

# NICU Certification Review

## HIGH – RISK MOMS AND HIGH – RISK BABIES

### Antepartum Conditions

- Pregnancy-Induced Hypertension
  - Incidence: 6-17% in primigravida women and 2-4% in multiparous women.
  - Etiology: unknown.
  - Predisposing factors: primip, < 18 and > 35 years of age, family history, low SES, malnutrition, obesity, diabetes, chronic hypertensive, renal disease, multiple gestation
  - Clinical Presentation:
    - BP > 140/90 after 20 weeks gestation. Severe is 160/110 and above.
    - Sudden/excessive weight gain. 33% do not have edema
    - Proteinuria
    - Other: headache, hyperreflexia with clonus, visual and retinal changes, irritability, nausea and vomiting, epigastric pain, dyspnea, and oliguria.
- Complications
  - Maternal: eclampsia, pulmonary edema, cardiopulmonary failure, stroke, DIC, HELLP syndrome, hepatic failure, renal cortical necrosis, retinal detachment
  - Fetal/Neonatal: premature placental aging, placental infarction, decreased amniotic fluid, abruptio, IUGR, fetal hypoxia and neurological injury, prematurity
  - Maternal Management
    - Seizure precautions
    - Prevention of complications
    - Birth of a live infant
      - Deliver the baby if severe preeclampsia presents after 34 weeks' gestation
    - Placental/fetal tests of wellbeing:
    - Medications:
      - Magnesium sulfate: CNS depressant to prevent seizures.
      - Antihypertensives:
      - Corticosteroids: increase lung maturity
      - Delivery: induction vs cesarean section
  - Neonatal Management
    - IUGR
    - Perinatal distress
    - Degree of prematurity
    - Hypermagnesemia: weakness, lethargic, hypotonic, flaccid, poor suck
  - Labetalol: hypotension, bradycardia, hypoglycemia

### Diabetes Mellitus:

- Incidence: 3% – 5% of pregnancies; 3-9% complicated by Gestational DM

- Etiology: 2<sup>nd</sup> half of pregnancy, pancreas can not meet increased need for insulin → hyperglycemia
- Predisposing factors: family history, > 25 years of age, ethnic groups with ↑ risk of diabetes (Hispanic, African American, Native North American, Pacific Islanders, South or East Asian), previous LGA who had congenital anomaly with hydramnios or was Stillborn
- Clinical Presentation
  - Controversy regarding abnormal blood values and fetal outcome
  - Prognostically “bad” signs: diabetic ketoacidosis (2<sup>nd</sup> trimester), PIH, pyelonephritis and maternal noncompliance
- Maternal Complications: progression of nephropathy, vasculopathy and retinopathy in existing diabetes
- Fetal/Neonatal Complications:
  - Macrosomia: > 4000 g.
    - Traumatic delivery
  - IUGR
  - RDS
  - Hypoglycemia, hypocalcemia, hypomagnesemia
  - Polycythemia, hyperviscosity, hyperbilirubinemia
  - Cardiomyopathy
  - Congenital malformations: 3-fold increase in incidence of congenital anomalies can be reduced significantly by preconception control of blood glucose levels.
- Neonatal Management
  - Assess for growth and gestational age
  - Respiratory Distress Syndrome
  - Hypoglycemia, hypocalcemia, hypomagnesemia
  - Polycythemia and hyperviscosity
    - Decreased blood flow, RBC hemolysis, thrombosis
  - Congenital malformations
  - Birth injuries
    - Fractured clavicle, brachial palsy, facial nerve paralysis, intracranial bleeding, skull fractures

## **INTRAPARTUM COMPLICATIONS**

### Preterm Labor

- Occurs >20 and < 37 completed weeks gestation
- Incidence: 11.7% of live births in the United States were preterm
- Etiology: unknown.
  - 70% associated with spontaneous premature rupture of membranes
- Predisposing Factors:
  - Age < 15 or > 35
  - Low Socioeconomic status
  - Inadequate prenatal care

- Maternal/Obstetrical history: preterm labor/birth, uterine anomalies, incompetent cervix, abruptio
- Lifestyle: substance abuse/use, stress at work and home
- Fetal factors: IUGR, congenital anomalies, death, multifetal gestation
- Clinical Presentation:
  - Uterine contractions
  - Low, dull, intermittent, constant backache
  - Intermittent pelvic pressure
  - Abdominal cramping, diarrhea
  - Increased vaginal discharge
  - Spontaneous premature rupture of membranes
- Complications:
  - Maternal: emotional distress
  - Neonatal:
    - Preterm birth—increase morbidity/mortality
    - Adverse reactions to tocolytics
      - Ritodrine and Terbutaline: tachycardia, hypoglycemia, pulmonary edema, hypotension, IVH
      - Magnesium sulphate: weakness, lethargy, hypotonia, flaccidity, poor suck
      - Indomethacin: pulmonary hypertension
      - Procardia: no effect on fetus/neonate

#### Abruptio Placenta

- Sudden, premature separation of placenta in varying degrees during pregnancy/labor. Is the most common cause of bleeding in 2<sup>nd</sup> half of pregnancy
- Incidence: 1% of deliveries
- Etiology: unknown
  - high association with hypertensive disorders
- Predisposing factors: uterine anomalies, polyhydramnios, multifetal pregnancy, trauma
- Presentation and Complications
  - Maternal: labor, cramping, dark or bright red vaginal bleeding ranging from spotting to frank hemorrhage
    - 20 - 30%: no evidence of bleeding
  - Fetus: signs of distress: decreased variability, tachycardia, bradycardia, loss of heart tones/movement
  - Neonatal Complications: perinatal distress, anemia, hypovolemia, cerebral palsy, risk of death
  - Neonatal Management: resuscitation as needed

#### Placenta Previa

- Placenta implanted in lower part of uterus near the cervix (marginal) or in varying degrees (partial or total) over the cervix
- Incidence: 0.5% of births
- Etiology: unknown.
- Presentation, Findings and Management:

- Similar to abruptio
- Treatment and Delivery Decisions:
  - based on bleeding, gestational age, condition and presentation of fetus
- Rh-negative woman: Kleihauer-Betke test and RhoGAM

### Shoulder Dystocia

- Delivery of the fetal head with an impaction of the fetal shoulder girdle or trunk against the pubic symphysis, making delivery impossible or difficult
- Incidence: .2% - 3% low risk population to 20% in high-risk groups
- Predisposing factors: maternal obesity, fetal macrosomia, diabetes mellitus
  - 50 - 60% have fetal weight < 4,000g
- Clinical Presentation:
  - Second stage > 2 hours with slow descent or no descent of head
  - After delivery of the head, the head recoils against the perineum → “turtling”
  - Complications:
    - Maternal: uterine rupture, perineal lacerations/tears, hemorrhage
    - Neonatal: birth injuries, perinatal depression, HIE, death

### Breech Delivery

- Incidence dependent upon gestational age
- Predisposing factors:
  - Maternal: polyhydramnios/oligohydramnios, Uterine anomalies, contracted pelvis
  - Fetal/placenta: multifetal gestation, IUGR, CNS anomalies, short cord, fetal death
- Clinical Presentation: fetal heart sounds above umbilicus, mom feels kicking in lower abdomen; vaginal exam → feel genitalia instead of suture lines
- Neonatal Complications:
  - Prolapsed cord
  - Perinatal depression
  - Aspiration of amniotic fluid
  - CNS injuries
    - IVH, injured spinal cord if head hyperextended
  - Assess: edematous genitalia, continuation of frank breech position

### Obstetrical Analgesia

- Stadal and Nubain most common
- IV or IM route
- Potential complications:
  - Maternal: respiratory depression, N & V, orthostatic hypotension
  - Neonatal: respiratory depression, respiratory acidosis, thermoregulatory concerns
- Neonatal Management
  - Have Narcan, oxygen, and ventilatory equipment available and ready in DR
  - Evaluate for respiratory depression
  - Ask OB nurse re use of analgesia
  - In the nursery, observe for side effects: hypothermia, increased work of breathing

### Obstetrical Anesthesia

- General:
  - Emergent Cesarean sections
  - Complicated vaginal deliveries
- Regional:
  - Continuous lumbar epidural, spinal and pudendal block
- Local:
  - Perineal infiltration for episiotomy, birth, perineal repair
- Complications:
  - General:
    - Mom: vomiting and aspiration; cardiopulmonary effects
    - Decreased fetal cardiac variability and movements
    - Neonatal respiratory depression/hypotonicity
  - Regional
    - Mom: Toxic reaction from overdose
    - Fetal compromise with prolonged maternal hypotension

### Cesarean Delivery

- Incidence: 32.8% in 2010.
  - The primary cesarean section rate was 23.6%
  - Vaginal birth after cesarean section (VBAC) rate was 9.2%
- Indications:
  - Maternal: CPD, previous classic Cesarean; PIH, cardiac disease, diabetes, active herpes
  - Placental: abruptio placentae, placenta previa, placental insufficiency
  - Fetal: distress, malpresentation, multifetal gestation, preterm delivery
    - Congenital anomalies: myelomeningocele; anterior abdominal wall defects
- Complications for neonate:
  - Iatrogenic preterm birth
  - RDS; PPHN
- Treatment for neonate: Resuscitation as needed

## **TRANSITION TO EXTRAUTERINE LIFE**

### Pneumocytes

- Type I:
  - Squamous cell
  - ~ 95% of alveolar surface
  - Cytoplasmic extensions—optimal for rapid gas exchange
- Type II:
  - Granular pneumocyte, cuboidal
  - ~ 5% of alveolar surface
  - First appears during terminal sac stage
  - Secrete surfactant

### Surfactant

- Detected between 25 – 30 weeks gestation.
- Lipoprotein
- Dipalmitoyl phosphatidylcholine (DPPC) → decreases surface tension to almost zero
- 8% Phosphatidylglycerol (PG)
  - Unique to lung cells, bronchoalveolar fluid
  - Marker for surfactant
- Remainder: intracellular transport, storage, exocytosis, adsorption, spreading of the monolayer, clearance at the alveolar lining and immunoprotection

### Glucocorticoids

- Accelerate surfactant synthesis and fetal lung maturation
  - Increase rate of glycogen depletion
  - Thins interalveolar septa
  - Increases size of alveoli
  - Increases number of Type II pneumocytes
  - Increases the lamellar bodies within those cells
- Increases glycerophospholipid biosynthesis
  - Increased surfactant production
- Role in early lung development:
  - Emphasis on surfactant synthesis
- Direct action on lung tissue
  - Increases the number of  $\beta$ -adrenergic receptors
  - Enhances elastin and collagen production
- Current recommendations:
  - Single course between 24 – 34 weeks if risk of delivery within 7 days
- Reduces RDS by ~50% and mortality by ~30%
- Decreases IVH and NEC

### Catecholamines

- Stimulate secretion of surfactant into alveolar space
  - Direct action of adrenergic compounds on Type II cells
  - Response occurs in less than an hour
  - Increased PC in lung fluid
  - Increased lung stability
  - Inhibits fetal lung fluid secretion

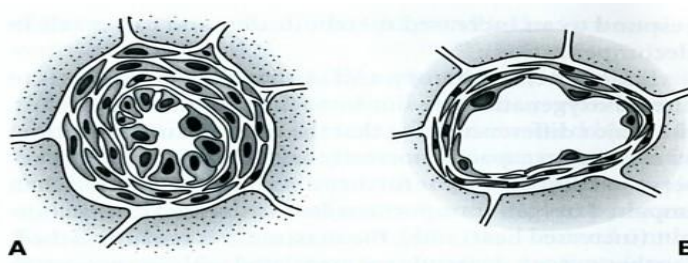
### Factors Inhibiting Lung Maturation

- Insulin:
  - ?? Hyperglycemia and/or hyperinsulinemia
  - Maturation of surfactant synthesis occurs at same time glycogen is depleted from lungs and liver.
  - Inhibits glycogen breakdown
  - Interferes with PC synthesis

- Androgens
  - Female lung 1 week more mature

### Pulmonary Vasculature

- Pulmonary artery muscle wall changes:
  - Wall very thick at birth due to low oxygen tension in utero
  - Wall thins postnatally as PaO<sub>2</sub> increases
- Pulmonary vein has very little elastic fibers
- Intrapulmonary arteries: dilate with postnatal increase in PaO<sub>2</sub> → PVR decreases



A: swollen endothelial cells and increased thickness of muscular layer. Within 24 hours of birth (B), luminal diameter is greatly increased: flattening of the endothelial cells, spreading of the smooth muscle cells and relaxation of the smooth muscles.

Figure 9-13, Blackburn, 2013, pg. 283.

### Fetal Lung Fluid

- Volume ~ size of the FRC
- Determines formation, size and shape of developing air spaces
- Absorption at birth:
  - Stimulated by catecholamines
  - Decreasing PVR aid in absorption

## **TRANSITIONAL EVENTS**

### Respiratory Conversion

- Lung aeration complete when lung liquid is replaced by air → establishes the functional residual capacity (FRC)
- Surfactant:
  - Decreases atelectasis
  - Promotes capillary circulation by increasing alveolar size
  - Improves alveolar fluid clearance
  - Protects the airway
- Postnatal breathing stimulated by:
  - Mild hypercapnia, hypoxia and acidosis due to stressors in labor
  - Decreased pH stimulates respiratory center
  - Low PaO<sub>2</sub> and high PaCO<sub>2</sub> stimulate central and peripheral chemoreceptors

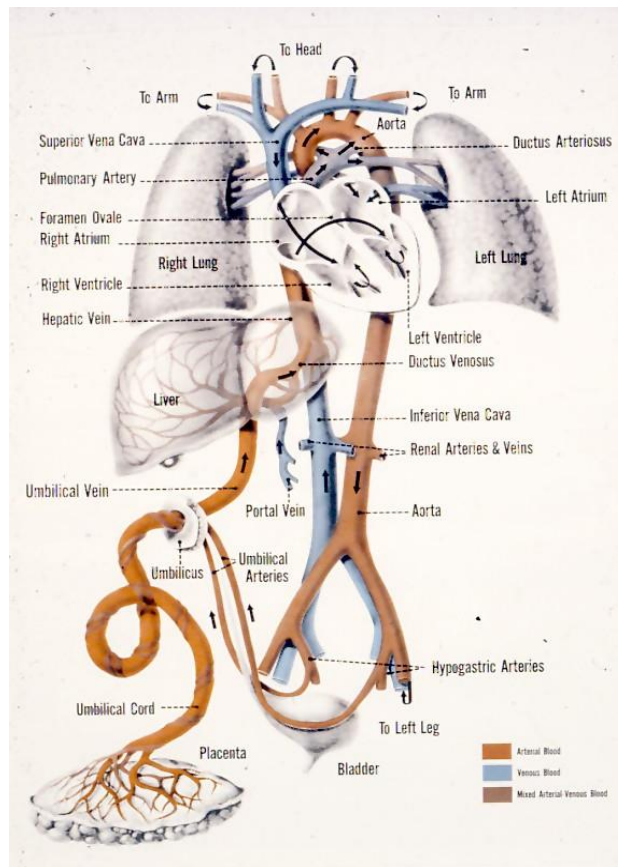
- Other stimuli: cold, light, noise, touch
- Mechanics of Respiratory Conversion:
  - Thoracic squeeze: aids in absorption of ~ 33% of fetal lung fluid
  - Recoil of chest wall → negative intrathoracic pressures > 80 cm H<sub>2</sub>O
    - Passive “inspiration” of air
    - Active expiration – contributes to FRC, even distribution of air and elimination of lung fluid
  - 2<sup>nd</sup> and 3<sup>rd</sup> breaths require less pressure
- Forces to overcome with 1<sup>st</sup> Breath
  - Viscosity of lung fluid column
  - Tissue resistive forces
  - Surface tension forces at air-liquid interface
    - First increases as lung fluid returns down conducting airways → bronchiole diameter reduced
    - Intraluminal pressure in terminal bronchioles highest → prevent closure by tension
  - Lung expansion facilitates surfactant secretion, alveolar stability and FRC formation
- Aeration of Lungs
  - Drives fluid into interstitium → absorbed through lymphatic and pulmonary circulations
  - Rate variable
    - Fine crackling rales auscultated
  - Pulmonary blood vessels dilate
    - PVR decreases progressively until 2 – 3 weeks of age

