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 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;
- explore 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 does not result in which of the following:
   a. Tachycardia
   b. Decreased urinary output
   c. Hypernatremia
   d. Hyperkalemia
4. Which of the following is true of hypothyroxinemia of prematurity?
   a. Is associated with a high TSH value
   b. Is treated with PTU
   c. Is associated with a normal TSH value
   d. Longer duration in less mature 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
The brain requires a constant supply of glucose. 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.
**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 – major form of stored glucose
  - Don’t begin until 27 weeks
  - Depleted by 3–12 hours
- Catecholamines and glucagon increase
- Insulin decreases

**Hormonal Control**

- Insulin
  - Changes cell wall permeability so glucose can enter
- Glucagon
  - Promotes glycogenolysis and gluconeogenesis
- Catecholamines
  - Increases glycogenolysis, gluconeogenesis, and glucagon secretion
  - Decreases secretion of insulin
  - Increases ketone level
  - Alternate source of fuel

**Best Practice For Glucose Infusion**

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

**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 level where neurologic damage occurs
- Critical threshold may be individualized
  - Gestational age
  - Chronological age
  - Underlying pathology
- Commonly accepted values
  - 40–47mg/dL
- Little correlation between level, symptoms and outcome

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

Yeah Sure You Will.....
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
- IUGR
- 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
Beckwith Wiedemann Syndrome

Hyperinsulinemia
- Inborn errors of metabolism
- Iatrogenic causes
  - Excess administration
  - UAC placement
- Endocrine deficiencies
  - Panhypopituitarism
  - Adrenal hemorrhage
  - Hypothyroidism

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 are 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

- Hydrocortisone
  - 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
  - Releases hepatic glycogen stores
  - Stimulates gluconeogenesis, ketogenesis and lipolysis
**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

- Not well defined
- Confusing due to underlying pathophysiology
- Neurological impairment is possible
  - Developmental delay
  - Seizures
  - Microcephaly
  - Attention deficit disorder
- Careful screening and treatment is imperative

**Infant Of Diabetic Mothers**

- Insulin resistance increases throughout gestation
- Can be gestational or chronic diabetes
- Glucose easily crosses placenta
- Insulin does not cross placenta
- Fetus increases insulin production
- Hypoglycemia occurs after delivery

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

**Clinical Manifestations**

- Hypoglycemia occurs after delivery
  - Macrosomia due to increased insulin levels
  - Small for gestational age
  - Round cherubic face
  - Plethoric
  - Hypertrichosis pinna
  - Visceral enlargement
Clinical Manifestations

- Birth trauma
- Respiratory distress
- Hypoglycemia (50%)
- Hypocalcemia (30–50%)
- Hypomagnesium (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

Caudal Regression Syndrome

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

Hypertrophic Cardiomyopathy

Normal heart
Hypertrophic cardiomyopathy

Caudal Regression Syndrome

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

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
- 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 to hyperosmolarity 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
  - 48 hours
    - PTH and Vitamin D increase
    - 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 GI absorption of calcium and phosphorous
- 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

Treatment of Hypocalcemia

- 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
**Etiology**
- Usually iatrogenic
- Hyperparathyroidism
- Decreased phosphorous
- Familial infantile hypercalcemia

**Diagnosis**
- Total calcium over 11 mg/dL
- Ionized calcium over 5.8 mg/dL

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

**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

The Adrenal Gland

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

Glucocorticoids

- Cortisol
  - Regulates blood sugar
  - Important for growth
  - Maintains cardiovascular function
  - Released in times of stress
    - Increases glucose
    - Increase cardiac output
    - 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

Clinical Manifestations

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

Diagnosis and Treatment

- Diagnosis
  - Cortisol levels (15mcg/dl)
  - Abnormally low and does not increase with stress
- Treatment
  - Hydrocortisone therapy
  - How much?
  - How long?
  - Should we give stress doses?
  - Short and long term complications

Thyroid Disorders
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

- Secretes 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
  - Stimulates secretion of 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

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 often subtle and nonspecific
- May be associated with chromosomal defects
- Post dates/LGA
- Defective skeletal maturation and growth
- Hypotonia
- Large tongue
**Congenital Hypothyroidism**

- Clinical manifestations
  - Umbilical hernia
  - Temperature instability
  - Poor feeding

**Thyroid Hormone Values**

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

**Diagnosis**

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

**Hypothyroxinemia of Prematurity**

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

**Treatment**

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

**Conclusion**

- Irreversible mental retardation if not treated
- Developmental follow up
Hypothyroxinemia of Prematurity

- T4 – Low
- TSH – Normal
- Free T4 – Low
- Nadir at 7-10 days
- Persists for 4-8 weeks

No proven benefit with treatment
- Possible decrease in mortality and improved developmental outcome
- AAP recommends treatment at 6 weeks
- Low T4 levels independently associated with cognitive delay

Hyperthyroidism (Neonatal Thyrotoxicosis)

- Thyroid gland secretes excessive thyroid hormone
- Due to maternal Graves disease
  - Transplacental transfer of thyroid stimulating immunoglobulins
  - Activates TSH
- May be transient or prolonged
- Onset during first week
- Considered a medical emergency

