Table 5-7 Principal Subgroups of Glycogenoses

Clinicopathologic Category	Specific Type	Enzyme Deficiency	Morphologic Changes	Clinical Features
Hepatic type	Hepatorenal—von Gierke disease (type I)	Glucose-6-phosphatase	Hepatomegaly—intracytoplasmic accumulations of glycogen and small amounts of lipid; intranuclear glycogen Renomegaly—intracytoplasmic accumulations of glycogen in cortical tubular epithelial cells	In untreated patients: failure to thrive, stunted growth, hepatomegaly, and renomegaly Hypoglycemia due to failure of glucose mobilization, often leading to convulsions Hyperlipidemia and hyperuricemia resulting from deranged glucose metabolism; many patients develop gout and skin xanthomas Bleeding tendency due to platelet dysfunction With treatment: Most survive and develop late complications (e.g., hepatic adenomas)
Myopathic type	McArdle disease (type V)	Muscle phosphorylase	Skeletal muscle only—accumulations of glycogen predominant in subsarcolemmal location	Painful cramps associated with strenuous exercise; myoglobinuria occurs in 50% of cases; onset in adulthood (>20 years); muscular exercise fails to raise lactate level in venous blood; serum creatine kinase always elevated; compatible with normal longevity
Miscellaneous types	Generalized glycogenosis—Pompe disease (type II)	Lysosomal glucosidase (acid maltase)	Mild hepatomegaly—ballooning of lysosomes with glycogen, creating lacy cytoplasmic pattern Cardiomegaly—glycogen within sarcoplasm as well as membrane-bound Skeletal muscle—similar to changes in heart	Massive cardiomegaly, muscle hypotonia, and cardiorespiratory failure within 2 years; a milder adult form with only skeletal muscle involvement, presenting with chronic myopathy; enzyme replacement therapy available

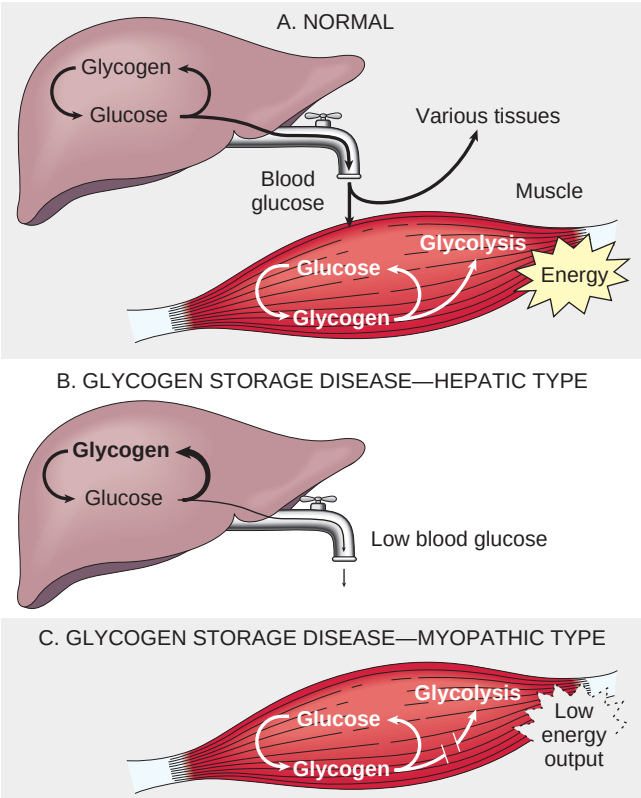

Figure 5-15 **A,** Normal glycogen metabolism in the liver and skeletal muscles. **B,** Effects of an inherited deficiency of hepatic enzymes involved in glycogen metabolism. **C,** Consequences of a genetic deficiency in the enzymes that metabolize glycogen in skeletal muscles.

KEY CONCEPTS

Glycogen Storage Diseases

- Inherited deficiency of enzymes involved in glycogen metabolism can result in storage of normal or abnormal forms of glycogen, predominantly in liver or muscles, but also in other tissues as well.
- In the **hepatic form** (von Gierke disease), liver cells store glycogen because of a lack of hepatic glucose-6-phosphatase. There are several **myopathic forms**, including McArdle disease, in which muscle phosphorylase lack gives rise to storage in skeletal muscles and cramps after exercise. In **Pompe disease** there is lack of lysosomal acid maltase, and all organs are affected, but heart involvement is predominant.

Disorders Associated with Defects in Proteins That Regulate Cell Growth

Normal growth and differentiation of cells are regulated by two classes of genes; proto-oncogenes and tumor suppressor genes, whose products promote or restrain cell growth (Chapter 7). It is now well established that mutations in these two classes of genes are important in the pathogenesis of tumors. In the vast majority of cases, cancer-causing mutations affect somatic cells and hence are not passed in the germ line. In approximately 5% of all cancers, however, mutations transmitted through the germ line contribute to the development of cancer. Most familial cancers are inherited in an autosomal dominant fashion, but a few recessive disorders have also been described. This subject is discussed in Chapter 7. Specific forms of familial tumors are described in various chapters.