### Cardiovascular Conversion

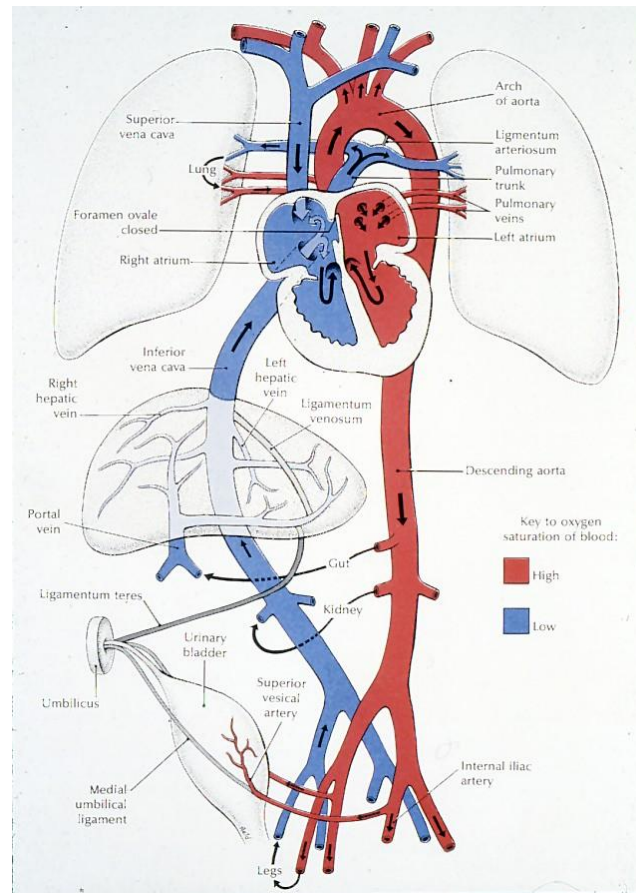
- Placenta
  - Gas exchange by simple diffusion
  - Uses ~ 33% of oxygen and glucose supplied by maternal circulation
  - Low-resistance circuit
  - PaCO<sub>2</sub> 38; PaO<sub>2</sub> 40-50; pH 7.36
- Fetal Blood Flow
  - Umbilical vein PaO<sub>2</sub> 30 mmHg
  - Ductus venosus: shunts 50 – 60% of umbilical venous blood into inferior vena cava (IVC)
  - IVC blood (PaO<sub>2</sub> 25-28 mmHg) enters right atrium. 60% shunted through foramen ovale into left atrium
  - Left atrium mixes right atrial blood and pulmonary vein return
  - Left ventricular blood (PaO<sub>2</sub> 20 – 25 mmHg) pumped through aorta to brain, coronary arteries and upper extremities
  - Superior vena cava (SVC) blood flow enters right atrium into right ventricle



- Right ventricle ( $\text{PaO}_2$  19 – 22 mmHg) ejects blood through ductus arteriosus to descending aorta



- Neonatal Blood Flow
  - Cord clamped → increase in pulmonary blood return to the heart
  - Foramen ovale closes due to increased left atrial pressure
  - Ductus venosus closes: no blood flow
  - Ductus arteriosus closes due to increase in  $\text{PaO}_2$  and decrease in prostaglandin



- Structural Changes in Pulmonary Circulation
  - First 24 hours
    - Recruitment of arteries
  - First 2 weeks
    - Reduced muscularity
  - After 2 weeks
    - Muscle tissue starts to reappear
    - Structural remodeling

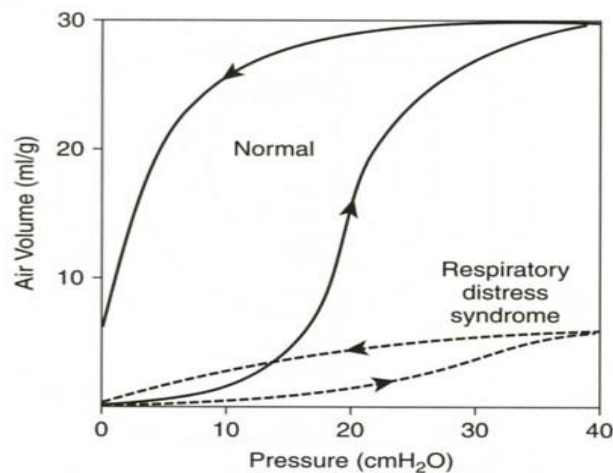
### Respiratory Physiology

- Control of Respiration
  - Peripheral Chemoreceptors:
    - Carotid and aortic bodies sense  $O_2$  and  $CO_2$  tensions
    - Central chemoreceptors in medulla: sensitive to  $PaCO_2 / [H^+]$  in extracellular fluid
    - When  $PaO_2$  falls, chemoreceptor stimulates ventilation
    - At birth, fetal  $PaO_2$  increases from 25 mmHg to 45-50 to 70 mmHg.
      - Relative hyperoxia
      - Chemoreceptors reset and become oxygen sensitive
    - More sensitive response to carbon dioxide

- Increases ventilation by 3 – 4 times baseline
  - Tolerates higher PaCO<sub>2</sub> levels initially
- The Respiratory Pump
  - Composed of the rib cage and respiratory muscles
- Rib Cage and Chest Wall Muscles
  - Muscles of rib cage:
    - External intercostal muscles → inspiration
    - Internal intercostal muscles → expiration
    - Accessory muscles → sternocleidomastoid, pectoral, scalene
  - Function: stabilize chest wall during diaphragmatic excursion. If they can't do this, the chest wall will collapse or be distorted upon inspiratory efforts
    - With stability: inspiratory muscles contribute to thoracic volume
- Diaphragm
  - Inserts on lower 6 ribs, sternum, and first 3 lumbar vertebrae
  - Innervated bilaterally by the phrenic nerve
  - Intercostals muscles stabilize rib cage
  - Abdominal muscles stabilize abdomen
  - Attached to very pliable chest wall
    - Distortion of lower portion of chest wall during expiration
    - Forceful expirations become less efficient, tidal volumes become smaller.  
Result: less effective ventilation

### Mechanical Properties of the Respiratory System

- Lung Compliance
  - Compliance: measurement of the elastic properties that oppose a change in volume (cc) per unit of change in pressure (cm H<sub>2</sub>O)

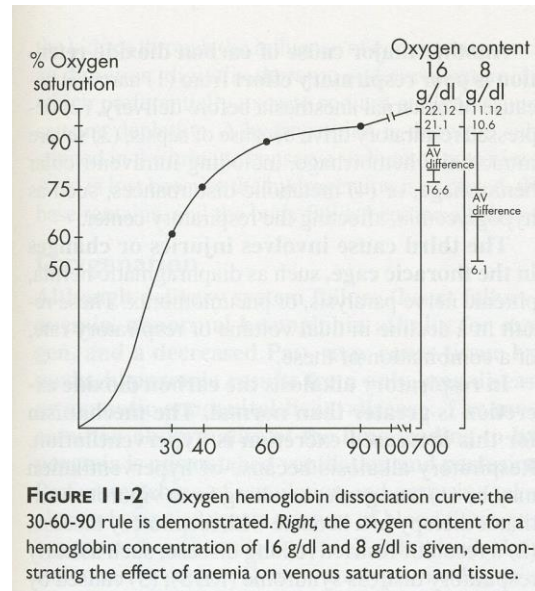


- Lung compliance depends on:
  - Tissue elastic characteristics of the parenchyma, connective tissue and blood vessels

- Surface tension in the alveoli
- Initial lung volume before inflation
- Air-liquid interface
- Presence of surfactant
  
- Lung Resistance
  - Depends on:
    - Size and geometric arrangement of the airways
    - Viscous resistance of the lung tissue
    - Proportion of laminar to turbulent airflow
  - Varies inversely with lung volume
  - Peripheral airways contribute the most to airway resistance
  - Increased resistance → increased ventilatory drive
  
- Alveolar Ventilation
  - Alveolar volume: all lung units capable of exchanging gas
  - At end-exhalation, the FRC is the sum of the volume of gas in the alveolar volume and in the anatomic dead space
  - Tidal volume ( $V_T$ ) = amount of gas entering and leaving the lung with each breath
  - Minute ventilation ( $V$ ) =  $V_T \times RR$
  - Alveolar ventilation ( $V_A$ ) =  $(V_T - V_D) \times RR$
  - Supplemental oxygen increases oxygen delivered to alveolar space. It has no effect on accumulation of  $CO_2$ , but may prevent hypoxemia
    - Example: a 1 kg neonate has a  $V_T$  of 6 cc, anatomic dead space of 2 cc and RR of 40 bpm.
      - Alveolar ventilation is 160 cc/min  $\{(6 \text{ cc} - 2 \text{ cc}) \times 40\}$ . In room air, he will deliver 33.6 cc of  $O_2$  to the alveolar space every minute (alveolar ventilation  $\times$  room air [.21])
      - If the RR is 20/min, the  $V_A$  decreases to 80 cc/min. 16.8 cc of  $O_2$  goes to alveolar space each minute →  $PAO_2$  and  $PaO_2$  will fall.
      - If RR is 20/min and he is now in 50%  $FiO_2$ , oxygen delivery to alveolar space increases to 40 cc/min →  $PAO_2$  and  $PaO_2$  increase
  
- Pleural Pressure
  - Majority of gas delivered to dependent portion of lung
  - Majority of pulmonary perfusion found in dependent regions → ventilation perfusion matching
  - Increases from apex to base
    - Alveoli smaller at the base – have the greatest increase in volume
  
- Closing Capacity
  - Dependent regions of the lung become closed from the main stem bronchi
  - When closing capacity exceeds the FRC, the ventilation-to-perfusion ratio decreases → hypoxia and hypercarbia
  - With total atelectasis, the closing capacity also exceeds the tidal volume

- CPAP and PEEP increase the FRC above the closing capacity
- Functional Residual Capacity
  - Rapidly established with the first successive breaths
  - Forms the alveolar reservoir at end expiration
  - Comprises 30 – 40% of total capacity of the lung
  - FRC stays low until lung disease resolves. Goal → keep FRC above the passive resting volume of the lung
  - Minimizes the work of breathing: optimizes system compliance and maintains a gas reservoir during expiration
- Ventilation-Perfusion Relationships
  - Alveolar ventilation dependent upon pulmonary vasculature
  - Interaction between ventilation and perfusion expressed as a ratio. A ratio of 1 indicates ideal efficiency.
  - Increased dead space. V/Q ratio = infinity. Rapid equilibrium occurs but it takes a large amount of ventilation to maintain this. This inefficient gas exchange will eventually result in CO<sub>2</sub> retention.
  - Alveolar underventilation. Ventilation is low in relation to perfusion. This inefficient gas exchange will result in an elevated PaCO<sub>2</sub> in arterial blood gases and a decreasing PaO<sub>2</sub>.
  - Intrapulmonary shunting and wasted ventilation. Often called the 4<sup>th</sup> compartment. This pattern adds mixed venous to mixed arterial blood.
- Oxygenation
  - Tissue hypoxia can be caused by:
    - Arterial hypoxemia
    - Venous hypoxemia
    - Decreased oxygen content
    - Abnormal affinity of oxygen to the hemoglobin molecule
- Oxygen Saturation:
  - The percentage of hemoglobin that is combined with oxygen
  - P<sub>50</sub> is the PaO<sub>2</sub> at which the Hgb is 50% saturated. It is low when the Hgb affinity is increased, and high when the Hgb affinity is decreased.
  - Factors that affect affinity:
    - Left: hypothermia, alkalemia, hypocapnia and fetal hemoglobin
    - Right: hyperthermia, acidemia and hypercapnia.
  - “30-60-90” rule is helpful in remembering saturation and reconstructing the Hgb dissociation curve. At a PaO<sub>2</sub> of 30 mm Hg, the oxygen saturation is 60%; at a PaO<sub>2</sub> of 60, the saturation is 90% and at 90 mm Hg, the saturation is 95%.
- Oxygen Content
  - Calculated from the Hgb saturation and Hgb concentration. 1 gm of Hgb binds 1.39 ml of oxygen. The oxygen content (cc/dl) = saturation percentage x Hgb (gm/dl)

- Example: an infant with a Hgb of 8 g/dl will have half the oxygen content of an infant with a Hgb of 16 g/dl at the same saturation.



Gardner, Carter, Enzman-Hines & Hernandez, 2016, pg. 149

- The neonate that has 16 g of Hgb that is 95% saturated carries 21.1 mL/dL oxygen (16 x 1.39). The baby with 8 g Hgb carries only 10.6 mL/dL oxygen.
- 4 – 5 ml/dl is needed by tissues for metabolism → venous blood contains 4 – 5 cc/dl less oxygen than does the arterial.
- The baby with 16 g of Hgb has a venous oxygen content of about 16 mL/dL → 75% saturation and PO<sub>2</sub> about 40 mmHg. The baby with 8 g of Hgb has a venous content of about 6 mL/dL oxygen—55% saturation and PO<sub>2</sub> < 30.

### Acid-Base Homeostasis and Oxygenation

- Evaluate acid base homeostasis: pH, PaCO<sub>2</sub>, base excess and bicarbonate
- Evaluate adequacy of oxygenation: PaO<sub>2</sub> saturation and hemoglobin
- Acid: hydrogen ion donor
- Base: hydrogen ion receptor
- Acid-base balance: determined by the pH
- Respiratory Contribution
  - CO<sub>2</sub> produced as a waste product of metabolism
  - Amount of CO<sub>2</sub> in the blood is due to a balance between metabolic rate (production) and the alveolar ventilation (excretion)
    - PaCO<sub>2</sub> accurately reflects alveolar ventilation
  - CO<sub>2</sub> combines with water to form carbonic acid, which divides into a hydrogen ion and a bicarb ion:  $\text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-$

- Metabolic (Non-respiratory) Contribution
  - Metabolic factors are regulated by generating fixed acids
  - Bicarb ion: is a hydrogen ion receptor (acid receptor)
  - Base excess:
    - Represent the actual excess or deficit of bicarb
    - Estimates the buffering action of the red blood cells
- Compensation
  - When one or more of the body's regulatory systems fail, other systems have a limited ability to maintain the acid-base equilibrium. When the pH is outside of the normal range, compensation has failed.
  - An acid-base deviation is respiratory if it is due to an abnormal PCO<sub>2</sub> and metabolic if due to an abnormal level of plasma HCO<sub>3</sub><sup>-</sup>.
  - With either the respiratory or non-respiratory acid-base system, the other system will become disturbed in the opposite direction in an attempt to balance the primary process.
  - The result is a change in pH toward normal despite an abnormal blood PCO<sub>2</sub> or HCO<sub>3</sub><sup>-</sup>
- Interpretation of ABG results:
  1. Look at pH. Determine direction of imbalance
  2. Classify: Metabolic → change in bicarb and base; Respiratory → change in PCO<sub>2</sub>
  3. Look at component not affected by primary disturbance to determine compensatory change
  4. Normal values:
 

pH	7.35 – 7.45
PaCO <sub>2</sub>	35 – 45 mm Hg
Bicarb	22 – 26 mEq/L
Base excess	- 4 – +4
PaO <sub>2</sub>	> 60 mm Hg
O <sub>2</sub> saturation	92% – 94%
- Respiratory Acidosis
  - Etiology: respiratory failure

	<u>Normal</u>	<u>Respiratory Acidosis</u>	<u>Compensated</u>
pH	7.40	7.23	7.40
Bicarb	24	24	36
PaCO <sub>2</sub>	40	60	60
BE	0	-4	+9

