# Metabolic Disorders Involving The CNS: A Case-Based Discussion

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## Case-Based Questions (please see page 3 for answers)

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| 1. | What is the public health rationale for expanded newborn screening for metabolic disorders? | |
| | a. | Collection and storage of DNA for medicolegal purposes |
| | b. | Expedited referral of patients to renal specialists |
| | c. | Identification of patients with increased risk for pediatric cancer |
| | d. | Rapid identification of diseases with potential interventions that can prevent morbidity |

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| 2. | Which of the following underlies Leigh Syndrome? | |
| | a. | Fatty acid oxidation defect |
| | b. | Glycogen storage disorder |
| | c. | Mitochondrial disorder |
| | d. | Peroxisomal storage disorder |

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| 3. | What ultrastructural finding would be typical of Niemann-Pick type C? | |
| | a. | Glycogen granules in endothelial cells |
| | b. | Mitochondrial paracrystalline inclusion in myocytes |
| | c. | Pleomorphic intracytoplasmic vacuoles in neurons |
| | d. | Sharp-cornered crystals in Schwann cells |

**Scroll to Page 3 for answers**

Question 1 Correct answer and rationale: **D) Rapid identification of diseases with potential interventions that can prevent morbidity**

Disorders evaluated in newborn screening generally have a treatment available and early therapy can often prevent severe effects of the disease. A key example is phenylketonuria, for which early dietary intervention can abrogate many of the developmental effects of the disease.

Question 2 Correct answer and rationale: **C) Mitochondrial disorder**

While Leigh Syndrome is associated with a variety of genetic alterations, the known causative genes are related to mitochondrial energy generation, with Complex I deficiency being the most common type.

Question 3 Correct answer and rationale: **C) Pleomorphic intracytoplasmic vacuoles in neurons**

Niemann-Pick type C is a lysosomal storage disorder, and electron microscopy should show storage inclusions in many cell types including neurons. The inclusions are typically pleomorphic and show electron lucent vacuoles with electron-dense curved short membranous structures.