# Chapter 20: Metabolic Disorders in Newborn

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## Overview

- Heterogenous group of disorders that typically present after 48 hours of life and after the initiation of feedings
- Often associated with hypoglycemia, hyperammonemia, and acidosis
- Presentation in the newborn period includes lethargy, emesis, poor feeding, hypotonia, tachypnea, temperature instability, seizures, coma, and apnea
- Always consider in a newborn who is being evaluated for sepsis
- May have family history of unexplained neonatal deaths
- Consanguineous matings (most are autosomal recessive)

## Diagnosis

- Initial labs
  - Blood glucose
  - Arterial blood gas
  - Lactate (arterial sample)
  - Electrolytes (look for acidosis and anion gap)
  - Ammonia (arterial sample, place immediately on ice)
  - Liver function tests
  - Urine ketones and reducing substances
  - Newborn screen
- Diagnostic labs
  - Plasma amino acids (amino acidopathies, urea cycle disorders)
  - Urine organic acids (fatty acid oxidation disorders, amino acidopathies)
  - Plasma acylcarnitine (fatty acid oxidation disorders, organic acidemias)
  - Serum carnitine (fatty acid oxidation disorders, organic acidemias, carnitine deficiency)

## Hyperammonemia

- Medical emergency
- Treatment:
  - Stop all feeds and discontinue all protein intake
  - Provide IV hydration with D10W

- Correct electrolyte disturbances
- Consult a metabolic specialist
- Promote an anabolic state with lipids
- IV arginine HCL, sodium benzoate, sodium phenylacetate
- Peritoneal or hemodialysis if above therapies are not effective
- Monitor for increased intracranial pressure

**alactosemia**

- Presentation: Progressive vomiting and lethargy, jaundice, encephalopathy, hepatomegaly
- Associated with E. coli sepsis
- Diagnosis: NBS, urine reducing substances
- Treatment: soy formula, galactose free diet

*able 1. Inborn Errors of Metabolism Associated With an **Acute Crisis***

| Diagnostic Clues | | |
|---|---|---|
| Primary | Secondary | Suggested Disorders |
| Acidosis | ± Hypoglycemia<br>± Lactic Acidosis<br>± Ketosis<br>± High ammonia<br>Increased Anion gap (AG) | Various Organic Acid Disorders |
| | Significant Lactic Acidosis<br>Normoglycemia | Mitochondrial disorders, Pyruvate dehydrogenase deficiency, Alpha-ketoglutarate dehydrogenase deficiency, Pyruvate carboxylase deficiency |
| | Sig. lactic acidosis<br>Hypoglycemia | Glycogen storage type I,<br>Fructose-1, 6-bisphosphatase deficiency |
| | Normal AG<br>Normal<br>lactate<br>No ketosis | Renal tubular acidosis |

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|---|---|---|
| Hyperammonemia | Alkalosis or normal pH<br>Normal lactate | Urea cycle disorders |
| | Reye-like illness (hypoglycemia, elevated LFTs, no ketones) | Fatty acid oxidation defects |
| | Acidosis<br>± Lactic acidosis<br>± Ketosis<br>± Hypoglycemia<br>Increased AG | Various organic acid disorders |
| Hypoglycemia | Acidosis<br>± Ketosis<br>± Lactic acidosis<br>± high ammonia<br>Increased AG | Various organic acid disorders |
| | Hepatomegaly<br>± Lactic acidosis | Glycogen storage disorders |
| | No acidosis or ketosis<br>No Lactic acidosis | Hyperinsulinemia<br>Fatty acid oxidation defects |
| | Hyponatremia<br>Hypotension | Adrenal insufficiency |
| | Signs of liver failure | Tyrosinemia<br>Glycogen storage disease type IV<br>Galactosemia<br>Niemann Pick type C |

*able 2. Characteristic of common Inborn Errors of Metabolism*

| Disorder | Fatty Acid Oxidation Disorders (MCAD, LCHAD, SCAD) | Amino-acidopathies (MSUD, PKU, tyrosinemia) | Organic Acidemias (pro-pionic acidemia, methylmalonic acidemia) | Urea Cycle Disorders (OTC deficiency) |
|---|---|---|---|---|
| Key Finding | Hypoketotic<br>Hypoglycemia | No acidosis, Nml ammonia, elevations in specific AAs | Metabolic acidosis + AG, hypogly, hyperammonemia | Hyperamonemia,<br>Resp alkalosis<br>No acidosis |

| Key Test | Acylcarnitine Profile | Plasma amino acids | Urine organic acids | Plasma amino acids |
|---|---|---|---|---|
| Supple-mental Tests | Carnitine Profile | Urine organic acids | Acylcarnitine profile | Urine organic acids |
| Signs/ Symptoms | Presents 6 mos-2 yr. VLCAD/LCHAD -rhabdomyolysis -cardiomyopathy -hypotonia, SIDS | MR, lethargy, coma, liver failure | Vomiting, lethargy, end organ dysfunction, be-gins with feeds | Lethargy, vomiting, coma |
| Acute Treatment | D10, early IVFs | Dextrose, special TPN, insulin | D10, early IVFs, no protein, +/- bicarbonate | D10, early IVFs, sodium benzoate, phenylacetate, arginine, insulin, dialysis |
| Chronic Treatment | Low fat diet, avoid prolonged fasts, nighttime feeds when sick, carnitine | Low protein diet, supplemental formula | Low protein diet, supplemental formula, carnitine, liver transplant | Low protein diet, supple- mental formula, phenyl acetate, arginine, liver transplant |

## References:


1. Gregory M. Rice, Robert D. Steiner. Inborn Errors of Metabolism (Metabolic Disorders). *Pediatrics in Review*. 2016;37;3.
2. Brodsky & Martin. Neonatology Review 3rd Ed. Vol 4. Inborn errors of metabolism. 2020

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|---|---|---|---|---|
| Key Finding | Hypoketotic Hypoglycemia | No acidosis or hyperam-monemia, elevations in specific amino acids | Metabolic acidosis with anion gap, hypoglycemia, hyperammonemia | Hyperam-monemia w/o acidosis, respiratory alkalosis |
| Key Test | Acylcarnitine Profile | Plasma amino acids | Urine organic acids | Plasma amino acids |
| Supple-mental Tests | Carnitine Profile | Urine organic acids | Acylcarnitine profile | Urine organic acids |
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*By taking care of a newborn we make a difference that lasts a lifetime!*

*–Neena Shah, MD*