Metabolic and Endocrine I and II

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Session Summary
This presentation provides a general overview of metabolic and endocrine function with common disorders to help the attendant prepare for NCC certification exams.

Session Objectives
Upon completion of this presentation, the participant will be able to:

- discuss abnormalities in calcium and magnesium homeostasis;
- recognize etiology, symptoms and treatment of glucose disorders;
- describe disorders of the thyroid and adrenal gland;
- recognize the pathophysiology, diagnosis and treatment of inborn errors of metabolism.

Test Questions

1. Symptoms of hypoglycemia do not include which of the following?
   a. Tachypnea
   b. Apnea
   c. Tachycardia
   d. Diarrhea

2. The Parathyroid hormone does which of the following;
   a. Mobilizes calcium and phosphorous from bone
   b. Increases urinary calcium excretion
   c. Inhibits calcium mobilization from bone
   d. Required for Vitamin D to work

3. Adrenal insufficiency in the VLBW infant can result in which of the following:
   a. Tachycardia
   b. Decreased urinary output
   c. Infection
   d. All of the above
4. Which of the following is true of hypothyroxinemia of prematurity?
   a. Should be treated at 3-4 weeks of age
   b. Is treated with PTU
   c. Is associated with a normal TSH value
   d. Only occurs in preterm infants

5. Which of the following are potential clues to the presence of an inborn error of metabolism?
   a. Respiratory distress at birth
   b. Coagulopathy
   c. Decreased urinary output
   d. Rapid progression of symptoms

References


Session Outline
See presentation handout on the following pages.
The brain requires a constant supply. Severe and/or persistent low levels can result in abnormal neurodevelopmental outcomes.

Glucose received completely from mom. Glucose crosses placenta. Insulin and glucagon do not cross. Fetal glucose levels are 80% of maternal glucose levels.
Postnatal Glucose Regulation

- Loss of maternal glucose stores
- Gluconeogenesis
  - Production of glucose from non-glucose sources
  - Delayed in VLBW infants for 2 hours
- Glycogen stores
  - Don’t begin until 27 weeks
  - Depleted by 3–12 hours
- Catecholamines and glucagon increase
- Insulin decreases

Hormonal Control

- Insulin
  - Changes permeability of the cell wall to enable glucose to enter cells
- Glucagon
  - Promotes glycogenolysis and gluconeogenesis
- Catecholamines
  - Increase glycogenolysis, gluconeogenesis, and glucagon secretion
  - Decreases the secretion of insulin

What is the Definition of Hypoglycemia?

- Nobody Seems to Have an Answer!
- May need to be individualized for each specific baby
  - Gestational age
  - Chronological age
  - Underlying pathology

Best Practice For Glucose Infusion

- Glucose infusion by 30 minutes
- Glucose nadir is 30–90 minutes

NEED IV ACCESS ASAP!!

Don’t Worry About the PIV, I’ll Slam that UAC in Within Minutes

Yeah Sure You Will.....

Definition of Hypoglycemia

- Nobody Seems to Have an Answer!
- “....one of the most confused and contentious issues in contemporary neonatology”
- Varies among institutions, clinicians and texts
Can You Give Me A Clue?

- The critical level where neurologic damage will occur
- Critical threshold may be individualized
  - Gestational age
  - Chronological age
  - Underlying pathology
- Commonly accepted values
  - 40–47mg/dL
- We’re working on it!

