Inborn Errors of Metabolism Involving Complex Molecules

Lysosomal and Peroxisomal Storage Diseases

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KEYWORDS

• Peroxisome • Lysosome • Storage disorder • Very long chain fatty acids

KEY POINTS

- Peroxisomes and lysosomes are distinct organelles that are implicated in a range of pediatric metabolic disorders.
- Peroxisomes and lysosomes share the pattern of involvement in complex macromolecule metabolism and a relationship between their functions and diseases.
- Peroxisomal disorders are multisystem diseases due to global or single enzyme loss of peroxisomal function.
- Lysosomal disorders lead to accumulation of storage material in lysosomes in multiple organs.

PEROXISOMES, LYSOSOMES, AND DISEASE

Eukaryotic cells perform several biological processes in organelles, which compartmentalize and organize key functions (**Fig. 1**). Peroxisomes and lysosomes perform distinct metabolic functions; however, they are very similar in size, such that they were discovered around the same time by similar methods of ultracentrifugation by Christian de Duve.[1] Both peroxisomes and lysosomes catalyze several metabolic

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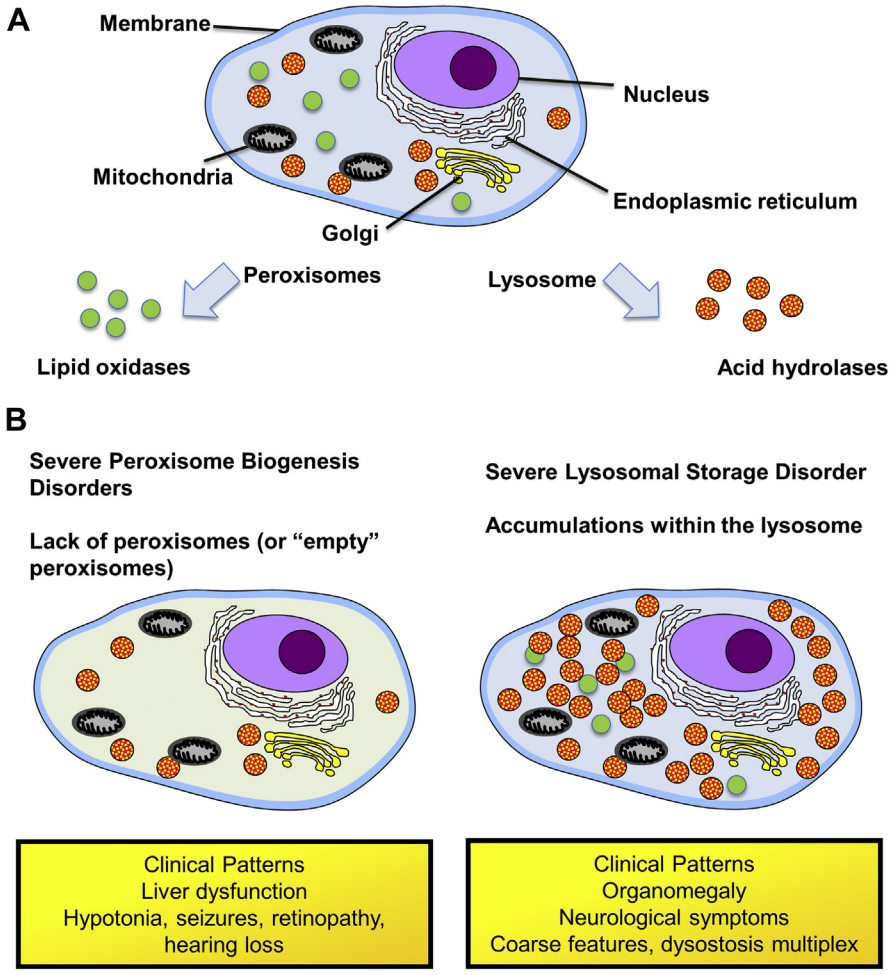

Fig. 1. Peroxisomes and lysosomes. (*A*) Eukaryotic cells have several organelles. Peroxisomes are shown in green and lysosomes are shown in yellow-red. The peroxisomes primarily contain lipid oxidases and perform complex lipid metabolism, whereas lysosomes contain enzymes, including acid hydrolases. (*B*) The most severe peroxisomal and lysosomal disease states. Severe peroxisome biogenesis disorders lead to lack of peroxisomes. The severe peroxisome biogenesis disorders have liver dysfunction, hypotonia, seizure, and retinopathy. Lysosomal storage disorders, in contrast, are characterized by lysosomal enzyme dysfunction and resultant substrate accumulation in the lysosome, resulting in organomegaly, neurologic symptoms, coarse features, and dysostosis multiplex due to bone involvement.

functions indispensable in cell biology. When these organelles are impaired they lead to several distinct pediatric metabolic disorders.[2] Although individually most of these disorders are rare, the careful clinical and cell biology characterization of these disorders has offered insight into the crucial role peroxisomes and lysosomes play in human health.[3–5] In addition, both organelles can produce a range of diseases that affect multiple organ systems, presenting to the pediatrician with an array of clinical presentations. Given the complexity of these disorders and the large number of biochemical pathways implicated, a general framework is needed for recognizing