Case 25
Glycogen Storage Diseases

Focus concept
Disturbances in glycogen utilization result if an enzyme involved in glycogen synthesis or degradation is missing.

Prerequisites
- Glycogen synthesis and degradation pathways.
- The link between glycogen metabolism and fat metabolism.

Background
Glycogen storage diseases are so named because a hallmark of the diseases is impaired glycogen storage due to a deficiency of one of the enzymes involved in either glycogen synthesis or glycogen degradation. Eight kinds of glycogen storage diseases have been identified so far. Each type is characterized by the lack of a specific enzyme. An understanding of glycogen metabolism is essential in the proper treatment of this disease, and identification of the deficient enzyme is required before a treatment protocol can be designed.

Your patient is a fifteen-year-old Caucasian male named Alex K. Alex’s mother has brought him to see you because she is concerned about his inability to perform any kind of strenuous exercise. During his physical education classes, Alex could not keep up with his classmates and often suffered painful muscle cramps if he did attempt to exercise. He appeared to be normal if at rest or performing light to moderate exercise. A physical examination reveals that his liver appears to be normal in size, but his muscles are flabby and poorly developed. A fasting glucose test showed that Alex was not hypo- or hyperglycemic. A number of biochemical tests were carried out to identify the type of glycogen storage disease in this patient.

Questions
1. You decide to try Alex’s response to glucagon. This test consists of injecting a high dose of glucagon intravenously and then drawing samples of blood periodically and measuring the glucose content of the samples. After the glucagon injection, Alex’s blood sugar rises dramatically. Is this the response you would expect in a normal person? Explain.

2. Liver and muscle biopsies are taken from Alex and analyzed. The biopsies reveal that glycogen content in the liver is normal, but muscle glycogen content is elevated. The biochemical structure of glycogen in both tissues appears to be normal. Suggest some possible explanations for these observations.
3. Next, you do another test where you have Alex perform ischemic exercise for as long as he is able to do so. Blood is withdrawn from the patient every few minutes or so during the exercise period.
   a. Alex’s blood samples are tested for lactate and compared with a control sample of a patient who does not suffer from a glycogen storage disease. The results are shown in Figure 25.1. Why does lactate concentration increase in the normal patient? Why is there no corresponding increase in Alex’s lactate concentration?

\[\text{Figure 25.1: Blood lactate concentration following ischemic exercise in a patient with a glycogen storage disease and a control patient (based on Stanbury, et al., 1978).}\]

b. Urine tests after Alex has completed his exercise reveal the presence of myoglobin in his urine. Myoglobin isn’t normally found in the urine, but in muscle cells. Why does Alex suffer from myoglobinuria following ischemic exercise?

c. Alex’s blood samples are also tested for alanine content. In a normal person, you would expect that blood alanine would increase during ischemic exercise. But in Alex’s blood samples, you see a decrease in alanine concentrations, leading you to believe that Alex’s muscle cells are taking up alanine rather than releasing it. Why would blood alanine concentrations increase in a normal person? Why do blood alanine concentrations decrease in your patient?

4. Alex’s enzyme deficiency does not cause him to suffer from either hypo- or hyperglycemia. Explain why.

5. As a treatment, you tell Alex that the best thing he can do is to avoid strenuous exercise. If he does wish to exercise, you advise him to consume sports drinks containing glucose or fructose frequently while exercising. Why would this help alleviate Alex’s suffering during exercise?
Reference