Risk Factors for Hypoglycemia

- Inadequate production or supply
  - Prematurity
  - Postmaturity
  - IUGR

Inadequate Production or Supply

- Delayed feeding or inadequate breastfeeding
  - Especially in the near term infant
- Asphyxia
  - Depletion of hepatic glycogen
  - Inefficient glucose use due to anaerobic metabolism
  - HIE + hypoglycemia——poorer prognosis

Inadequate Production or Supply

- Increased metabolic rate
  - Respiratory distress
  - Hyperthermia
  - Cold stress
  - Sepsis
  - Perinatal stress

Hyperinsulinemia

- Infant of a diabetic mother
- Islet cell dysplasia
- Pancreatic tumors
- Increased maternal glucose infusion

Beckwith Wiedemann Syndrome

- Macroglossia
- Abdominal wall defects
  - Omphalocele
  - Umbilical hernia
- Macrosomia
- Organomegaly including pancreas
- Severe unremitting hypoglycemia
Inborn errors of metabolism
- lactic acidosis
- glycogen storage diseases
- urea cycle disorders
- disorders of lipid metabolism

Iatrogenic causes
- Excess administration
- UAC placement

Endocrine deficiencies
- Panhypopituitarism
- Adrenal hemorrhage
- Hypothroidism

Hyperinsulinemia
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- Iatrogenic causes
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- Endocrine deficiencies
  - Panhypopituitarism
  - Adrenal hemorrhage
  - Hypothroidism

Symptoms of Hypoglycemia
- Apnea
- Irritability
- Lethargy
- Tachycardia and tachypnea
- Abnormal neurological examination
- Most symptoms are nonspecific
- Most infants are asymptomatic

Diagnosis of Hypoglycemia
- Intermittent acuchecks
- Undetected abnormalities common
- Abnormal levels may be at limits of accuracy
- Continuous glucose measurement systems

Treatment of Hypoglycemia
- Prevention is the key
- Identify and screen at risk infants
- Early feeding or glucose infusion
  - 2–3 ml/kg D10W
    - Severe hypoglycemia
    - Not corrected by feeding
  - Continuous dextrose may be required
    - 6–8mg/kg/min
    - Titrate as necessary
**Treatment of Hypoglycemia**

- Hydrocortisone
  - 5 to 15 mg/kg per day in 2-3 doses
  - Decreases peripheral glucose utilization
  - Increases blood glucose concentration
  - Systemic side effects common
  - Consider with glucose requirements > 15 mg/kg/min
- Diaoxide
  - Decreases insulin secretion
- Somatostatin
  - Inhibits insulin and growth hormone release
- Glucagon

**Prognosis of Hypoglycemia**

- Glucose is essential for cerebral metabolism
- Prognosis dependent on several factors
  - Duration
  - Frequency
  - Age
  - Presence and severity of symptoms
  - Presence of alternate sources
    - Ketones
    - Glycogen stores

**Infant Of Diabetic Mothers**

- Mother increasingly insulin resistant
- Can be gestational or chronic diabetes
- Glucose easily crosses placenta
- Insulin does not cross placenta
- Fetus increases insulin production
- Hypoglycemia occurs after delivery

**Clinical Manifestations**

- Macrosomia due to increased insulin levels
- Small for gestational age
- Round cherubic face
- Plethoric
- Hypertrichosis pinna
- Visceral enlargement

**Infant Of Diabetic Mothers**

- Macrosomia due to increased insulin levels
- Small for gestational age
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- Hypertrichosis pinna
- Visceral enlargement
Infant Of Diabetic Mothers

Clinical Manifestations
- Birth trauma
- Respiratory distress
- Hypoglycemia (50%)
- Hypocalcemia (30–50%)
- Hypomagnesemia (30–50%)
- Hyperbilirubinemia
- Feeding difficulties

Clinical Manifestations
- Congenital anomalies (3–4X the risk)
- Neural tube defects
- Congenital heart disease (VSD, TGV)
- Hypertrophic Cardiomyopathy
  - 30% affected

Hypertrophic Cardiomyopathy
- Enlarged left ventricle
- Aortic outflow obstruction
- Symptoms
  - Decreased perfusion
  - Hypotension
- Diagnosis – echo
- Treatment

Hypertrophic Cardiomyopathy

Caudal Regression Syndrome
- Abnormalities in lower extremities
- Scoliosis to “mermaid syndrome”
- Other anomalies common
  - Anal atresia
  - Menigomyelocele
  - GI abnormalities
  - GU abnormalities
Caudal Regression Syndrome