- Respiratory Alkalosis
  - Etiology: iatrogenic in the NICU
  - Decreased PaCO<sub>2</sub> results in less “acid”, causing the pH to increase
  - Treatment: decrease ventilator support
  - Compensation takes place after several days by excretion of HCO<sub>3</sub> in urine

	<u>Normal</u>	<u>Respiratory Alkalosis</u>	<u>Compensated</u>
pH	7.40	7.52	7.40
Bicarb	24	24	18
PaCO <sub>2</sub>	40	30	30
BE	0	+ 2	-5

- Metabolic Acidosis
  - Accumulation of acids in excess of base
  - Acute: anaerobic metabolism → lactic acid → reacts with HCO<sub>2</sub> → serum bicarb level falls → base deficit
  - Acute pH changes → prompt compensatory increase in ventilation
  - Renal adjustments occur over a longer period
    - Very low birth weight infant has a limited response

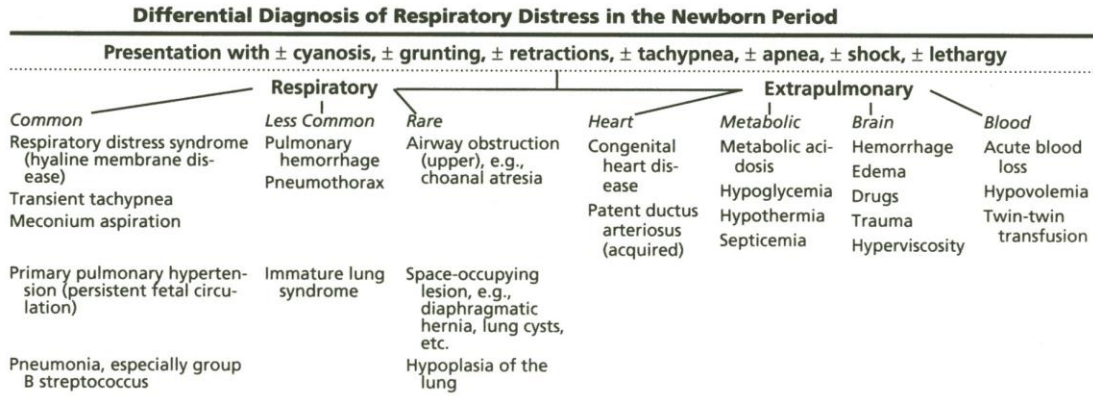
	<u>Normal</u>	<u>Metabolic Acidosis</u>	<u>Compensated</u>
pH	7.40	7.10	7.40
Bicarb	24	12	12
PaCO <sub>2</sub>	40	40	20
BE	0	-17	-10

- Metabolic Alkalosis
  - Etiology: excess of bicarb or from a loss of acid.
  - Gain of bicarb from overcorrection of acidosis with sodium bicarb
  - Loss of H<sup>+</sup>: vomiting, gastric suction
  - Increased renal acid loss from diuretic therapy
  - Rapid ECF reduction

	<u>Normal</u>	<u>Metabolic Alkalosis</u>	<u>Compensated</u>
pH	7.40	7.57	7.40
Bicarb	24	36	36
PaCO <sub>2</sub>	40	40	60
BE	0	+13	+9



## PULMONARY SYSTEM OVERVIEW



Modified from: Klaus, MH, Fanaroff, AV, and Martin, RJ: Respiratory Problems. *in* Klaus, MH, and Fanaroff, AV, eds., Care of the High Risk Neonate, Philadelphia, W.B. Saunders Co., 1979; from: Polin RA, and Burg FO: Workbook in Practical Neonatology, Philadelphia, 1983, W.B. Saunders, p. 103. Reprinted with permission.

### Respiratory System Examination

- Effort: normally is irregular, abdominal. Rate = 30 – 60 breaths/min
- Bradypnea: rate < 30 breaths/min
  - ? insult to respiratory center
- Tachypnea: rate > 60 breaths/min
  - Earliest symptom
  - Attempts to maintain alveolar ventilation
  - Increases oxygen demand and work of breathing
- Periodic breathing: cyclic pattern of breathing and pauses
  - Rate: 30 – 60 breaths/min
- Apnea: respiratory pause > 20 seconds
  - May be less than 20 seconds if accompanied by colour change, hypotonia and bradycardia
- Use of accessory muscles:
  - Retractions are seen because the neonate's cartilage is soft. Airway resistance or lung disease result in increased work of breathing
  - Intercostal: between the ribs
  - Subcostal: immediately below the ribcage
  - Sternal, suprasternal and subxiphoid retractions with severe distress
- Nasal flaring:
  - During inspiration widens the nasal alae in an attempt to decrease upper airway resistance
- Grunting:
  - Sound produced when air is exhaled against a partially closed glottis
  - Stabilizes alveoli → increases transpulmonary pressure
  - Delays expiration → increases gas exchange by increasing end-expiratory pressure and lung volume
- Colour

- Acrocyanosis: normal x 24 hours
- Pallor → expect hypotension if poor peripheral circulation is present
- Ruddy, plethoric → hyperviscosity syndrome; polycythemia
- Cyanosis: peripheral vs central
  - Not a reliable sign of hypoxemia in neonates
- Chest symmetry:
  - Round or barrel shape
  - Distress → increase in anterior-posterior diameter
- Auscultation:
  - Compare and contrast each side of the chest for equality of breath sounds
  - Sound is very easily transmitted through the small chest of the neonate
  - Presence/absence of fine/coarse rales, wheezes, grunting, other extraneous sounds

#### Non-Respiratory Examination

- Progression from flexion to flaccidity → progression of hypoxia and increased work of breathing
- Cardiac findings: signs of congestive heart failure or congenital defects
- Scaphoid abdomen → diaphragmatic hernia

#### Laboratory data:

- Chest xray
- Blood gases
- Hematocrit
- WBC and differential
- Blood/plasma glucose
- EKG and echocardiogram
- EEG and ultrasound
- Serum electrolytes

#### General Treatment Strategies

- Supplemental oxygen:
  - Indications: anytime the neonate is unable to maintain adequate oxygenation
  - Principles for oxygen administration:
    - No “safe” concentration
    - Maintain PaO<sub>2</sub> 60 – 80 mm Hg
    - Continuous monitoring of oxygenation status
    - Oxygen humidified and warmed
    - Oxygen concentration monitored.
    - Stable concentration necessary to maintain PaO<sub>2</sub> within normal limits.
      - Rule of 7: estimated percentage change in inspired oxygen is equal to the desired change in arterial oxygen divided by 7
      - %O<sub>2</sub> change =  $\frac{\text{New PaO}_2 - \text{Old PaO}_2}{7}$

To get a PaO<sub>2</sub> of 90 mm Hg with a PaO<sub>2</sub> of 160 mmHg, you would have to decrease the FiO<sub>2</sub> by 10%:  $\frac{90 - 160}{7} = -10\%$

- Clinical observations,  $\text{FiO}_2$  concentrations, time of adjustments must be described, documented and reported
- Blow-by Oxygen
  - Free-flow oxygen
  - Indications: short-term oxygen delivery to an infant who is breathing spontaneously but needs an oxygen enriched atmosphere
  - Disadvantages: no way to determine the exact content of oxygen delivered.
- Oxygen Hood
  - Used when the neonate has sufficient ventilation to maintain a normal arterial carbon dioxide tension
  - Indications: cyanosis, hypoxemia, apnea, respiratory difficulty
  - Warmed, humidified oxygen
  - Disadvantages:
    - Secondary source of oxygen may be needed when out of the hood
    - Confines movement
    - Temperature instability due to dampness
    - $\text{CO}_2$  buildup if inadequate flow to wash  $\text{CO}_2$  out of hood
    - Complications: hyperoxia
- Nasal Cannula:
  - Humidified oxygen is delivered at a set flow rate via a cannula positioned across upper lip and secured to face, with the flow directed into the nares.
  - Conventional nasal cannula:
    - Oxygen is regulated by the flow.
    - Low-flow meters can deliver amounts as small as 0.02 l/minute.
    - Oxygen concentration can be 100% or regulated via a blender
  - High Flow Nasal Cannula (HFNC)
    - Flow is greater than 1.5 to 2 L/min, with oxygen blended to a known concentration.
    - High flow rates result in the delivery of various levels of continuous positive airway pressure (CPAP) depending on the type of cannula, size of the infant, whether the infant's mouth is open or closed, and the flow rate used
    - Adequate humidification is essential to prevent drying and damage to the nasal passages.
    - Comparable to nasal CPAP in level of respiratory support supplied
    - Use blender to adjust the concentration of oxygen being delivered
      - Amount of oxygen entering the infant's lungs cannot be accurately determined because of the entrainment of room air around the cannula.
  - Indications:
    - Low oxygen requirement oxygen hood
    - Prolonged oxygen requirement
    - Increased mobility of the baby for developmental activities

- Titrate flow rate: monitor PaO<sub>2</sub>, oxygen saturation, body temperature, weight gain, clinical status
- Disadvantages: unable to measure exact concentration of oxygen
- Complications: hyperoxia, pressure-related tissue damage, hypoxemia with displacement of cannula
  
- Continuous Distending Pressure
  - Increases FRC and PaO<sub>2</sub>
  - Improves oxygenation by decreasing intrapulmonary shunting and ventilation-perfusion mismatching
  - Improves lung compliance
  - Decreases work of breathing
  - Mask CPAP
    - Delivers 5 – 8 cmH<sub>2</sub>O pressure with variable amounts of O<sub>2</sub> via face or nasal mask.
    - Requires appropriate-sized mask and tight seal around the nose/nose and mouth.
    - Indications: atelectasis, apnea, respiratory distress, and pulmonary edema.
    - Advantages:
      - Short-term use to assist with alveolar expansion and to inhibit atelectasis
      - Intubation not required.
      - May be useful in infants whose nares are too small to accommodate CPAP prongs.
      - Alternating between nasal prong CPAP and nasal mask CPAP may help to reduce skin breakdown around the nares in low birth weight infants
    - Complications:
      - Carbon dioxide retention in the dead space of the mask
      - Pulmonary hyperexpansion potentially leading to air leaks
      - Aspiration of stomach contents
      - Gastric distention.
  
- Nasal CPAP
  - Started at 5 to 6 cm H<sub>2</sub>O pressure and titrated up to 8 cm H<sub>2</sub>O pressure
  - Delivered by prongs that fit into the nares, in addition to a measured concentration of oxygen.
  - Indications: atelectasis, apnea, mild to moderate respiratory distress, and pulmonary edema.
  - Advantage: intubation not required.
  - Complications:
    - Ineffective ventilation
    - Pneumothorax
    - Variable pressure delivery when infant's mouth is open
    - Molding of the head from securing straps
    - Erosion of the septum from poorly fitting prongs
    - Nasal obstruction as a result of increased secretions
    - Agitation
    - Dislodging of prongs by an active infant
    - Gastric distention and perforation.

- Bilevel CPAP
  - Provides continuous positive pressure at two separate CPAP levels.
  - Background or baseline CPAP set at 4 to 7 cm H<sub>2</sub>O
  - Sighs / brief periods of increased pressure set 2 to 4 cm of H<sub>2</sub>O higher than baseline.
  - Indications: atelectasis, apnea, moderate respiratory distress, and pulmonary edema.
    - May facilitate extubation in very low birth weight infants.
  - Advantage:
    - Intubation not required.
    - Higher MAPs may stabilize airways and assist in the recruitment of alveoli
  - Complications:
    - Ineffective ventilation, pneumothorax
    - Variable pressure delivery when infant's mouth is open
    - Erosion of the septum from poorly fitting prongs
    - Agitation; dislodging of prongs by an active infant
    - Feeding intolerance
    - Gastric distention.
- Nasal intermittent positive pressure ventilation (NIPPV)
  - Combines nasal CPAP with ventilator breaths delivered at a set peak pressure
  - Breaths delivered through nasal CPAP prongs or nasal CPAP mask.
  - Indications: apnea, atelectasis, moderate respiratory distress.
  - Advantages:
    - Compared to nasal CPAP, NIPPV has been shown to reduce work of breathing
    - Decreases the need for mechanical ventilation in the first 72 hours of life
  - Complications: ineffective ventilation, pneumothorax, variable pressure delivery when infant's mouth is open, erosion of the septum from poorly fitting prongs, agitation, dislodging of prongs by an active infant, feeding intolerance, and gastric distention.
- Mechanical Ventilation:
  - Indications:
    - Respiratory failure
    - Pulmonary insufficiency
    - Surfactant administration
    - Severe apnea and bradycardia episodes
    - Cardiovascular support
    - CNS disease
    - Surgery
  - Advantages:
    - Consistent deliver of assisted ventilation and oxygen therapy
    - Decreases work of breathing
    - Stabilizes airway

- Disadvantages
  - Intubation
  - Xray examination: confirm placement
  - Intermittent xray examinations: verify placement
  - Continuous physiologic monitoring
  - Exposure of lung tissue to potential volutrauma/barotrauma

**TABLE 23-4** **COMPLICATIONS OF ENDOTRACHEAL INTUBATION**

COMPLICATIONS	COMMENTS
<b>IMMEDIATE</b>	
<b>Malposition</b>	
Too low	Usually in right mainstem bronchus; no or diminished breath sounds in left chest or upper right lobe; asymmetric chest movement; atelectasis (withdraw tube until breath sounds are heard bilaterally and equally).
Too high	Inadequate ventilation bilaterally; especially at lung bases.
Esophageal	Air movement auscultated in stomach with no or inadequate breath sounds.
<b>Obstruction</b>	
Plug	Partial—no change or diminished breath sounds audible. Complete—distant or no breath sounds audible.
<b>Kinking of the tube</b>	
Head position	Flexion or extension of the head results in diminished or blocked airflow.
<b>Perforation</b>	
Vocal cords	
Trachea	
Pharynx	
Esophagus/gastric	
<b>Pulmonary hemorrhage</b>	
Infection	Colonization in the neonatal airway increases with the duration of intubation; presence of ETT longer than 72 hours is associated with colonization; this biofilm may contribute to the chondritis that precedes subglottic stenosis; MRSA tracheal infection causes subglottic stenosis. <sup>406</sup> Late-onset sepsis is more common in VLBW infants with prolonged ventilation <sup>353</sup> ; mechanical ventilation is a risk factor for nosocomial infection. <sup>192</sup>
Air leak	ETT displacement (e.g., into the right mainstem bronchus or to the level of the carina) is a major factor in the development of air leaks. <sup>267</sup>
Increased intracranial pressure	Suctioning increases mean BP, which increases cerebral blood flow velocity and intracranial pressure, which increases the risk for IVH/PVL (see Box 23-2).
<b>Post-extubation</b>	
Migratory lobar collapse	Prevent and treat with pulmonary hygiene.
Diffuse microatelectasis	In VLBW infants may be associated with apnea; treatable by pulmonary hygiene or nasal CPAP, or both.
<b>LONG-TERM</b>	
<b>General</b>	
	Vocal cord inflammation, stenosis, and eventual dysfunction; tracheobronchial fistula; subglottic stenosis; tracheal inflammation and stenosis; necrotizing tracheobronchitis; contributes to CLD/BPD.
<b>Specific to the type of tube</b>	
Orotracheal	Abnormal dentition; gingival and palatal erosion; palatal grooves.
Nasotracheal	Otitis media; erosion of alae nasi and nasal septum; nasal stenosis.

BP, Blood pressure; CLD/BPD, chronic lung disease/bronchopulmonary dysplasia; CPAP, continuous positive airway pressure; ETT, endotracheal tube; IVH, intraventricular hemorrhage; MRSA, methicillin-resistant *Staphylococcus aureus*; PVL, periventricular leukomalacia; VLBW, very-low-birth-weight.