Clinical manifestation
- IUGR
- Irritability
- Tachycardia and tachypnea
- Cardiac failure
- Hyperthermia
- Vomiting and diarrhea
- Failure to thrive
- Goiter

Goiter

Neonatal Goiter
Diagnosis and Treatment

- **Diagnosis**
  - High T4 and T3
  - Low TSH

- **Treatment**
  - Chronic treatment – Lugol’s solution
  - Acute treatment – PTU (propylthiouracil)

Hyperthyroidism (Neonatal Thyrotoxicosis)

We Need a Break Here

Osteopenia of Prematurity

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

Etiology

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

Etiology

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

- 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 intestinal absorption of calcium and phosphorous
- Phosphorous
  - Stimulates bone formation
  - Inhibit reabsorption of bone
- Calcium

Clinical Manifestations

- High or normal calcium levels
- Normal to low phosphorous
  - < 3.5 mg/dL
- 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 xray delays diagnosis
  - Lag time of 2-6 weeks
- Fractures of the long bones and ribs

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

Self-resolving

Increased incidence of BPD

Decreased linear growth
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

Precursor ↔ Substrate

"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
- Electrolytes
  - Anion gap
    - Anion Gap = Sodium – (Chloride + Bicarbonate)
    - 3-11 mEq/L
- Arterial blood gas
- Ammonia level
- Lactate
- Urine for reducing substances

The most important aspect of diagnosis and treatment is just thinking about it

Diagnosis
- Plasma amino acids
- Urine organic acids
- More specific testing
  - Enzyme analysis
  - Molecular testing of blood, urine, and skin

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

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 hyperammonemia
Disorders of Amino Acid Metabolism

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

Phenylketonuria (PKU)
- Deficiency of Phenylalanine hydroxylase
- Incidence is 1:12,000
- 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
- Branched-chain amino acids
- Toxic accumulation occurs
- 1:180,000

Symptoms
- Urine smells like maple syrup (12 hours)
- Vomiting and irritability (2–3d)
- Metabolic acidosis (2–3d)
- Severe neurologic symptoms (4–5d)
- Coma (7–10 d)

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
  - Intermediate breakdown products of amino acids
  - Deficiency of an enzyme which breaks down specific organic acids
  - Incidence 1:50–100,000
  - Examples
    - Propionic academia
    - Methylmatonic acidemia

Symptoms
- Metabolic acidosis with an elevated anion gap
- Feeding difficulties
- CNS deterioration
- Hypoglycemia
- Hyperammonemia

Diagnosis
- State screen
- Urine organic acids

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

**Galactosemia**
- Diagnosis
  - Newborn screening
  - Increased serum galactose
  - Measurement of enzyme activity
- Treatment
  - Withhold all lactose containing feeds
- Prognosis
  - Untreated
    - Irreversible brain damage
    - Cataracts
    - Cirrhosis
  - Complications even in treated patients

**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)**
- 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
  - Generally presents between 3 and 24 months
  - May present days after birth

Disorders of Fatty Acid Oxidation

- Presentation
  - Sudden and unexplained death
  - Metabolic crisis
- Treatment
  - Avoid even brief periods of fasting
  - Frequent small meals
  - Constant glucose infusion if fasting
- Prognosis
  - Excellent if diagnosed

Disorders of Fatty Acid Oxidation

- 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 a urea cycle pathway
- Urea cycle responsibilities
  - Metabolism of waste nitrogen
  - Detoxification of ammonia
Disorders of Hyperammonemia

- Symptoms
  - Normal at birth
  - Poor feeding and emesis
  - Progressive CNS deterioration
  - Greatly elevated ammonia levels
- Treatment
  - Stop all protein intake
  - Dialysis
  - Diet modification
- Prognosis

Cystic Fibrosis

- Disorder causing dysfunction of exocrine glands
  - 1 in 3500 white infants
  - Autosomal recessive

Cystic Fibrosis

- Affects any organ which secretes mucus
  - Lungs
  - Pancreas
  - Intestines
  - Biliary tract
  - GU tract

Clinical Manifestations

- Mucus produced by these organs is viscous and thick
- 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
Clinical Manifestations

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

Meconium Ilius

Diagnosis

- Newborn screening available in some states
- Early diagnosis
  - Improves nutritional status and growth
  - Decreases infections
  - Possible improved pulmonary status
  - Increased trust in the health care system

Diagnosis

- Sweat test
  - Gold standard
  - Performed after 1 week in term infants
- DNA testing

Treatment

- Optimal nutrition
- Pancreatic enzymes
- CPT
- Prompt treatment of infections
- Salt supplementation

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)
- X–linked
- G6PD
  - Reduces NADP to NADPH. NADPH protects RBCs
  - Glutathione protects the RBC from oxidation
- Most common enzyme deficiency
- Affects 400,000,000 people world wide
- At risk: African, Middle East and Asian descent

G6PD Deficiency
- RBC are damaged by oxidative substances
  - Certain medication
  - Infection – oxidizing agents
- Hemolytic anemia
- Subsequent hyperbilirubinemia
  - Early and later–onset
  - Persistent
  - Unusual severity
- Prognosis
  - Risk of kernicterus
  - Risk of readmission

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