Small Left Colon Syndrome
- Constriction at the sigmoid and descending colon
- Symptoms of intestinal obstruction
- Diagnosis – contrast enema
- Treatment

Small Left Colon Syndrome

Hyperglycemia
- Transient phenomenon in the ELBW infant
- No clear definition
- 125–150? The level associated with complications?
  - Unsure when this occurs
  - May be individualized
- Failure of glucose autoregulation
  - Hepatic immaturity
  - Pancreatic immaturity

Etiology of Hyperglycemia
- Poorly understood
- Extreme prematurity
- Excessive glucose load
- Insulin resistance and deficiency
- Stress
  - Surgery, NEC, IVH
- Medications
  - Steroids
  - Vasoactive drugs, theophylline
- Sepsis

Clinical Manifestations of Hyperglycemia
- Usual onset prior to three days
- Glycosuria due to low renal threshold
- Osmotic diuresis
  - Tubular reabsorption
### Treatment of Hyperglycemia
- What a dilemma!
- Decrease glucose load
  - Need to maintain 6 mg/k/min
- Administer insulin
  - Used for chemstrips above 300
  - Subcutaneous
  - IV dose
  - IV infusion
- Monitor and minimize fluid losses

### Is Insulin Therapy Effective?
- Nurture study
  - 389 infants VLBW infants
  - Received standard care vs. extra glucose + insulin
  - Insulin group had higher glucose rates and growth
  - Insulin group had increased mortality and hypoglycemia
- Cochrane review (2009)
  - No evidence that treating hyperglycemia decreases mortality or morbidity

### Complications of Hyperglycemia
- Dehydration
- Neurologic injury
  - Due hyperosmolality effects on brain
- Increased mortality rate
- Less positive neurodevelopmental outcome
- Especially problematic if over 300 mg/dl
- Studies are all retrospective
- Hyperglycemia vs. illness severity

### Complications of Insulin
- Hypoglycemia
- Difficulty with insulin administration
  - Prime tubing
  - 100% bioavailability at 8 hours
  - Circuit changes likely to affect delivery

### Calcium Regulation
- Imperative in numerous physiologic processes
  - Maintenance of cell membrane permeability
  - Activation of enzyme reactions for muscle contraction
  - Nerve transmission
  - Blood clotting
  - Normal skeletal function and development

### Calcium Regulation
- Fetus completely dependent on placenta
- Postnatal relative hypocalcemia
  - Supply ceases at birth
  - Nadir at 24 hours
  - At 48 hours the PTH and Vitamin D increase and calcitonin decreases
  - Exaggerated in unstable infants
**Introduction of the Players**

- Parathyroid hormone (PTH)
  - Mobilizes calcium and phosphorous from bone
  - Decreases renal excretion
- 1.25 Dihydroxycholecalciferol (Vitamin D)
  - Required for PTH to work
  - Increases absorption of calcium and phosphorous from the gut
- Calcitonin
  - Inhibits calcium mobilization from bone
  - Increases calcium excretion

**Types of Calcium**

- Protein Bound (40%)
- Inactivated (10%)
- Free ionized calcium (50%)

**Factors Influencing Calcium Levels**

- Acidosis increases level
- Alkalosis decreases level
- Phosphorous inhibits absorption of calcium
- A normal magnesium level is mandatory
  - Required for PTH to function

**Hypocalcemia**

- Etiology and Risk Factors
  - Inadequate stores
    - VLBW infant (90%)
    - SGA
  - Placental insufficiency
  - Immature hormonal control
  - Asphyxia (35%)
  - IDM (50%)

**Symptoms of Hypocalcemia**

- Most often asymptomatic
- Hyperexcitability of the central and peripheral nervous system
  - Jittery
  - Increased sensory response
  - Seizures
- Neonatal tetany