Gardner, Carter, Enzman-Hines & Hernandez, 2016, pg 586

## Types of Assisted Ventilation

- Positive Pressure Devices

- Bag-and-mask ventilation
  - Positive pressure and O<sub>2</sub> are delivered via face mask applied with an adequate seal around the mouth and nose
  - Maximal pressure relief valves should be present to prevent administration of excessive pressure
  - Manometer measures pressure delivered to the patient
  - Does not require intubation
- T-Piece resuscitator
  - Levels of positive pressure and PEEP are preset
  - Breaths are delivered by occluding the PEEP cap (T-piece)
  - Gas source is required
  - Advantage
    - Controls the amount of pressure applied with each breath
- Criteria for Intubation
  - Blood gases:
    - Severe hypoxemia:
      - PaO<sub>2</sub> <50-60 mm Hg with FiO<sub>2</sub> > 60%
      - PaO<sub>2</sub> < 60 mm Hg with FiO<sub>2</sub> > 40% in infants < 1250 g
    - Severe hypercapnia:
      - PaCO<sub>2</sub> > 55 – 65 mm Hg with pH < 7.20 – 7.25
  - Evaluation of clinical presentation
- Ventilator Parameters
  - Rate:
    - How often a volume of gas is delivered
    - Initial setting: 30 - 40 breaths/min for respiratory failure
    - Affects PaCO<sub>2</sub>
  - Peak Inspiratory Pressure (PIP):
    - Maximal amount of positive pressure delivered on inspiration
    - Primary factor used to determine tidal volume → affects oxygenation
    - Initial setting: 18 – 20 mm Hg.
  - Tidal Volume (V<sub>T</sub>):
    - Primary factor affecting both oxygenation and ventilation.
    - Volume targeted ventilation (volume guarantee): determine the desired volume to be delivered with each breath rather than setting the PIP.
    - Based on weight: 4 – 5 cc/kg
  - Positive End Expiratory Pressure (PEEP):
    - Continuous distending pressure
    - Aids in maintaining the FRC, stabilizing and recruiting atelectatic areas for gas exchange, improving compliance and improving ventilation-perfusion matching.
    - Initial setting: 4 – 5 cm H<sub>2</sub>O.
  - Inspiratory/Expiratory (I/E) ratio:
    - Ratio of time spent in inspiration and time spent in expiration
    - Based on underlying reason for ventilation



- Non-diseased lung: I/E ratio 1:2 or 1:3
  - Affects oxygenation and ventilation.
- Flow Rate:
  - Flow of gas (L/min) through the ventilator circuit
  - Initial setting: 5 – 10 L/min. Faster flow rates needed for severely compromised lungs.
  - Affects oxygenation
- Mean Airway Pressure (MAP)
  - Average distending pressure throughout a complete respiratory cycle.
  - Affects oxygenation
  - Most affected by changes in PEEP, PIP and I/E ratio.
  - High MAP → increased barotrauma

### Types of Assisted Ventilation

- Intermittent Mandatory Ventilation
  - Breaths are delivered at a predetermined rate, regardless of where the patient is in the respiratory cycle
  - Allows spontaneous respirations.
  - May “stack” ventilator breaths
    - Air trapping, air leak, CNS dysfunction
    - Irregularity of blood pressure and cerebral blood flow
- Patient Triggered Ventilation
  - Mechanical breaths are delivered in response to spontaneous respiratory effort from the patient
  - Goal: to avoid asynchrony of breathing
  - Improves gas exchange, decreases need and duration of ventilation, decreases incidence of air leaks and provides ventilation that better matches the baby’s own efforts.
  - Types of PTV:
    - Synchronized intermittent mandatory ventilation:
      - Present number of ventilator breaths is synchronized with the onset of the neonate’s spontaneous breaths
      - Associated with a decrease in:
        - Supplemental oxygen
        - Duration of ventilator therapy
        - Incidence of chronic lung disease
        - Severity of IVH
      - Also associated with fewer episodes of hypoxia and better oxygenation due to improved ventilation-perfusion and an increased functional residual capacity
    - Assist/control mode of ventilation
      - Computerized assisted control enables rapid digital feedback circuits to adjust PIP to control tidal volume and ventilatory rate to control minute ventilation
      - Indications:
        - Preterm infants with RDS

- Infants with a strong ventilatory drive
  - Infants who are not heavily sedated
- Volume-guarantee ventilation
  - Preset target tidal volume is maintained by the ventilator because the pressure limit varies inversely with the lung compliance and the baby's respiratory efforts
  - Typically set at 4-5 mL/kg
- Mandatory Minute ventilation
  - Provides mechanically generated breaths only if the neonate's spontaneous breathing doesn't meet the minimum level of minute ventilation chosen by the MD/NNP
  - Enables the baby to control the rate, flow and inspiratory time of the ventilator which enhances synchrony
  - Ensures a "backup" system to help with the work of breathing if the baby can't maintain an adequate minute ventilation
- Pressure-Support Ventilation
  - Supports breaths initiated by the baby by triggering a mechanical breath, preset to a specific pressure
  - Decreases work of breathing by assisting the activity of the infant's respiratory muscles
  - Has a variable inspiratory time that allows the baby greater control and synchrony with the ventilator
  - Flow cycled: when inspiratory flow decreases, inspiration ends
  - Used alone if the baby has effective respiratory drive or in conjunction with SIMV
  - Very useful in weaning ventilator dependent infants
- Neurally assisted ventilation (neurally adjusted ventilatory assist [NAVA]).
  - Uses measured electrical activity in the diaphragm to detect the onset of a breath and trigger the ventilator to support the breath
  - Each breath is supported in proportion to the intensity of the infant's inspiratory effort in an attempt to optimize synchrony
- High-Frequency Ventilation
  - Any of several forms of mechanical ventilation that uses small tidal volumes and rapid ventilator rates to ventilate patients with severe respiratory failure.
  - Advantage of HFV over conventional ventilation: ability to deliver adequate minute volumes with lower proximal airway pressures.
  - Types:
    - High-Frequency Jet Ventilation
      - Rapid high-velocity pulses from pressurized sources directly
      - Conventional ventilator used in tandem to provide gas for entrainment, provide PEEP and background ventilation
    - High-Frequency Oscillatory Ventilation
      - Piston or vibrating diaphragm moves a small volume of gas toward and then away from patient
      - Allows for use of higher MAP with less barotrauma

- Expiratory phase is active
- High-Frequency Flow-Interrupted Ventilation
  - Have both high-frequency and conventional options
  - Are neither oscillators nor jet ventilators.
  - Use a microprocessor-controlled pneumatic valve to interrupt the gas flow to achieve a pulsatile flow
- Indications for Use of HFV:
  - Severe lung disease unresponsive to conventional
  - Pulmonary air leaks
  - Hypoplastic lungs, diaphragmatic hernia
  - PPHN, meconium aspiration syndrome
- HFV parameters
  - Mean airway pressure
    - Affects oxygenation
    - Initial MAP should be adjusted to about 1-2 cm H<sub>2</sub>O above the one on the conventional ventilator
  - Amplitude
    - Size of pressure wave produced by the oscillator
    - Based on the clinical assessment of chest wall movement. Get an ABG after ~ 10 minutes to determine the changes in the PaO<sub>2</sub> and PaCO<sub>2</sub>
  - Rate (Hz)
    - Oscillator: 600-900 breaths/minute (10-15 Hz) 1Hz= 60 cycles.
      - A faster rate is used for a baby < 1.5 Kg (12-15) and 10-12 Hz for term babies
    - Jet: 240-660 breaths/min (4-11 Hz). Conventional ventilator has a back-up rate that provides sigh breaths
  - Inspiratory Time
    - Typically set at .33

### Medications Used During Ventilation Therapy

- Surfactant
  - Dose: 4 – 5 cc /kg/dose, depending on product used
  - Administration: suction 10 – 15 minutes prior to surfactant administration
    - Ensure position of ETT
    - Follow manufacturer’s recommendations
  - Continuous monitoring: cardiac, respiratory and oxygen saturation during and after administration, vital signs, ongoing assessment of air entry and chest excursion
  - Side effects: hypoxia, bradycardia or distress
  - ETT suctioning should be delayed for at least 1 – 2 hours after dosing to prevent removal of the medication
- Bronchodilators
  - Methylxanthines
    - Improve respiratory drive, increase contractility of the diaphragm; enhance chemoreceptor sensitivity to carbon dioxide

- Improve renal and pulmonary blood flow, causing a mild diuresis and bronchodilation, and increased heart rate and cardiac output.
  - Caffeine
    - Less of a bronchodilator and diuretic action
    - Dose: loading: 10 mg/kg; maintenance 2.5 mg/k every 24 hours
    - Serum concentration: not routinely monitored
    - Side effects: rare
  - Albuterol
    - Bronchodilator effect similar to aminophylline
    - Enhances clearance of mucociliary secretions
    - Dose: aerosol: 0.5 – 1 mg/kg/dose every 4 hrs via nebulized solution; metered dose inhaler: 1 or 2 puffs every 6 hours
    - Serum concentration not determined
    - Signs of toxicity: tachycardia, arrhythmia, tremors, irritability
- Diuretics
  - Furosemide (Lasix)
    - Affects chloride transport
    - Causes loss of sodium, chloride, potassium, calcium
    - Diuresis may decrease pulmonary blood flow, decrease vascular resistance and increase pulmonary compliance
    - Dose: 1 – 2 mg/kg/dose IV or po every 24 hrs (preterm) and every 12 hrs (term); every 6-8 hrs (chronic infant older than 1 month). Long-term therapy: once every 2<sup>nd</sup> day
    - Monitor: intake and output; frequent electrolyte values
    - Side effects: ototoxic, with transient and permanent hearing loss, renal calculi with long term use
  - Spironolactone (Aldactone)
    - Inhibitory effect on renal tubules → increased sodium losses; sparing of potassium
    - Dose: 1 - 3 mg/kg/dose po every 24 hours
    - Monitor: intake and output, electrolyte values after 72 hours
    - Side effects: rash, vomiting, diarrhea
    - Use with caution in infant with impaired renal function
  - Chlorothiazide (Diuril)
    - Inhibits sodium reabsorption in distal tubule, calcium sparing
    - Potentiating effect on Lasix
    - Dose: 10 – 30 mg/kg/dose po every 12 hours
    - Monitor: intake and output, electrolytes
    - Side effects: electrolyte disturbances and hyperglycemia
  - Hydrochlorothiazide with spironolactone (Aldactazide)
    - Inhibits sodium reabsorption in distal nephron
    - Spironolactone: helps to prevent potassium excretion and hypokalemia
    - Dose: 1 – 3 mg/kg/day every day or BID
    - Monitor: intake and output, signs of dehydration, electrolytes
    - Side effects: hyperglycemia

- Corticosteroids
  - Dexamethasone (Decadron)
  - Long-acting anti-inflammatory medication used to treat chronic lung disease and tracheal edema before and after extubation
  - Studies have shown increased risk of poor neurodevelopmental outcomes in infants receiving systemic steroid therapy
  - Routine use of chronic lung disease in the LBW infant not recommended
  
- Paralytic Agents
  - Pancuronium (Pavulon)
  - Pharmacologic relaxation/paralysis of skeletal muscle
    - Improved mechanical ventilation with improved oxygenation/ventilation
    - Decreased barotrauma
    - Decreased fluctuations in cerebral blood flow.
  - Dose: 0.1 mg/kg/dose every 1 – 4 hours
  - Monitor: vital signs continuously
  - Side effects: tachycardia, hypertension/hypotension
  - Eye lubricant necessary
  - Vecuronium:
    - Dose: 0.1 mg/kg/dose every 1 to 2 hours
  
- Analgesia/Sedation
  - Induce analgesia by acting at various levels of CNS
    - Spinal cord: impair/inhibit transmission of nociceptive input from periphery to CNS
    - Basal ganglia: activate a descending inhibitory system
    - Limbic system: alter the emotional response to pain, making it more tolerable
  - Fentanyl:
    - Dose: bolus: 1 – 4 mcg/kg/dose every 2 - 4 hours slow IV push
    - Continuous infusion: 1 – 5 mcg/kg/hour
    - Side effects: respiratory depression, chest wall rigidity, tolerance and dependence; urinary retention
  - Morphine:
    - Dose: bolus: 0.05 – 0.2 mg/kg/dose slow IV push, IM or subcutaneous route every 4 hours
    - Continuous infusion: loading dose of 100 – 150 mcg/kg over 1 hour, followed by continuous infusion of 10 – 20 mcg/kg/hr
    - Side effects: respiratory depression, hypotension, bradycardia, transient hypertonia, ileus, delayed gastric emptying, urinary retention, tolerance and dependence
  - Midazolam (Versed)
    - Short-acting synthetic benzodiazepine
    - Use: sedation
    - Dose: 0.07 – 0.2 mg/kg slow IV push; 2 – 8 mcg/kg/min continuous infusion
    - Monitoring: same as Morphine
    - Side effects: respiratory depression

- Inhaled Nitric Oxide
  - Endogenous nitric oxide is released from the endothelium and causes vascular smooth muscle relaxation
  - Used to promote relaxation of pulmonary smooth muscle to facilitate perfusion of the lung and gas exchange
  - Approved for treatment of PPHN in late preterm and term infants
  - Use of iNO in preterm infants remains experimental.
  - Dose:
    - Initial 20 parts per million (ppm)
    - After 4 hours, reduce dose to 6 ppm.
    - iNO is then weaned by 20% in a stepwise fashion to a dose of 1 ppm before discontinuation
    - Duration of therapy usually less than 5 days.
  - Monitor:
    - Vital signs, including blood pressure, continuously
    - Complete blood count
    - Methemoglobin levels
    - Environmental levels of nitric oxide.
  - Considerations: may cause methemoglobinemia, decreased platelet aggregation.

#### Weaning From Conventional Ventilation

- Indications:
  - Clinical status of infant consistent with beginning resolution of pulmonary condition
  - Ventilation becomes easier with less support
  - Less PIP need to achieve desired tidal volume
  - ABGs stable and physiologically normal
  - Spontaneous respiratory efforts
  - Increased activity and muscle tone
- Techniques:
  - PIP and FiO<sub>2</sub> usually lowered before other parameters
  - If PaO<sub>2</sub> above desired range: decrease PIP, FiO<sub>2</sub>, inspiratory time, PEEP or flow rate. Then reassess
  - If PaCO<sub>2</sub> is below desired range: decrease rate, then reassess
  - Minimal ventilatory support: PIP < 14 - 18, FiO<sub>2</sub> < .30 VR < 10 – 20 breaths/min

## ■ SPECIFIC EFFECTS OF DIFFERENT VENTILATOR CHANGES

### **Increasing PIP**

1. Increases  $V_T$  and  $V_e$
2. Adds little to MAP unless combined with a reversal of I/E ratio or prolongation of IT
3. Affects maximum dilation of alveoli already open, contributing to barotrauma
4. Opens alveoli with high critical opening pressures

### **Reversing I/E Ratio (for lengthening IT while respiratory rate is kept constant)**

1. Has little effect on  $V_T$  or  $V_e$  beyond the minimum IT needed to deliver  $V_T$  or reach desired PIP level (or both)
2. Can contribute on more than one-to-one basis to MAP, depending on original PIP and degree of reversal of I/E ratio
3. Allows expansion of atelectatic alveoli at lower PIP
4. May cause inadvertent PEEP, overinflation of alveoli, and reduction of pulmonary blood flow

### **Increasing Background CPAP or PEEP**

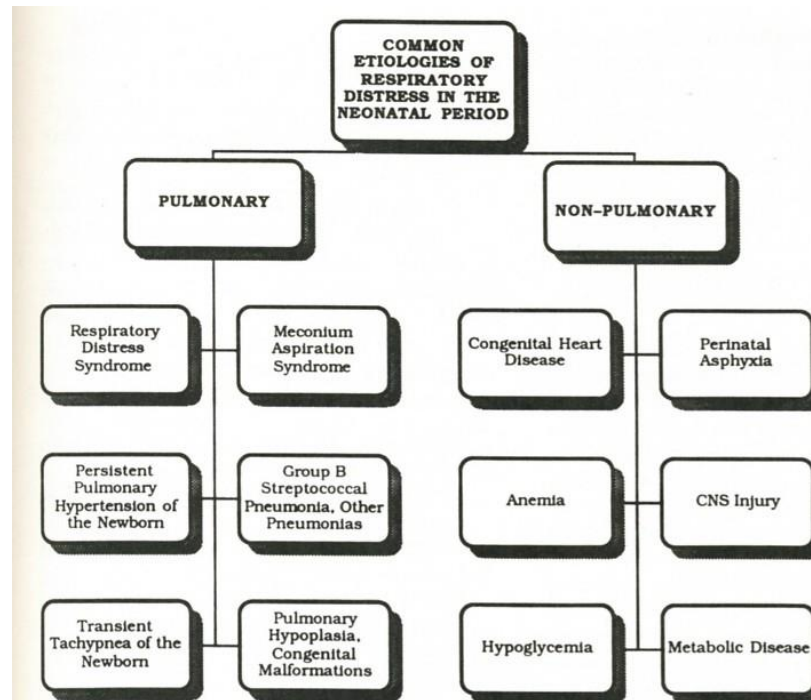
1. Decreases  $V_T$  and  $V_e$  unless significant atelectasis is overcome
2. Adds to MAP on a one-to-one basis
3. Holds open alveoli and terminal airways on end-expiration, thus raising closing volume and aiding in equal distribution of ventilation
4. Reduces likelihood of inadvertent PEEP

*CPAP*, Continuous positive airway pressure; *I/E*, inspiratory/expiratory; *IT*, inspiratory time; *MAP*, mean airway pressure; *PEEP*, positive end-expiratory pressure; *PIP*, peak inspiratory pressure;  $V_T$ , tidal volume;  $V_e$ , expired volume per unit time.

