Table I-58

Testing used to establish the diagnosis of Pompe disease

- **Acid alpha-glucosidase (GAA) enzyme activity.** GAA enzyme activity analysis can be performed on dried blood spots thus permitting rapid and sensitive analysis. Standard conditions for assay of GAA in blood samples have been proposed by a Pompe Disease Diagnostic Working Group. Confirmation by measurement of GAA activity in another tissue (e.g., culture skin fibroblasts) or molecular analysis is recommended. Historically, measurement of GAA enzyme activity has been performed using cultured skin fibroblasts, but it may take four to six weeks to obtain results, and delayed diagnosis and initiation of treatment, particularly in infants, may affect outcome.
    - Complete deficiency (activity less than 1% of normal controls) of GAA enzyme activity is associated with classic infantile-onset Pompe disease.
    - Partial deficiency (activity 2% to 40% of normal controls) of GAA enzyme activity is associated with the non-classic infantile-onset and the late-onset

Note: (1) As a general rule, the lower the GAA enzyme activity the earlier the age of onset of disease. (2) GAA enzyme activity can be assayed in muscle; however, this invasive procedure usually requires anesthesia, which may not be tolerated in those who have infantile Pompe disease and cardiopulmonary compromise. (3) Peripheral leukocytes have been used to measure GAA enzyme activity but alternate isoenzymes such as maltase-glucoamylase may interfere with the assay. (4) GAA enzyme activity analysis can be performed on dried blood spots thus permitting rapid and sensitive analysis that is potentially useful for newborn screening

- **Acid alpha-glucosidase protein quantitation** can be performed by an antibody-based method in cultured fibroblasts. Such testing may be important in determining if an affected individual produces cross-reactive immunologic material (CRIM). CRIM status affects response to ERT and CRIM-negative individuals need an altered plan for enzyme
- **Muscle biopsy.** In contrast to the other glycogen storage disorders, GSD II is also a lysosomal storage disease. In GSD II glycogen storage may be observed in the lysosomes of muscle cells as vacuoles of varying severity that stain positively with periodic acid-Schiff. However, 20%-30% of

individuals with late-onset Pompe disease with documented partial enzyme deficiency may not show these muscle-specific changes

Newborn screening. Newborn screening for GSD II, using GAA enzyme activity in dried blood spots as a primary screening tool.