**Diagnosis of Hypocalcemia**

- Diagnosis
  - Total calcium less than 7 mg/dL
  - Ionized calcium
    - Less than 3–4.4 mg/dL
    - Less than 0.75–1.1 mmol/L
**Symptomatic**
- 10% calcium gluconate over 20–30 minutes, given until symptoms subside
- Cutaneous necrosis
- Bradycardia
- Cardiac arrest

**Asymptomatic**
- To treat or not to treat: that is the question
- Oral elemental calcium
- IV Calcium infusion

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**Clinical Manifestations**
- Due to effect of the calcium on the CNS
- Hypotonia or irritability
- Poor feeding
- Constipation
- Seizures
- Polyuria and dehydration
- Renal stones
- Bradycardia and arrhythmias

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**Treatment of Hypercalcemia**
- Hydrate
- Promote excretion with lasix
- Decrease calcium and vitamin D intake
- Increase phosphorous intake

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**Magnesium**
- Assists in maintenance of normal muscle and nerve function
- Supports the immune system
- Important in bone formation
- Involved in energy metabolism and protein synthesis

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**Hypomagnesemia**
- Etiology
  - Low maternal level
  - Placental insufficiency
  - Prematurity and IUGR
  - Increased losses with renal or intestinal disorders
  - Hypoparathyroidism
Hypomagnesemia
- Symptoms
  - Tremors
  - Irritability
  - Hyperreflexia
  - Seizures
  - Hypocalcemia
- Treatment
  - Administer Magnesium (IV, PO)

Hypermagnesemia
- Etiology
  - Prenatal magnesium administration
  - Iatrogenic
- Presentation
  - Hypotonia
  - Respiratory depression
  - Poor feeding
  - Decreased GI motility
- Treatment
  - Just wait it out

Adrenal Insufficiency
- Adrenal Medulla
  - Secretes catecholamines (epi and norepi)
  - “Fight or Flight” response
- Adrenal Cortex
  - Glucocorticoids
  - Mineralcorticoids
  - Androgens

The Adrenal Gland
- Carotid
- Medulla

Adrenal Insufficiency
- Adrenal Medulla
  - Secretes catecholamines (epi and norepi)
  - “Fight or Flight” response

Glucocorticoids
- Cortisol
  - Regulates blood sugar
  - Important for growth
  - Maintains cardiovascular function
  - Released in times of stress to increase glucose, increase cardiac output and maintain vascular tone
**Mineralcorticoids**

- Aldosterone
  - Regulates fluid and electrolyte balance
  - Stimulates reabsorption of sodium and water in the distal collecting tubules
  - Inhibits secretion of potassium
  - Maintains blood pressure, intravascular volume, cardiac function and electrolytes

**Adrenal Insufficiency**

- A transient phenomenon in the ELBW infant
- Related to hypothalamic–pituitary–adrenal immaturity

**The Hypothalamic–Pituitary–Adrenal System**

The diagram shows the hypothalamus, anterior pituitary, and adrenal gland with corresponding hormones (ACTH, CRF) indicated.

**Clinical Manifestations**

- Glucose abnormalities
- Refractory hypotension
- Decreased cardiac output, acidosis and shock
- Decreased UOP
- Hyponatremia, hyperkalemia
- Tachycardia

**Diagnosis and Treatment**

**Diagnosis**
- Cortisol levels (15 mcg/dl)
- Abnormally low and do not increase with stress

**Treatment**
- Hydrocortisone therapy
  - How much?
  - How long?
- Should we give stress doses?
- Short and long term complications
Complications of Adrenal Insufficiency

- Recovery by 14 days
- Association with BPD

Thyroid Disorders

Thyroid Physiology

- Thyroid hormones affect nearly every tissue and organ system
- Essential for normal skeletal growth
- Essential for normal maturation of the CNS
- Control of basal metabolic rate
- Calcium regulation
- Regulation of temperature