From Goldsmith, J.P. and Karotkin, E.H. (Eds.): *Assisted ventilation of the neonate* (3rd ed.). Philadelphia, 1996, W.B. Saunders, p. 62.

- Extubation
  - Remove tube on inspiration → adequate lung expansion
  - Remove tube on expiration → secretions “blown away”
  - ABG 30 – 60 minutes post-extubation
  - Chest xray: document lung expansion/atelectasis

## PULMONARY CONDITIONS



### Apnea

- Cessation of breathing for 20 seconds, or less if accompanied by cyanosis, pallor, hypotonia or bradycardia
- Central
  - Absence of airflow and respiratory effort
  - Contributing factors:
    - Chest wall afferent neuromuscular signals and chest wall instability
    - Diaphragmatic fatigue
    - Immature, paradoxical response to hypoxia and hypercapnia
    - Altered levels of local neurotransmitters in brain stem region of CNS
- Obstructive
  - Absence of airflow with continued respiratory effort, associated with blockage of airway at pharynx and/or larynx
  - Hyperextension or flexion of the neck may induce obstruction of the airway
- Mixed
  - Combination of central and obstructive, with obstruction usually at the level of the pharynx



- Apnea of Prematurity
  - Diagnosis after exclusion of pathologic processes in the premature infant
  - Onset within first week of life, usually at 24 to 48 hours.
  - If not present within first week, not likely to appear
  - Cease by 36-38 weeks in 95%
  
- Causes of Apnea
  - Prematurity
  - Hypoxia
  - Respiratory Disorders
  - Cardiovascular Disorders
  - Sepsis
  - CNS Disorders
  - Medications
  - Metabolic Disorders
  - Hematopoietic disorders
  - Reflex stimulation
  - Environmental factors
  
- Evaluation for Apnea
  - History:
    - Perinatal Risk Factors: fetal hypoxia, trauma
    - Neonatal Risk Factors
      - Prematurity
      - Cardiopulmonary disease
      - Metabolic abnormalities
      - Temperature instability
      - Infection
      - Environmental causes
      - CNS Disorders
  - Physical Examination
    - Complete physical and neurological examination
    - Observe for presence of risk factors
  - Documentation of Apneic Episodes
    - Detect any pattern
    - Duration
    - Time of episode and relation to any activities
    - Infant's position
    - Associated bradycardia, colour change, oxygen desaturations
    - Type of stimulation needed to resolve episode
  - Laboratory evaluation:
    - Basic evaluation to assess for sepsis, respiratory deterioration, metabolic issues
      - CBC with differential and platelet count
      - Blood gas
      - Serum glucose, electrolytes, calcium

- Blood culture
  - Echocardiogram
  - Chest xray
  - Barium swallow and pH study
- Management Strategies
  - Treat underlying cause
  - Avoid triggering reflexes
  - Prone position: only those infants with upper airway disorders or impaired airway protective mechanisms for whom the risk of death due to gastroesophageal reflux is greater than the risk of SIDS
  - Maintain neck in neutral position
  - Continuous distending pressure
    - Splints upper airway and weak chest wall
  - Pharmacologic treatment
    - Caffeine

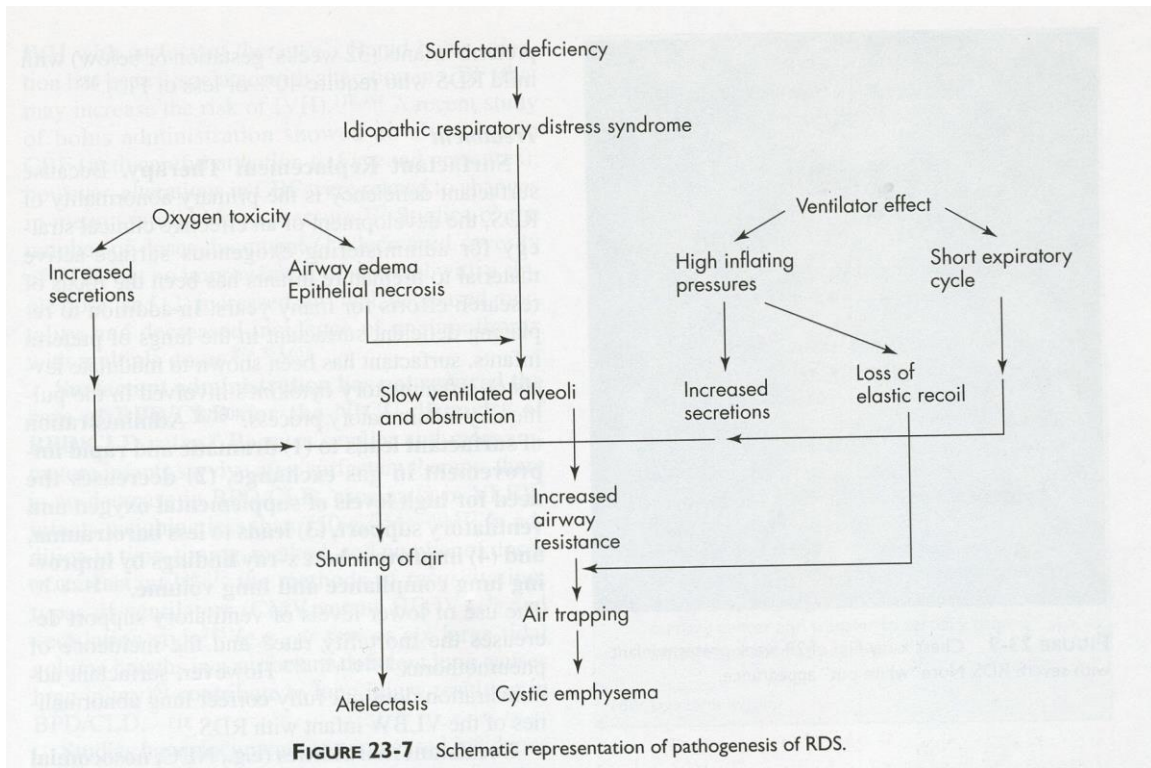
### Transient Tachypnea of the Newborn

- Retained Lung Fluid Syndromes
- Affects late preterm and term infants
- Presents with pulmonary edema from retained lung fluid
  - may complicate surfactant deficiency
- No history of asphyxia
- Substernal retraction and expiratory grunting may be present
- Presentation:
  - Normal respiratory rate for first hour of life, then gradually increases over next 4 – 6 hrs
  - Rate peaks between 6 – 36 hours
  - Gradually returns to normal by 48 – 72 hours
  - Mild hypercarbia, hypoxia and acidosis
  - ABG's: mild respiratory alkalemia
  - Hypoxemia: maldistribution of ventilation
  - Physical examination: appears barrel-chested
    - Subcostal retractions less prominent
    - Retained lung fluid may obstruct lower airways
- Etiology and Pathophysiology
  - Due to delayed postnatal reabsorption of normal lung fluid
  - After birth, lung fluid moves to interstitial space to pool in the interlobar fissures.
  - Predisposing Factors
    - Prematurity:
      - Premature labor
      - Cesarean section without labor
      - Hypervolemia:
        - increased capillary and lymphatic hydrostatic pressure

- Hypoproteinemia:
      - lower plasma oncotic pressure delays absorption
      - air trapping and hyperinflation
      - increased pulmonary vascular resistance
      - shunting through the ductus arteriosus and foramen ovale
- Radiographic Findings:
  - Characteristic:
    - Prominent perihilar streaking and fluid in the interlobar fissures
    - Hyperaeration:
      - Flattened hemidiaphragms
      - Increased anterior-posterior diameter of the chest
    - Should be normal within 48 – 72 hours
- Treatment Strategies:
  - Self-limited condition
    - Supportive care
    - Supplemental oxygen
  - Monitor oxygen saturations to assess oxygenation
  - Fluid, electrolyte and glucose needs met with IV fluids
  - Septic workup with antibiotics if sepsis/pneumonia suspected
  - PPHN may complicate clinical condition

### Respiratory Distress Syndrome

- Disease of immature lung anatomy and physiology
- Etiology:
  - Surfactant deficiency
  - Pulmonary hypoperfusion
  - Anatomic immaturity
  - Cesarean section without labor
  - Maternal diabetes
  - Second born twin
  - Male/female ratio of 2:1
- Pathophysiology



Gardner, Carter, Enzman-Hines and Hernandez, 2016, pg. 616

- Production of surfactant is inadequate
- Leads to diffuse alveolar atelectasis, pulmonary edema and cell injury.
- Progressive worsening contributes of loss of FRC, ventilation-perfusion mismatching
- Serum proteins leak into alveoli → inhibit surfactant function
- Alveolar spaces are generally collapsed
- Additional contributors:
  - Increased water content
  - Immature mechanism for clearing lung fluid
  - Decreased surface area for gas exchange
  - Increased distance between alveoli and capillaries impairs gas diffusion
- Clinical Presentation
  - Preterm infant with tachypnea and increased work of breathing
  - Distress present at or soon after birth
  - Tachypnea often first sign
  - Audible expiratory grunt
  - Significant substernal, suprasternal and intercostal retractions
  - Use of accessory muscles → paradoxical breathing
  - Cyanosis with increasing hypoxemia
  - Breath sounds decrease → usually described as “poor air entry”
- Diagnosis:

- Signs/symptoms above
- ABGs: hypoxemia and acidosis
- Increasing oxygen dependence and poor lung function peaks during first 48-72 hours
- Chest xray: low lung volumes, hazy lung fields
  - fine reticulogranular pattern of density with air bronchograms
  - evidence of PDA: enlarged heart, left to right shunt vessels, especially in R hilum, haziness
- Septic work up
- Electrolytes, glucose
- Treatment Strategies
  - Surfactant replacement
  - Warm, humidified oxygen
  - Assisted ventilation for profound hypoxemia ( $\text{PaO}_2 < 50$ ) and/or hypercapnia ( $\text{PaCO}_2 > 60$ )
  - Monitor oxygenation
  - Monitor pulmonary status
  - Physiologic support and maintenance of homeostasis:
    - Thermoregulation
    - Fluids, electrolytes, glucose, calories
- Complications
  - Pulmonary: Air leak, Pulmonary edema, BPD
  - Cardiovascular: PDA, systemic hypotension
  - Renal: Oliguria
  - Anemia
  - Neurologic: seizures due to hypoglycemia or IVH
  - Retinopathy of prematurity
- Outcome
  - Chronic lung disease. Long-term sequelae are related to specific complications such as BPD, IVH, ROP
  - Infants weighing  $> 1500$  g with mild to moderate RDS have same developmental outcome as those without RDS.
  - Most severe developmental outcomes are those who weigh  $< 1500$  g with an IVH

### Meconium Aspiration Syndrome

- Etiology:
  - With intrauterine stress/asphyxia, peristalsis is stimulated, anal sphincter relaxes and meconium is released into amniotic fluid
- Pathophysiology:
  - Meconium is aspirated into trachea and large bronchi
  - Mechanical obstruction of airways results in ball-valve phenomenon

- Complete obstruction of smaller airways → atelectasis
- Partial obstruction → on inspiration air passes around the obstruction. With expiration, airway collapses trapping residual air distally
- Air leaks occur when overdistranded alveoli rupture
- Chemical composition of meconium causes local toxic effects

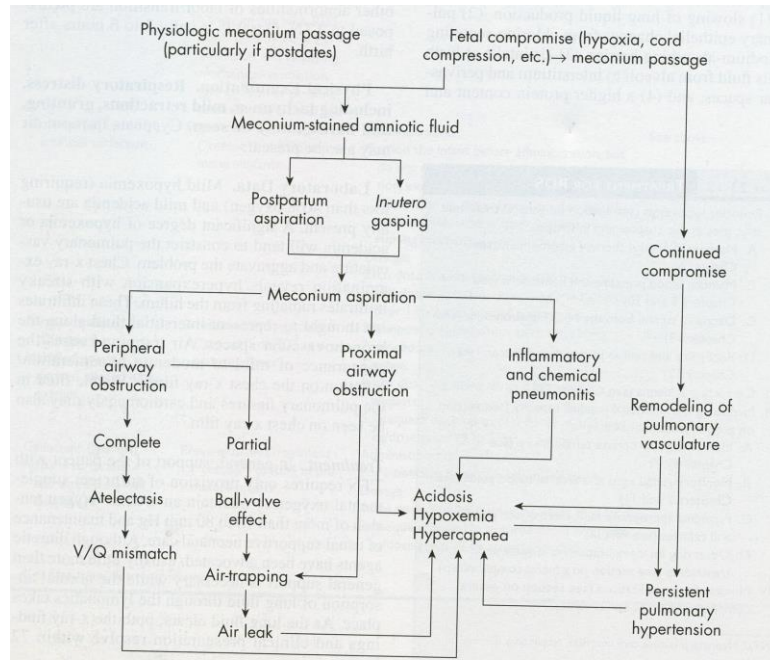


FIGURE 23-10 Pathophysiology of meconium passage and the meconium aspiration syndrome. (From Wiswell T, Bent R: *Pediatr Clin North Am* 4:957, 1993.)

