cells including the sodium-potassium pump that maintains the amount of potassium in cells (Figure 1)
- red blood cells lack mitochondria, the energy-producing compartment found in most cells, and hence can only derive energy from **glycolysis**
- **pyruvate kinase** is the last enzymatic reaction in glycolysis and when deficient in the red blood cell, prevents the cell from producing sufficient amounts of ATP for cell survival, in large part due to the loss of potassium (Figure 1)
- the defective red cells are destroyed in the spleen causing anemia and the spleen enlarges (splenomegaly) because it is overworked
- the excessive destruction of red blood cells (hemolysis) results in the breakdown of hemoglobin stored in these cells
  - a by product of hemoglobin breakdown is bilirubin, which when overproduced causes a yellowing of the skin and sclera of the eyes (jaundice)
  - liver processes bilirubin for excretion and the excessive excretion causes inflammation of the gallbladder (cholecystitis) leading to formation of bilirubin-containing gallstones (cholelithiasis) (Figure 2)
**Figure 1.** Glycolysis produces usable energy as ATP at two reactions. In the red blood cell this energy is largely used to drive the sodium (Na)-potassium (K) pump to maintain the proper amount of potassium inside the cell. In this disease (right), pyruvate kinase is deficient (X). This deficiency causes the entire glycolysis pathway to cease working so that little to no ATP is produced. Consequently the NA-K pump does not function (X) and because potassium does not re-enter the cell the amount inside the cell is markedly lowered. The red blood cells cannot then survive for their normal 120 days and this excessive breakdown of red blood cells (hemolysis) by the spleen leads to fewer cells in the blood (anemia). Excess hemolysis leads to jaundice and gallstones (see Fig. 2).

**Figure 2.** The normal process of red blood cell destruction by the spleen leads to production of small amounts of bilirubin, which is then excreted by the liver via the bile duct. This diagram shows the consequences of excess hemolysis due to the pyruvate kinase deficiency in the red blood cells. The spleen is overworked and becomes enlarged (splenomegaly). The bilirubin produced exceeds the capacity of the liver to process and excrete it resulting in yellowing of skin and sclera of the eyes (jaundice). Excessive bilirubin is excreted and taken up by the gall bladder, which becomes inflamed (cholecystitis) and forms bilirubin-containing gallstones (cholelithiasis).