Thyroid Physiology

- Secrete two hormones
  - Classified according to number of iodine atoms
    - Thyroxine (T4)
    - Triiodothyronine (T3)
  - More potent
  - Much of T4 is converted to T3
  - 99% are bound to proteins
  - 1% is free and able to produce effects
- Thyroid stimulating hormone (TSH)
  - Secreted from anterior pituitary and stimulates thyroid gland to secrete thyroid hormones

Hypothalamic Pituitary–Thyroid Axis

Congenital Hypothyroidism

- Most preventable cause of severe mental retardation
- Most common endocrine disorder
- 1 in 3 - 4,000 live births
Congenital Hypothyroidism

- **Etiology**
  - Maternal iodine deficiency
  - Dysgenic or absent thyroid gland
  - Deficient synthesis of thyroid hormones
  - Maldevelopment or absence of the anterior pituitary gland

**Clinical Manifestations**

- Often asymptomatic at birth
- Symptoms are often subtle and nonspecific
- May be associated with chromosomal defects
- Post dates/LGA
- Defective skeletal maturation and growth
- Hypotonia
- Large tongue

**Clinical manifestations**

- Umbilical hernia
- Temperature instability
- Poor feeding

**Diagnosis**

- State screen
- Low T4 and high TSH
- Free T4

**Thyroid Hormone Values**

<table>
<thead>
<tr>
<th>Test</th>
<th>Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>&lt; 7 mU/liter</td>
</tr>
<tr>
<td>T4</td>
<td>6.4-23.2 μg/dl</td>
</tr>
<tr>
<td></td>
<td>82.4-298.6 nmol/liter</td>
</tr>
<tr>
<td>Free T4</td>
<td>2.6-6.3 mg/dl</td>
</tr>
<tr>
<td></td>
<td>33.5-81.3 nmol/liter</td>
</tr>
<tr>
<td>T3</td>
<td>100-740 mg/dl</td>
</tr>
<tr>
<td></td>
<td>1.5-11.4 nmol/liter</td>
</tr>
</tbody>
</table>

**Treatment**

- Consult endocrine
- L-Thyroxine (a synthetic T4)
- Monitor levels
- Irreversible mental retardation if not treated
- Developmental follow up

**Diagnosis and Treatment**
**Congenital Hypothyroidism**

- A transient phenomena due to immaturity
- T4 levels increase with advancing gestation
- Occurs in 50% of infants < 30 weeks
- Severity dependant on gestational age

**Hypothyroxinemia of Prematurity**

- T4 – Low
- TSH – Normal
- Free T4 may be low or normal
- Persists for 4–8 weeks

**Hyperthyroidism (Neonatal Thyrotoxicosis)**

- Thyroid gland secretes excessive thyroid hormone
- Due to maternal Graves disease
  - Thyroid-stimulating hormones activate TSH and increase thyroid hormone production
- Transplacental transfer of thyroid stimulating immunoglobulins
- May be transient or prolonged
- Considered a medical emergency

**Hypothyroxinemia of Prematurity**

- No proven benefit with treatment
  - Possible decrease in mortality and improved developmental outcome
- AAP recommends treatment at 6 weeks
- Low T4 levels have been associated with increased mortality and morbidity

**Hyperthyroidism (Neonatal Thyrotoxicosis)**

- Clinical manifestation
  - IUGR
  - Irritability
  - Tachycardia and tachypynea
  - Cardiac failure
  - Hypertension
  - Vomiting and diarrhea
  - Failure to thrive
  - Goiter
Diagnosis and Treatment

- Diagnosis
  - High T4
  - Low TSH
- Treatment
  - Chronic treatment – Lugol’s solution
  - Acute treatment – PTU (propylthiouracil)

Osteopenia of Prematurity

- Bone thinning and under-mineralization
- 16–55% of infants < 1000 grams
- Peak is 2–3 months of age
**Etiology of Osteopenia of Prematurity**