Gardner, Carter, Enzman-Hines and Hernandez, 2016, pg 623

- Clinical Presentation
  - Term or post-term infant
  - History of fetal distress and meconium stained amniotic fluid
  - Vigorous resuscitation in delivery room needed
  - Signs of weight loss with little subcutaneous fat remaining
  - Nails, umbilical cord, and skin may be meconium stained
  - Respiratory distress variable
    - Mild: hypoxemia easily corrected with minimal oxygen therapy. Tachypnea resolves in 72 hours.
    - Severe: Neurologic and respiratory depression at birth
      - Respiratory distress with cyanosis, nasal flaring, grunting, retracting, tachypnea,
      - Appears barrel-chested
      - Fine and coarse rales common
      - Expiration phase of respirations prolonged
      - ABGs: respiratory and metabolic acidosis. Hypoxemia even with 100% oxygen
- Chest Xray:
  - Coarse, patchy, irregular pulmonary infiltrates

- Areas of irregular aeration
  - Hyperaeration with flattening of diaphragm
  - Pneumothorax and pneumomediastinum common
  - Chemical pneumonitis apparent after 48 hours
- Treatment Strategies
    - Delivery room management according to NRP Guidelines
    - Improve oxygenation
      - Ventilator therapy. Same parameters as with RDS but with a low PEEP and a slightly higher rate
      - May require high-frequency ventilation
      - Surfactant administration therapy every 6 hours for up to four doses has been shown to reduce the risk of air leaks, lessen the need for ECMO, and improve gas exchange
      - Lung lavage with surfactant has been shown to improve clinical outcome
    - iNO if PPHN develops
    - Sedatives and paralytics
    - Fluid balance critical: cerebral edema and inappropriate secretion of antidiuretic hormone occur following asphyxia
    - Observe for seizure activity and metabolic derangements if severe MAS
  - Complications
    - Pulmonary air leaks
    - PPHN
    - Pulmonary barotrauma/BPD
    - Metabolic: acidosis, hypoglycemia, hypocalcemia
    - Neurologic: depends on degree of asphyxia
  - Outcome
    - Mild cases have excellent prognosis
    - Severe: neurologic sequelae common

### Persistent Pulmonary Hypertension of the Newborn

- Definition:
  - PPHN is caused by right-to-left shunting through the fetal shunts at the atrial and ductal levels, secondary to persistent elevation of pulmonary vascular resistance and pulmonary artery pressure
  - 77% are diagnosed in the first 24 hours of life, 93% diagnosed by 48 hours of life, and 97% of the infants by 72 hours of life
  - Incidence is 1.9 per 1000 live births
- Etiology:

- Maladaptation: PVR stays high due to active vasoconstriction which may be transient or persistent
  - Hypoxia/perinatal asphyxia
  - Pulmonary parenchymal disease
  - Bacterial sepsis: endotoxin-mediated myocardial depression and pulmonary vasospasm
  - Prenatal pulmonary hypertension: premature closure of ductus arteriosus.
- Maldevelopment:
  - Abnormal pulmonary blood vessels. Musculature is hypertrophied and extends into normally nonmuscularized arteries.
    - Intrauterine asphyxia: increases systemic arterial blood pressure in the fetus and diverts more blood to the lung
    - Fetal ductal closure
    - Congenital heart disease
    - Underdevelopment: decreased number of pulmonary blood vessels.
      - Pulmonary hypoplasia
      - Space-occupying lesions
- Pathophysiology
  - Pulmonary arterial pressure remains elevated
  - Blood shunted right to left across the ductus arteriosus and foramen ovale
  - Persistently high PVR increases right ventricular afterload and oxygen demand
    - At same time blood flow to the lung is decreased → hypoxemia, acidemia and lactic acidosis
  - Impairs oxygen delivery to the right ventricle, posterior wall of left ventricle and subendocardial regions of right ventricle
  - Increased right ventricular afterload displaces septum into the left ventricle, which impairs left ventricular filling and decreases cardiac output
- Clinical Presentation
  - Late preterm, term or post-term neonate with worsening cyanosis in first 24 hours
  - History of hypoxia/asphyxia
  - Tachypnea, retractions
  - Cyanosis intense at birth, or becomes progressively worse due to increasing right to left shunting
  - Despite increasing FiO<sub>2</sub>, neonate continues to have hypoxemia
  - Severe cases: decreased peripheral perfusion and hypotension
  - Cardiovascular abnormalities
    - Blood pressure is usually lower than normal.
    - Electrocardiogram will show a right axis deviation.
    - Systolic murmur is frequently heard, usually from a PDA, foramen ovale, or tricuspid insufficiency.
    - Echocardiogram: dilated right side of the heart, evidence of pulmonary hypertension and shunting across the foramen ovale.



- Diagnosis
  - Suspect on basis of history and clinical presentation
  - Arterial blood gases: acidosis, hypoxia and increased PaCO<sub>2</sub>
    - Simultaneous pre- and post-ductal ABGs: difference of > 15 mm Hg documents ductal shunting
    - Pre- and post-ductal pulse oximetry
  - CBC with differential to detect:
    - Anemia
    - Polycythemia
    - Sepsis/pneumonia
  - Chest xray:
    - Prominent main pulmonary artery segment
    - Mild to moderate cardiomegaly
    - Variable pulmonary vasculature
    - Signs of left ventricular dysfunction → pulmonary venous congestion and cardiomegaly
  - Echocardiogram: rules out structural heart defects, evaluates cardiac function, measures pulmonary artery pressures and diagnoses right to left shunting at the level of the foramen ovale and ductus arteriosus

#### Treatment Strategies

- Main goal: correct hypoxia and acidosis, promote pulmonary vascular dilation
- Management depends on the cause of PPHN
- Supportive Care:
  - Usual NICU care
- UAC placement: continuous blood pressure monitoring
- Pre-and post-ductal pulse oximetry/transcutaneous monitoring
- Ventilation: Conventional or High-frequency
  - Oxygen: keep PaO<sub>2</sub> > 90 mm Hg
  - Hyperventilation to keep PaCO<sub>2</sub> in low normal range
  - iNO: selective pulmonary vasodilator
  - ECMO
- Minimal stimulation and handling
- Pharmacologic Support
  - Sedatives, paralytics and analgesics
  - Pulmonary vasodilators (iNO previously discussed)
    - Phosphodiesterase inhibitors
      - Sildenafil may be as effective as iNO in improving pulmonary vasodilation.
        - It has been suggested as adjunctive therapy to facilitate weaning of iNO.
      - Milrinone improves oxygenation without decreasing systemic blood pressure. Loading dosage: 75 mcg/kg given over 1 hour followed by 0.5 to 0.75 mcg/kg/min

- Vasopressors

Table 23-21 VASOPRESSOR RESPONSE IN THE NEONATE	
DRUG DOSE	DISADVANTAGES
<b>Dopamine</b>	
<4 µg/kg/min: renal vasodilation, mesenteric and cerebral vasodilation (effects unknown) plus increase in cardiac output	May decrease systemic arterial pressure
5-20 µg/kg/min: increase in cardiac output depending on myocardial norepinephrine	Loss of renal and mesenteric perfusion
>20 µg/kg/min: systemic arterial pressure increases more than pulmonary artery pressure	Cardiac output may decrease Myocardial oxygen consumption increases Marked increase in left ventricular afterload Dysrhythmias noted
<b>Dobutamine</b>	
10 µg/kg/min: increases cardiac contractility directly; cardiac output increases depending on myocardial catecholamine stores	No selective renal or mesenteric vasodilation Tends to increase skeletal blood flow at the expense of viscera Increase in pulmonary artery pressure
<b>Isoproterenol</b>	
0.05-1.0 µg/kg/min: lowers pulmonary vascular resistance in pulmonary hypertensive and vascular disease in child and adult; lowers hypoxemia-induced pulmonary vascular resistance in animal models	Dysrhythmias No specific vasodilation effects
<b>Nitroprusside</b>	
0.4-5.0 µg/kg/min: cardiac output increases because of decreased left ventricular afterload; systemic vascular resistance (indicated by blood pressure) decreases because of decrease in left ventricular afterload	Systemic vascular resistance remains constant if CO <sub>2</sub> increases

Modified from Drummond W: *Clin Perinatol* 11:715, 1984.

Gardner, Carter, Enzman-Hines and Hernandez, 2016, pg 635

- Outcome
  - iNO has reduced the need for ECMO and has reduced the occurrence of chronic lung disease
  - Sensorineural hearing loss higher for those with PPHN
  - Need for remedial assistance in school is increased in PPHN survivors

### Pneumonia

- Infection of the lung
- Etiology:
  - Intrauterine
    - Infection of fetal membranes, transplacental transmission
    - Aspiration of infected amniotic fluid
    - Prolonged rupture of membrane
  - Neonatal
    - Acquired during nursery stay → equipment, caregivers, etc
  - Risk greatest in premature due to immature immune system and lack of maternal antibodies.
  - Immature ciliary system in lung
  - Insufficient macrophages for bacterial clearance

- Pathophysiology
  - Congenital Pneumonia:
    - Evidence of chorioamnionitis
    - Prolonged rupture of membranes > 24 hrs → ascending infection. If mom in active labor, contamination occurs faster
    - Usually has evidence of illness from birth
  - Neonatal Pneumonia
    - Infection occurs days to weeks after birth
    - Organism acquired from caregivers, parents, equipment, etc
    - Bacterial and viral pathogens responsible
    - Common bacterial: Group B streptococcus, *E. coli*, *Klebsiella*, *Pseudomonas*, *Serratia marcescens*, *Staphylococcus epidemidis*, *Listeria*, *Enterobacter*, *Treponema pallidum* and *Staphylococcus aureus*
    - Common viral: herpes, CMV, varicella zoster, respiratory syncytial virus, enterovirus, adenovirus
- Clinical Presentation
  - Prolonged labor/prolonged rupture of membranes
  - Maternal fever, foul smelling amniotic fluid; Fetal tachycardia
  - May require resuscitation in delivery room
  - Tachypnea, grunting, retractions, cyanosis, hypoxemia, hypercapnia
  - Decreased breaths sounds, fine/coarse rales
  - Severe involvement: shock-like syndrome within first 24 hours
  - Chest xray: variable
- Diagnosis
  - Blood cultures
  - Urine: latex particle agglutination (LPA) and counterimmunoelectrophoresis (CIE) to detect GBS.
  - Polymerase chain reaction (PCR): herpes
  - CBC and differential
  - ABGs: metabolic acidosis
  - Tracheal aspirate for culture
  - Lumbar puncture when stable
- Treatment Strategies
  - Antibiotics
  - Oxygen/assisted ventilation – correct respiratory and metabolic acidosis
  - Monitor blood pressure/treat hypotension
  - Maintain temperature
  - Observe for disseminated intravascular coagulation if shock present
- Complications
  - Meningitis
  - Septic Shock
  - DIC

- PPHN

### Bronchopulmonary Dysplasia

- Definition: BPD Criteria establishes criteria for mild, moderate and severe BPD

<b>Definition of Bronchopulmonary Dysplasia: Diagnostic Criteria</b>		
<b>Gestational Age</b>	<b>&lt;32 Weeks</b>	<b>≥32 Weeks</b>
Time point of assessment	36 weeks' PMA or discharge to home, whichever comes first	>28 days but <56 days of postnasal age or discharge to home, whichever comes first
	Treatment with oxygen >21% for at least 28 days <b>plus</b>	
Mild BPD	Breathing room air at 36 weeks' PMA or discharge, whichever comes first	Breathing room air by 56 days' postnatal age or discharge, whichever comes first
Moderate BPD	Need* for <30% oxygen at 36 weeks' PMA or discharge, whichever comes first	Need* for <30% oxygen at 56 days' postnatal age or discharge, whichever comes first
Severe BPD	Need* for ≥30% oxygen and/or positive pressure (PPV or NCPAP) at 36 weeks' PMA or discharge, whichever comes first	Need* for ≥30% oxygen and/or positive pressure (PPV or NCPAP) at 56 days' postnatal age or discharge, whichever comes first

Jobe AH & Bancalari E (2001). Bronchopulmonary dysplasia. *American Journal of Respiratory and Critical Care Medicine*, 163, 1723-1729.

- Incidence:
  - Estimates suggest that the rate of BPD is 42% in infants 501 to 750 g, 25% in infants 751 to 1000 g, and 11% in infants 1001 to 1250 g at birth
- Etiology/Pathophysiology:
  - Multifactorial, resulting from acute lung injury, arrested lung development, and abnormal repair processes that occur in the lung.
  - Maternal chorioamnionitis triggers an inflammatory response that may alter cell signaling pathways critical to development of lung alveoli and capillaries
  - Oxygen toxicity
    - Preterm infant has lower levels of antioxidant mediators and vitamins C and E, which have anti-inflammatory properties
    - High inspired oxygen concentrations
      - Cause production of reactive oxygen species (ROS) and release of chemotactic factors that attract neutrophils to the lung, initiating the inflammatory cycle.
      - Ongoing inflammatory process in the lung causes and continues parenchymal damage
      - Low birth weight infants receiving little or no oxygen in the first week of life are still at risk of developing BPD
      - When ROS injure epithelial and endothelial cells, pulmonary edema and activation of inflammatory cells results
      - Pulmonary edema results in a leak of proteins into the alveoli, which inactivates surfactant, exacerbating the surfactant deficiency of prematurity
  - Assisted ventilation with positive pressure results in lung damage

- Intubation interrupts normal pulmonary function
      - Mucociliary function is damaged
      - Dead space is increased
    - Barotrauma
      - Related to the intensity and amount of time exposed to positive pressure ventilation
      - Repeated distention of distal airways during mechanical ventilation of infants with poor alveolar compliance results in ischemia.
      - Alveolar capillary unit is further disrupted by mechanical ventilation, leading to pulmonary edema.
    - Ventilation using volumes that are too low results in cycles of alveolar collapse (atelectrauma), which is as damaging as overventilation
  - Increased shunting (left to right) via a PDA
  - Excessive fluid intake
  - Gestational age
    - More likely in infants weighing less than 1500 g.
    - Damage may occur with less exposure to the previously noted factors in the infant less than 1250 g.
  - Nutritional deficits
    - Adequate caloric and protein intake is required for cell growth and division.
    - Vitamin A is essential for differentiation, integrity, and repair of respiratory epithelial cells.
    - Poor nutrition may impair macrophages and neutrophil and lymphocyte function.
    - Infants who develop BPD are more likely to have had a lower protein intake and received fewer calories in the first week of life
  - Clinical presentation.
    - Predisposing risk factors.
      - Oxygen, intubation, and assisted ventilation.
      - Gestational age less than 32 weeks.
      - Nutritional deficiencies.
      - Underlying lung disease.
      - Air leaks.
      - Infection.
      - PDA.
    - Increase in ventilatory requirements or inability to be weaned from ventilator.
    - Hypoxia, hypercapnia, and respiratory acidosis.
    - Audible crackles and wheezing.
    - Retractions.
    - Increased secretions
    - Bronchospasm
    - Electrocardiogram showing right ventricular hypertrophy and right axis deviation.
    - CXR showing hyperinflation, infiltrates, blebs, and cardiomegaly.
    - Fluid intolerance, as evidenced by increase in weight, edema, and decrease in urine output, despite no change in fluid intake.