- Prematurity of course!
  - 80% of bone mineralization occurs during the third trimester
  - Calcium and phosphorous are maximally acquired
  - Intrauterine mineral accretion > extraterine
  - Inadequate postnatal bone mineralization

- Almost impossible to meet demands
  - Inadequate calcium, phosphorous and vitamin D intake
  - Prolonged TPN use
  - Feeding intolerance

**Lasix**
- Increases renal calcium loss
- Stimulates calcium reabsorption from bone

**Aminophylline**
- Increases urinary calcium excretion

**Phenobarbital and dilantin**
- Enhance vitamin D metabolism

**Steroids**
- Inhibits bone growth and longitudinal growth

**Immobility**
- Fetus undergoes continual mechanical stimuli
- Stresses fetal bones
- Stimulates bone formation and growth
- Immobilized in incubators
- Minimal physical stimulation
- Results in bone reabsorption and demineralization

**What is Needed to Make Bones?**

- Vitamin D
  - 1,25 dihydroxyvitamin D
  - Stimulates absorption of calcium and phosphorous from the intestines

- Phosphorous
  - Stimulates bone formation
  - Inhibit reabsorption of bone

- Calcium

**Clinical Manifestations of Osteopenia of Prematurity**

- Normal calcium levels
- Normal to low phosphorous
  - < 3.5 mg/dL
- Increased alkaline phosphatase ( > 499)
- Increased alkaline phosphatase ( > 499)
  - A glycoprotein
  - Derived from various tissues
  - Bone, liver, kidney, intestines
  - Concurrent cholestasis also elevates level
  - Elevation precedes radiographic changes
  - > 700 IU/L at 3 weeks predictive of osteopenia
Clinical Manifestations

- Cupping and fraying of the metaphysis
- Decreased bone density
  - Apparent with 20% reduction in mineralization
  - Reliance on x-ray delays diagnosis
- Fractures of the long bones and ribs

Osteopenia of Prematurity

Cupping and Fraying of the Metaphysis

Fractures of the long bones and ribs

Osteopenia of Prematurity

Fracture of the Femur

Fracture of the Rib
Treatment of Osteopenia of Prematurity

- PREVENTION, PREVENTION, PREVENTION!
  - Adequate amounts of calcium and phosphorous
  - Adequate kcal and protein
  - 400 IU of vitamin D
  - Fortify breastmilk/use premature formulas
- Passive ROM

Prognosis of Osteopenia of Prematurity

- Self-resolving
- Increased incidence of BPD
- Decreased linear growth

Inborn Errors of Metabolism

- An autosomal recessive genetic defect
- Due to the absence of an enzyme, cofactor, or transport protein which either degrades or converts one substance into another
- This absence results in either a toxic accumulation of the substrate or the deficiency itself can be toxic

Inborn Errors of Metabolism

![Enzyme Diagram]

Enzyme → Precursor → Substrate

Inborn Errors of Metabolism

Enzyme

↑ Precursor ← Substrate ↓
Inborn Errors of Metabolism

"The unexpected and mysterious deterioration of a child after a normal initial period is the most important signal of the presence of an inborn error"

Saudubray, 1997

Clues to Suggest the Presence of an Inborn Error of Metabolism

- Normal at birth
- Acute onset
- Rapid progression
- Unusual severity and intractability
- Failure of other treatments
- Family history

Clinical Presentation

- Prolonged and unexplained jaundice
- Seizures
- GI disturbances – vomiting, poor feeding
- Failure to thrive
- Disturbed acid/base status
- Hypoglycemia
- Reducing substances in the urine
- Neurologic deterioration
- Cardiac disorders – cardiomyopathy and arrhythmias
- Acute liver disease

Diagnosis

- The most important aspect of diagnosis and treatment is just thinking about it
- CBC and diff
- Electrolytes
- Arterial blood gas
- Ammonia level
- Lactate
- Urine for reducing substances
- Plasma amino acids
- Urine organic acids
- Enzyme analysis and molecular testing of blood, urine, and skin

Diagnosis

- Initial stabilization
  - Aggressive fluid and electrolyte therapy
  - Withhold all protein feeds
  - Optimize nutrition
  - Consult genetics
  - Dialysis
  - Exchange transfusion
  - Chronic therapy

Treatment
**Categories of Inborn Errors of Metabolism**

- Inborn errors of amino acid metabolism
- Inborn errors of organic acid metabolism
- Disorders of CHO metabolism
- Disorders of fatty acid oxidation
- Disorders of hyperammonemia

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**Disorders of Amino Acid Metabolism**

1. Phenylketonuria (PKU)
2. Maple syrup urine disease

**Phenylketonuria (PKU)**

- Deficiency of Phenylalanine hydroxylase
- Incidence is 1:12000
- Converts phenylalanine to tyrosine
- Excess phenylalanine is toxic to CNS
- Tyrosine deficiency

**Early Symptoms of PKU**

- Vomiting and poor feeding
- Irritability
- Musty smelling urine
- Eczema
Late Symptoms of PKU
- Profound mental retardation
- Unusually fair skin, hair, and eyes
- Musty body odor
- Hyperactivity
- Seizures
- Aggressive behavior

Diagnosis and Treatment
- Diagnosis
  - Neonatal screening
  - Serum phenylalanine level > 25 mg/dL
- Treatment
  - If treatment doesn’t begin prior to 3–4 months, permanent deficits
  - Limit intake of phenylalanine
    - Lofenlac

Maple Syrup Urine Disease (MSUD)
- Deficiency of the enzyme which breaks down leucine, isoleucine, and valine
- Toxic accumulation occurs
- 1:180,000

Maple Syrup Urine Disease
- Symptoms
  - Severe neurologic symptoms
  - Vomiting
  - Metabolic acidosis
  - Urine smells like maple syrup
- Diagnosis
  - Increased levels of leucine on urine amino acids
- Treatment
  - Severely restrict amino acids
- Prognosis

Categories of Inborn Errors of Metabolism
- Inborn errors of amino acid metabolism
- Inborn errors of organic acid metabolism
- Disorders of CHO metabolism
- Disorders of fatty acid oxidation
- Disorders of hyperammonemia

Disorders of Organic Acid Metabolism
- Organic acids are intermediate breakdown products of amino acids
- Deficiency of an enzyme which breaks down specific organic acids
- Examples include propionic acidemia and methylmalonic acidemia
Disorders of Organic Acid Metabolism

- Symptoms
  - Metabolic acidosis
  - Feeding difficulties
  - CNS deterioration
  - Hypoglycemia
  - Hyperammonemia
- Hallmark is an elevated anion gap
- Treatment – protein restriction
- Prognosis

Categories of Inborn Errors of Metabolism

- Inborn errors of amino acid metabolism
- Inborn errors of organic acid metabolism
- Disorders of CHO metabolism
- Disorders of fatty acid oxidation
- Disorders of hyperammonemia

Galactosemia

- A disorder of carbohydrate metabolism
- Lack of the enzyme necessary for the breakdown of galactose to glucose
- Increased levels of galactose are toxic
  - 1:155,000
- Symptoms
  - Poor weight gain
  - Vomiting/diarrhea
  - Lethargy
  - Jaundice
  - Hypoglycemia
  - Reducing substances in the urine
  - Increased susceptibility to infections
  - Cataracts
  - Cirrhosis of the liver
- Diagnosis
  - Newborn screening
  - Increased serum galactose
  - Measurement of enzyme activity
- Treatment
  - Withhold all lactose containing feeds
- Prognosis
  - Untreated leads to irreversible brain damage, cataracts and cirrhosis
  - Even treated patients frequently have complications
Categories of Inborn Errors of Metabolism