- Diagnosis
  - Diagnosis of exclusion.
  - CXR findings
  - Clinical signs: tachypnea, hypercapnia, hypoxia, crackles
- Complications
  - Intermittent bronchospasm.
  - Inability to be weaned from ventilator and/or oxygen supplementation.
  - Recurrent infections.
    - Pneumonia.
    - Upper respiratory tract infections
    - Otitis media.
  - Congestive heart failure from cor pulmonale.
  - BPD “spells.”
    - Becomes irritable, agitated, and dusky; has increased respiratory effort, hypoxia, and hypercapnia.
  - Gastroesophageal reflux.
  - Developmental delays.
- Prevention
  - Prevention of preterm birth is the single most important strategy
  - Prophylactic surfactant therapy
  - Routine use of steroids for prevention or treatment of chronic lung disease in preterm infants is not recommended
  - Gentle ventilation, permissive hypercapnia, and early extubation
    - Synchronized intermittent mandatory ventilation is associated with less severe BPD
  - Aggressive nutrition to promote lung growth, maturation, and repair, and protect the damaged lung from infection
- Management
  - Minimize length of exposure to mechanical ventilation.
  - Intubation for surfactant administration and extubation to nCPAP
  - Continue respiratory support as needed.
    - Some very low birth weight infants can be supported by nCPAP
    - Use synchronized modes of ventilation with the minimal amount of pressure and volume needed to deliver adequate tidal volumes
  - Oxygen administered as needed to prevent hypoxia and avoid cor pulmonale.
    - Appropriate target for oxygen saturation has not been established.
      - Current recommendations: 88% to 92%
    - Avoid large variations in oxygen saturation
    - Wean using pulse oximetry and occasional monitoring of blood gas.
  - Diuretics may be used to control fluid retention leading to pulmonary edema.
    - Furosemide (Lasix) is used most often.
      - Decreased calcium reabsorption leads to hypercalciuria, bone demineralization, and renal calcifications
      - Metabolic alkalosis may result in compensatory hypoventilation
      - Ototoxicity may occur

- Monitor for hyponatremia, hypokalemia, and metabolic alkalosis.
  - Fluid restriction may help reduce pulmonary edema and right-sided heart failure.
- Cardiac evaluation for complications.
  - Cor pulmonale (right ventricular hypertrophy) due to prolonged pulmonary hypertension.
  - Electrocardiography and echocardiography should be performed periodically to evaluate the progression/development of right ventricular hypertrophy.
- Optimal nutrition to compensate for increased work of breathing and fluid restriction.
  - May need 150 to 180 kcal/kg/day.
- Complications
  - Impairment of growth
  - Possible increase in neurodevelopmental abnormalities
  - Hypertension
  - Myocardial hypertrophy
  - Gastrointestinal hemorrhage and perforation
  - Gastric ulcerations
  - Nosocomial sepsis
  - Hyperglycemia
  - Transient adrenal suppression
  - High risk for RSV outbreaks
    - Require Palivizumab (Synagis)
- Outcome
  - Pulmonary function:
    - Abnormalities of the chest wall, alveoli, and small airways persist
    - Asthma is more prevalent
  - Neurologic and developmental sequelae.
    - Demonstrate deficits in intelligence; reading, mathematics, and gross motor skills; and special education services may be required.
    - Cerebral palsy
  - Sensorineural hearing loss and visual difficulties

### Air Leak Syndromes

- Etiology/Pathophysiology
  - Most common serious complication of assisted ventilation
  - Incidence: 1% to 2% of all newborns; however, many are asymptomatic
    - In infants receiving CPAP, bag-and-mask ventilation, or mechanical ventilation, the incidence ranges from 16% to 36%
  - Alveoli become overdistended → connective tissue around pulmonary blood vessels attempt to expand with alveoli, blood vessels stay the same size → unbalanced forces across the base of the alveoli → rupture

- With rupture, air moves from alveoli into connective tissue surrounding arterioles, traveling to the hilum
- Presentation/Diagnosis/Treatment
  - Pulmonary Interstitial Emphysema
    - Gas trapped in the interstitium or lymphatics
    - Decreases compliance, tidal volume, alveolar ventilation
    - Can progress to pneumomediastinum and pneumothorax
    - Impairs cardiac output and increases PVR
    - Diagnosis
      - Chest xray: microcystic areas throughout lung extending out from hilum
        - Flattened diaphragm and hyperinflated lungs
      - Unilateral: overdistention of affected lung, mediastinal displacement, compression atelectasis of contralateral lung, and ventilation/perfusion inequalities
    - Treatment:
      - Short  $I_T$  - 0.15 sec
      - High-frequency ventilation
      - Place affected side in dependent position
  - Pneumomediastinum
    - Doesn't usually have enough tension to cause distress
    - Anticipate with meconium aspiration
    - Symptoms: tachypnea, muffled heart sounds, cyanosis
    - Increased anteriorposterior diameter of chest
    - Indistinct heart sounds
    - Diagnosis:
      - Chest xray: "spinnaker sail sign": thymus lifted from heart
    - Treatment:
      - Usually not treated
      - Typically resolves spontaneously
  - Pneumothorax
    - Spontaneous:
      - Leak into intrapleural space
      - Typically asymptomatic
    - Tension:
      - Interpleural collection of air above atmospheric pressure
      - Pressure may collapse the affected lobe/lung, shift the mediastinum and compress heart/blood vessels
      - Risk factors: early gestational age, RDS, high PIPs, PIE and/or pneumomediastinum
      - Symptoms:
        - Rapid deterioration
        - Hypoxia and hypercapnia occur with circulatory collapses
        - Sudden cyanosis



- Hypotension, bradycardia/tachycardia, decreased pulse pressures
- Decreased breath sounds, bulging of the affected side, shift of the PMI
- Abdomen becomes tense and distended
- Treatment:
  - Transillumination
  - Confirm by chest xray stat
  - Needle aspiration
  - Chest tubes connected to underwater seal drainage with continuous negative pressure of 10 – 15 cm H<sub>2</sub>O
    - Leave in place until air stops bubbling for at least 24 hours
    - Place to water seal x 24 hours and observe for reaccumulation of air
  - Remove chest tube 12 – 24 hours after tube placed to water seal if free from symptoms
  - Continued ventilatory management:
    - Conventional: decrease pressures, increase oxygen, decrease I<sub>T</sub>
    - Use of high-frequency ventilation
- Pneumopericardium
  - Interstitial air moves along the great vessels and ruptures into pericardial sac
  - Life threatening
  - Symptoms:
    - Bradycardia, cyanosis, muffled/absent heart sounds
    - Hypotension, weak pulses, decreased pulse pressures
    - Metabolic acidosis
  - Diagnosis:
    - Chest xray: halo appearance around the heart
  - Treatment:
    - Emergency treatment by placing a long catheter or chest tube into the pericardial sac with continuous negative pressure

#### Pneumoperitoneum

- Etiology:
  - Pulmonary
    - Directly related to ventilator therapy
    - Associated with pneumomediastinum and pneumothorax
  - GI etiology: perforation
    - Requires surgical intervention
- Diagnosis:
  - Xray: air appears as dark cloud in peritoneum
- Treatment:
  - Paracentesis only necessary if venous return to heart impeded or respiratory status compromised

## Pulmonary Hemorrhage

- Localized areas of bleeding into alveoli
- Etiology
  - Occurs as a complication of other disorders:
    - Prematurity, IVH, asphyxia, PDA, surfactant replacement
  - Trauma due to improper suctioning technique
  - Due to large increase in capillary hydrostatic pressure
    - Causes capillary rupture and fluid transudation from other capillaries
- Clinical Presentation/Diagnosis
  - Sudden, severe respiratory distress
  - Bright red blood suctioned from trachea
- Treatment
  - Assisted ventilation to maintain gas exchange and PEEP
  - Evaluate hemoglobin/hematocrit.
  - Identify any clotting abnormalities
  - Treat underlying disease
- Complications/Outcome
  - Death if massive hemorrhage
  - Small hemorrhage: outcome dependent on underlying disease

## Non-Pulmonary Causes of Respiratory Distress

### Choanal Atresia

- Etiology/Pathophysiology
  - Persistence of the bucconasal membrane causing blockage or narrowing
  - May be membranous or bony
  - Associated with anomalies
    - CHARGE (Colobomas of the eyes, congenital Heart disease, choanal Atresia, Retardation of physical and mental growth, and Ear anomalies associated with deafness)
    - Treacher Collins
- Clinical Presentation
  - Signs of distress may be intermittent if unilateral
  - Chest retractions and cyanosis, especially during feedings
  - Distress is relieved when the mouth is open/crying
  - Catheter cannot be passed through the nasal passages to the posterior oropharynx → diagnostic
- Diagnosis:
  - Computed tomography (CT)
- Treatment:
  - Use of oral airway and keeping prone position

- Intubation if placement of an oral airway is difficult
- Surgical correction:
  - Perforation of the obstruction and serial dilation by use of obturators

Other non-pulmonary causes of respiratory distress:

- Upper Airway
  - Micrognathia
    - Defined as mandibular undergrowth.
    - Occurs with certain syndromes and sequences such as Pierre Robin syndrome, trisomy 18, trisomy 22, and cri-du-chat syndrome
    - Airway distress may be alleviated by prone positioning.
    - Use of an oral airway or endotracheal tube
    - Generally mandibular growth “catches up” by 6 to 12 months of age.
  - Cystic hygroma
    - Form of cystic lymphangioma, with benign water cysts occurring most frequently in the neck (80%)
    - Usually seen at birth
    - Mass will occupy the submandibular region and may compromise the airway in 25% of cases.
    - Symptoms depend on the size and location.
    - Treatment is related to complications.
      - If infant is free of symptoms, surgical excision is performed between 4 and 12 months of age.
  - Obstruction of larynx or trachea
  - Tracheoesophageal fistula

Thoracic Conditions

- Cystic adenomatoid malformation
- Congenital lobar emphysema

## HEMATOLOGIC SYSTEM REVIEW

Development of Blood Cells

- Hematopoiesis
  - Formation, production and maintenance of blood cells
- Erythropoiesis
  - Production of red blood cells
  - Regulated by erythropoietin, which is regulated by hypoxia
    - Produced in liver and extrarenal sites during fetal life
    - Postnatally, produced in kidney
    - Increase production: hypoxia; anemia
    - Decrease production: hypertransfusion

- Increased: Down Syndrome, IUGR and those born to women with diabetes and PIH
- Hemoglobin
  - Major iron-containing component of RBCs
  - Carries oxygen to tissues
- Hematocrit
  - Percentage of RBCs in a given volume of blood
  - Normal: 48 – 60%
- Red Blood Cells
  - Function
    - Oxygen transport via oxyhemoglobin
    - Carbon dioxide transport via carboxyhemoglobin
    - Carbon dioxide reacts with water to form carbonic acid; reaction catalyzed by carbonic anhydrase in cytoplasm of RBCs
    - Carbonic acid dissociation to form bicarbonate ions
    - Buffering protons: binding with hemoglobin to form acid hemoglobin and by reaction with bicarbonate ions
  - Life span proportional to gestational age
    - Term: 60- 70 days
    - Preterm: 30 – 50 days
  - Nucleated RBCs
    - Circulating immature RBCs
    - Increase: hemolysis, acute blood loss, hypoxemia, sepsis
- Platelets
  - Small, nonnucleated, disk-shaped cells
  - Aid in hemostasis, coagulation and thrombus formation
  - Circulate for 7 – 10 days prior to being removed by the spleen
  - Normal: 150,000 – 400,000 / mm<sup>3</sup>
- Blood Volume
  - Factors affecting blood volume
    - Gestational age
      - Term: ~ 80-100 ml/kg
      - Preterm: ~ 90 - 105 ml/kg
    - Placental transfusion
  - Maternal-fetal hemorrhage
  - Twin-twin transfusion
  - Placenta previa or abruptio placenta
  - Nuchal cord
  - Iatrogenic loss

### **Anemia**

- Decreased hemoglobin concentration and/or decreased number of RBCs
- Decreases the ability of blood to carry oxygen to the tissues
- Etiology:
  - 3 major causes: hemorrhage, hemolysis, underproduction of RBCs
  - Hemorrhage

- Fetal-maternal
- Twin to twin: hemoglobin difference > 5 g/dl between twins
- Placental: placenta previa; abruptio; umbilical cord rupture
- Internal: IVH, subgaleal, organ rupture (adrenal, kidney)
- External: phlebotomy; iatrogenic (catheter losses)
- Hemolysis
  - Blood group incompatibilities
    - Rh incompatibility
      - Fetal blood cells with Rh antigen enter maternal circulation
      - Maternal immune system produces antibodies against the foreign fetal antigen
      - Subsequent pregnancies, maternal antibodies enter fetal circulation and destroy fetal RBCs
      - Predisposing factors
        - Previous pregnancy or abortion
        - Fetal-maternal hemorrhage during pregnancy
        - Delivery
        - Amniocentesis, chorionic villus sampling
      - Clinical presentation
        - Anemia
        - Tissue hypoxia, acidosis
        - Congestive heart failure and hydrops fetalis
        - Ascites, pleural effusion
        - Hepatosplenomegaly
        - Petechiae
        - Hypoglycemia
        - Positive direct Coombs test result
      - Treatment Strategy
        - Anti-D immune globulin (RhoGAM)
          - Destroys fetal RBCs in maternal circulation
          - 90% effective in prevention of sensitization
    - ABO incompatibility
      - Mother with O blood type; fetus with A or B blood type
      - Maternal anti-A and anti-B antibodies destroy fetal RBCs
      - Protective against Rh disease
      - Clinical presentation
        - Mild hemolysis, anemia, reticulocytosis
        - Hyperbilirubinemia
    - Glucose-6-phosphate dehydrogenase (G6PD) deficiency
      - Most common inherited disorder of RBCs
      - Interaction of intracellular abnormality (deficiency of red cell enzyme) and extracellular factor (exposure to oxidant stressor) causes hemolysis and shortened RBC life
      - Most common in American Black neonates (10-15%)
    - Infection
  - Underproduction: Anemia of Prematurity

- During first 2 – 3 months, hemoglobin concentration decreases to its lowest values
    - Rates of decline and nadir are inversely proportional to gestational age
  - Iatrogenic postnatal phlebotomy
    - Excessive amounts of blood removed for diagnostic tests
- Clinical Presentation
  - Varies with volume of hemorrhage and time period over which blood is lost
  - Acute blood loss
    - Pallor initially, then cyanosis, desaturations
    - Shallow, rapid, irregular respirations
    - Tachycardia, weak peripheral pulses, hypotension
    - Hemoglobin concentration may be normal initially
  - Chronic blood loss
    - Pallor without signs of distress
    - Normal blood pressure
    - Low hemoglobin
- Treatment Strategies
  - Family history
  - Maternal blood type
  - Physical examination: Cephalohematoma, jaundice, abdominal distension or mass (liver, spleen rupture), petechiae, etc
  - Diagnostic testing
    - Hemoglobin. Values < 13 g/dl abnormal in first week of life
    - Reticulocyte count: persistently elevated with ongoing RBC destruction
    - Blood type
    - Coombs test:
      - Positive result on direct Coombs: presence of maternal IgG antibodies on neonatal RBC
      - Positive result on indirect Coombs: antibodies against infant's RBCs are present in maternal blood
    - Kleihauer-Betke test: fetal hemoglobin in maternal blood
  - Emergent replacement for acute loss resulting in hypovolemia
    - Whole blood or combination of packed red blood cells with crystalloid or colloid
      - Group O, Rh negative
      - 10 – 20 ml/kg
  - Non-emergent replacement transfusion
    - Clinical decision based on adequacy of tissue oxygenation

### **Mechanisms of Blood Coagulation**

- Deficiencies in newborn clotting mechanisms:
  - Transient decreased platelet function
  - Transient deficiency of clotting factors II, VII, IX, X, XI and XII
    - Immaturity of hepatic enzymes
    - Transient deficiency of vitamin K

- Hemostatic mechanisms
  - Vascular
    - Damaged vessel contracts
  - Intravascular
    - Platelet plug formation
  - Extravascular
    - Compression by surrounding tissue
    - Release of tissue thromboplastin by injured tissue

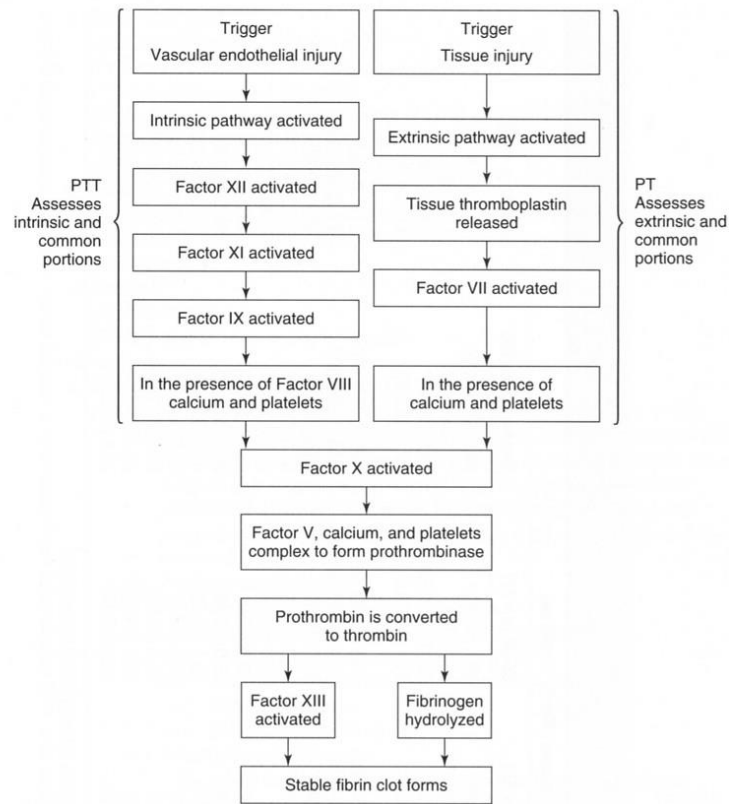


Figure 31-2 Fibrin clot formation through activation of intrinsic or extrinsic pathways of coagulation process

Verklan and Walden, 2015, p 668

- Exposed collagen from broken blood vessel → vessel constriction and adhesion of platelets → primary hemostatic plug
  - Clotting factors activated (XII and XI) → activate factor X
  - Intrinsic system
- Damage to tissue around damaged blood vessel releases tissue thromboplastin → factor VII → activates factor X
  - Extrinsic system
- Activated factor X with factor V converts factor II (prothrombin) to thrombin → fibrinogen (factor I) broken into loose fibrin and converted into fibrin by factor XIII

- Antithrombin III, protein S and protein C control clotting
  - Block activity of thrombin
  - Neutralize activated factors V and VIII
- Plasminogen activated to plasmin → dissolves fibrin into fibrin-split products → have an anticoagulant effect

### Screening coagulation tests

- Platelet count
- Partial thromboplastin time
  - Measures the time until a fibrin clot forms
  - Prolonged
    - Defect in intrinsic pathway (VIII, IX, XI or XII)
    - Defect in common pathway (I, II, V, X)
- Prothrombin time
  - Measures time until formation of fibrin clot
  - Measures factor VII (extrinsic system) and common pathway
- Fibrinogen
  - Evaluates circulating level of fibrinogen
  - Required for clot formation
- FSPs
  - Used to assess fibrinolytic activity

DESCRIPTION	PTT	PT	TT	FIB	D-DIMER	PLT Ct
Healthy term	N-↑	N-↑	↑	NL	Neg	NL
Healthy preterm	↑↑	N-↑	↑	NL	Neg	NL
Vit K deficiency	↑↑	↑↑↑	↑	NL	Neg	NL
Liver disease	↑↑	↑↑↑	↑↑-↑↑↑	↓	Pos	↓
Hemophilia	↑↑↑	N-↑	↑	NL	Neg	NL
DIC	↑↑↑	↑↑	↑↑	↓	Pos	↓↓

*Fib*, Fibrinogen; *N*, normal; *Plt Ct*, platelet count; *PT*, prothrombin time; *PTT*, partial thromboplastin time; *TT*, thrombin time; ↑, mildly prolonged; ↑↑, moderately prolonged; ↑↑↑, severely prolonged; ↓, decreased.