- Inborn errors of amino acid metabolism
- Inborn errors of organic acid metabolism
- Disorders of CHO metabolism
- Disorders of fatty acid oxidation
- Disorders of hyperammonemia

Disorders of Fatty Acid Oxidation (FAO)

- The most common type of inborn error
- Fatty acids are oxidized to produce energy during periods of fasting
- Instead of a drop in blood sugar you have a life-threatening situation

Disorders of Fatty Acid Oxidation

- Symptoms
  - Severe hypoglycemia
  - Unexplained neonatal death
- Diagnosis
  - Not usually on state screen
  - Hypoglycemia
  - Metabolic acidosis
  - Organic aciduria

Disorders of Fatty Acid Oxidation

- Medium-Chain Acyl-CoA Dehydrogenase Deficiency (MCADD)
  - Autosomal recessive
  - Inability to break down medium chain fatty acids

Disorders of Fatty Acid Oxidation

- Treatment
  - Avoid even brief periods of fasting
  - Frequent small meals
  - Constant glucose infusion if fasting

Categories of Inborn Errors of Metabolism

- Inborn errors of amino acid metabolism
- Inborn errors of organic acid metabolism
- Disorders of CHO metabolism
- Disorders of fatty acid oxidation
- Disorders of hyperammonemia
Disorders of Hyperammonemia

- A defect in one of the pathways of the urea cycle
- The urea cycle is responsible for the breakdown of amino acids and the detoxification of ammonia

Symptoms
- Poor feeding and emesis
- Progressive CNS deterioration
- Greatly elevated ammonia levels

Treatment
- Stop all protein intake
- Dialysis
- Diet modification

Prognosis

Cystic Fibrosis

- A disorder which causes dysfunction of the exocrine gland
- 1 in 3500 white infants
- Autosomal recessive

Clinical Manifestations

- The mucus produced by these organs is viscous and thick
- The glands and ducts become plugged
- Results in damage and dysfunction
- Infection is common
### Clinical Manifestations
- Failure to thrive
- Bulky/fatty stools
- Recurrent intestinal blockage
- Prolonged jaundice
- Early respiratory infections
- Salty taste

### Meconium Ilius
- Neonates are usually asymptomatic
- 10–20% present with a meconium ilius
  - Thick viscous mucous block intestines
  - Results in intestinal obstruction

### Diagnosis
- Newborn screening available in some states
  - Early diagnosis improves nutritional status, growth and decreases infections
  - Possible improved pulmonary status
  - Increased trust in the health care system

### Treatment and Complications
- Treatment
  - Optimal nutrition
  - Pancreatic enzymes
  - CPT
  - Prompt treatment of infections
  - Salt supplementation

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**Sweat test**
- Gold standard
- Performed after 1 week in term infants
- DNA testing
Treatment and Complications

- Recurrent pneumonia
- Malabsorption and malnutrition
- Anemia from vitamin E deficiency
- Protein and calorie malnutrition
- Mineral and fat malnutrition
- Severe dehydration

Glucose–6–Phosphate–Dehydrogenase Deficiency (G6PD)

- G6PD is an enzyme which causes the conversion of glucose 6 phosphate to glutathione
- Glutathione protects the RBC from oxidative substances
- Most common enzyme deficiency
- Affects 400,000,000 people worldwide

G6PD Deficiency

- RBC are damaged with exposure to oxidative substances
  - Certain medication
  - Infection – oxidizing agents
- Results in hemolytic anemia and subsequent hyperbilirubinemia

G6PD Deficiency

- Diagnosis
  - G6PD levels
  - Hematocrit
  - Reticulocyte count
  - Bilirubin level

G6PD Deficiency

- Treatment
  - Phototherapy
  - Blood transfusion
  - Vitamin E
  - Life long process
  - Mild or severe hemolytic anemia
  - Avoid triggering agents