Gardner, Carter, Enzman-Hines and Hernandez, 2011, pg 523

### Vitamin K-Dependent Bleeding

- Etiology
  - Primary vitamin K deficiency
    - Required for activation of clotting factors II, VII, IX and X, and of proteins C and S after liver synthesis
  - Suppression of bacterial synthesis
    - Intestinal flora is required for Vitamin K synthesis
    - Antibiotic therapy can alter normal intestinal colonization
- Clinical Presentation
  - Bleeding that begins at 24-72 hours of age, and is localized or diffuse
  - Local or diffuse oozing



- Diffuse ecchymosis, petechiae
- Abdominal distention
- Jaundice
- Diagnostic Studies
  - PT and PTT are prolonged
  - Levels of Vitamin K-dependent factors are low
- Differential Diagnosis
  - Decreased absorption of Vitamin A
    - Biliary atresia
    - Cystic fibrosis
    - Cholestasis
  - Pharmacologic antagonism of Vitamin K
    - Anticonvulsants and anticoagulants
      - Induce hepatic enzymes and increase vitamin K degradation
      - Inhibit vitamin K transport across the placenta
      - Depress vitamin K-dependent coagulation factors
- Complications
  - Anemia
  - Intraventricular hemorrhage
- Patient Care Strategies
  - Administer vitamin K 0.5 – 1 mg IM

### **Disseminated Intravascular Coagulation**

- Is a secondary process related to a variety of primary disease states
- Etiology
  - Inappropriate, systemic activation of coagulation → generation of excess thrombin and decreased production of anticoagulant factors
  - These changes lead to diffuse intravascular thrombus formation and consumption of coagulation factors and platelets
  - Inhibition of fibrinolytic pathway due to increased concentrations of plasminogen activator inhibitors prevents removal of fibrin from small blood vessels → extensive thrombosis and organ failure
  - Consumption of platelets and coagulation factors may cause severe, diffuse hemorrhage
  - Precipitating factors: sepsis, hypoxia/acidosis, tissue injury (birth trauma), thrombocytopenia
- Clinical Presentation
  - Sick neonate
  - May have laboratory evidence with no/little clinical signs
  - Multiorgan failure and bleeding from multiple sites
    - Oozing from mucus membranes, sites of invasive procedures
    - Petechiae, ecchymosis, hematuria
    - Hemorrhage
  - Platelet count decreased
  - PT and PTT significantly prolonged

- Fibrinogen low
- Fibrinogen-degradation products increased but are not specific markers of DIC.
- D-Dimer is a sensitive marker for endogenous thrombin/plasmin production
  - Detect much milder forms of DIC.
- Treatment Strategies
  - Aggressive treatment of underlying primary disorder
  - Replacement transfusion with significant bleeding
    - Whole blood:
    - PRBCs
    - Platelets
  - Replacement of clotting factors
    - FFP
    - Platelets
    - Cryoprecipitate
    - Antithrombin III
  - Heparin therapy controversial
- Complications
  - Microvascular thrombosis
  - Organ failure due to ischemia and necrosis

### **Thrombocytopenia**

- Significant decrease in platelet count to  $< 100,000/\text{mm}^3$
- Incidence: 1% to 2% of healthy term neonates; up to 35% of critically ill neonates
- Etiology
  - Platelet destruction
    - Maternal autoantibodies
      - Idiopathic thrombocytopenic purpura
      - Systemic lupus erythematosus
    - Neonatal conditions
      - Neonatal alloimmune thrombocytopenia
        - Fetal platelets contain an antigen lacking in the mother
        - Fetal platelets enter the maternal circulation—mom produces antibodies—maternal antibodies cross into fetal circulation and destroy fetal platelets
      - Infection
        - Bacterial or TORCH
      - Thrombotic disorders
        - Renal vein thrombosis
        - Microvascular disease
      - Birth asphyxia
  - Impaired platelet production (very rare)
  - Platelet interference
    - Maternal drug ingestion
- Clinical presentation

- Petechiae, purpura
- Ecchymosis over presenting part
- Cephalohematoma
- Bleeding
- Jaundice
- IUGR, microcephaly, hepatosplenomegaly
- Platelet count low
- PT and PTT normal
- Bleeding time prolonged
- Treatment Strategies
  - Treatment of underlying disease. Most thrombocytopenias are secondary to other disorders
  - Platelet transfusion
    - Keep platelet count > 30,000 first 24 hours, > 50,000 if surgery necessary or at risk for IVH
- Complications
  - Increased incidence of IVH in infants < 1250 g
  - Entrapped hemorrhage
  - Anemia
  - Hyperbilirubinemia

### **Polycythemia**

- a condition in which there is too much circulating RBC mass.
- Blood viscosity increases when
  - Hematocrit is > 65%
  - Venous hemoglobin is > 22 g/dl
- Incidence: 0.4% to 12% of healthy term newborns
- Etiology:
  - Intrauterine hypoxia, placental insufficiency
  - Maternal-fetal and twin-to-twin transfusion
  - Maternal diabetes
  - Delayed cord clamping
- Clinical Presentation
  - Asymptomatic
  - Plethoric
  - Cyanosis
  - Respiratory distress
  - Tachycardia, congestive heart failure
  - Hypoglycemia
  - CNS abnormalities
- Diagnostic studies
  - Physical examination: normal except for plethora and possibly cyanosis
  - Venous hemoglobin concentration and hematocrit are elevated
- Treatment Strategies

- Normal saline bolus 10 ml/kg for asymptomatic infants with a hematocrit greater than 70% or those with symptoms and a hematocrit between 65% and 70%
- Partial exchange transfusion
  - Not typically done for asymptomatic infants
  - Reduce the hemocrit level to < 60%
- Supportive treatment of symptoms—hypoglycemia, resp distress, etc.
- Complications
  - Hyperbilirubinemia
  - Hypoglycemia
  - Hyperviscosity syndrome—decreased blood flow, vascular thrombosis (renal, cerebral, mesenteric), neurological sequelae
  - Outcome:
    - Neonates with proven hyperviscosity are at risk of an adverse neurologic outcome

### **Transfusion Therapies**

- Recommendations for use of blood components:
  - Develop and document criteria indicating need.
  - Use only the blood components required for therapy.
  - Use crystalloid or nonblood colloid whenever possible.
  - Use Universal Precautions when handling blood products
- Informed consent
  - Infection
    - Blood is screened for HIV types 1 and 2, hepatitis B virus, hepatitis C virus, human T-cell leukemia/lymphoma virus (HTLV), *Treponema pallidum* (syphilis), Chagas' disease (*Trypanosoma cruzi*), human T-lymphotropic virus and West Nile virus
    - Cytomegalovirus transmission can be prevented by using leukocyte-depleted, irradiated products or CMV seronegative blood
  - Transfusion Reactions are rare in the neonate
    - Transfusion-related acute lung injury (TRALI)
      - Pulmonary edema occurring within 6 hours following a transfusion.
  - Graft-versus-host disease
    - Immature immune system may not reject foreign lymphocytes; donor lymphocytes proliferate and damage the host
    - Clinical symptoms
      - appear within 100 days of transfusion
      - Rash, diarrhea, hepatic dysfunction and bone marrow suppression with generalized reduction in all cell lines
    - Gamma irradiation of blood products will prevent lymphocyte proliferation
- Hemodynamic complications
  - Fluid overload
    - Volumes should not exceed 20 mL/kg
  - Hypoglycemia, metabolic acidosis, hyperkalemia, and hypocalcemia.

- NEC: transfusion-related acute gut injury (TRAGI)
  - Possible relationship between RBC transfusions and late-onset NEC in low birth weight infants
- Replacement of blood volume
  - Whole blood
    - Increases Hct by ~ 35%
    - Treatment of massive hemorrhage, exchange transfusion
    - Amount will depend on reason for transfusion
  - PRBC
    - Improved oxygen-carrying capacity and tissue oxygenation
    - Relief of symptoms of anemia
    - Treatment of active bleeding, hemolytic disease
    - Volume: 10 – 20 ml/kg
  - Platelets
    - Improve coagulation
    - Treatment of hemorrhage caused by thrombocytopenia or platelet dysfunction
    - One unit provides ~  $5 \times 10^{10}$  platelets; should increase platelet count by 75,000
  - FFP
    - Replacement of clotting factors
    - Transfused in increments of 10 ml/kg to minimize fluid overload
  - Cryoprecipitate
    - Replaces factor I, factor VIII and factor XIII
    - Volume is 1 unit/kg = 15 ml
  - Albumin
    - Treatment of hypovolemia, third-space losses
    - 5% albumin 10 ml/kg

# CARDIOVASCULAR SYSTEM REVIEW

## Cardiac Physiology

### Fetal and Transitional Circulation

- Previously reviewed
  
- Cardiac Depolarization
  - Results from the electrical discharge across the myocardial cell
  - Measured by the ECG
  - Contraction usually follows depolarization
  - Strength of cardiac contraction measured by blood pressure or arterial pulse palpation
  - Cardiac electrical activity doesn't ensure adequate cardiac function
    - Congenital defects may result in arrhythmias or heart block
    - Electrolyte disturbances affect electrical activity
      - Hypokalemia / Hyperkalemia
      - Hypocalcemia / Hypercalcemia
      - Hypoxia
      - Acidosis
  
- Cardiac Output
  - Volume of blood ejected in one minute
  - $CO = \text{stroke volume} \times \text{heart rate (L/min)}$ 
    - Tachycardia improves CO if diastolic filling time is not decreased
  - Stroke volume fixed. Depends on 3 factors:
    - Preload:
      - Volume of blood in ventricles before contraction
      - Increased volume → lengthens contractile fibers → improved stroke volume
      - Neonatal heart has less contractile tissue and decreased myocardial compliance → difficult to increase cardiac output with volume infusion
    - Contractility:
      - Speed of ventricular contraction
      - Decreased contraction time → increased diastole → increased ventricular filling time (preload)
      - Influenced by:
        - Exogenous catecholamine → increases BP and CO
        - Decreased by acidosis, hypoxia, electrolyte disturbances, hypoglycemia
    - Afterload:
      - Resistance to blood leaving the ventricle
      - Increased with increased systemic/pulmonary vascular resistance → decreased stroke volume
      - Decreased by vasodilators

- Systemic: nitroprusside
- Pulmonary: Dobutamine, iNO
- Concepts of Blood Flow
  - Flow is directly proportional to pressure/resistance
  - Blood flow will always take the path of least resistance
  - If heart action remains unchanged, but vasoconstriction or dilation, or obstruction to flow changes, flow will change
  - Normal decline of PVR after delivery is influenced by prematurity, low birth weight and hypoxia episodes

## **Evaluation of the Cardiovascular System**

### History

- Age at which symptoms presented
- Feeding history
- Tachypnea and dyspnea
- Excessive perspiration
- Acrocyanosis vs cyanosis
- Maternal illness
  - Uncontrolled Diabetes
    - TGV.
    - VSD.
    - Cardiomyopathy.
    - Complex congenital heart disease.
  - Lupus
    - Congenital heart block and cardiomyopathy.
  - Viral and bacterial illnesses may directly and indirectly affect the fetal cardiovascular system.
- Family history
  - Incidence increases by 3- to 4-fold when a first-order relative (parent or sibling) has CHD
  - Risk increases by 10-fold if two first-order relatives have CHD

### Physical Examination

- Observation
  - Presence of stigmata
- Weight: regain birthweight by 7 – 10 days; gain an average of 30 g /day
- Vital signs recorded while asleep/resting
  - > 180 bpm → CHF, tachyarrhythmia
  - < 80 bpm → increased vagal tone, bradyarrhythmia
  - BP: both arms and a leg
- Universal pulse oximetry screening
  - To identify newborns at risk for HLHS, TOF, TGV, TAPVR, pulmonary atresia, critical aortic stenosis, truncus arteriosus
  - Implementation

- Should not be done until  $\geq 24$  hours of age in well-baby and intermediate care nurseries.
    - Monitor pulse oximetry of both the right hand (RH) (preductal) and either foot (postductal).
  - Negative screen – discharge home
    - Pulse oximeter reading is  $>95\%$  in RH or foot and difference between RH and foot is  $<3\%$ .
  - Suspicious screen – repeat screen in 1 hour.
    - Reading is  $90\%$  to  $95\%$  in RH and foot or there is  $\geq 3\%$  difference between RH and foot, repeat in 1 hour.
    - If second reading is the same, then repeat again in 1 hour.
  - Positive screen – refer for further testing
    - If pulse oximeter reading in RH or foot is less than  $90\%$ , further testing warranted.
- Evaluate colour of skin and mucus membranes
- Thorax:
  - Cardiac impulse
  - Palpate precordium
    - Tapping or rocking  $\rightarrow$  volume overload
    - Thrill  $\rightarrow$  AV valve regurgitation, VSD, PDA
- Auscultation
  - $S_1$ : loudest at apex at 4<sup>th</sup> intercostal space
    - Represent tricuspid and mitral closure
    - Usually heard as single sound
    - Split  $S_1 \rightarrow$  delayed tricuspid closure
    - Accentuated  $S_1$ 
      - Increased CO
      - Increased flow across atrioventricular valves
      - PDA, VSD with increased mitral flow, TAPVR, Tetralogy of Fallot
    - Diminished  $S_1$ 
      - Congestive heart failure
      - Myocarditis
      - Decreased atrioventricular conduction
  - $S_2$ : best heard at left upper sternal border
    - Represents aortic and pulmonic valve closure
    - Split sound is normal
    - Single sound with increased PVR
    - Splitting influenced by:
      - Abnormalities of aortic or pulmonic valves
      - Conditions altering PVR or systemic vascular resistance
    - Wide splitting
      - ASD, TAPVR, Tetralogy, pulmonary stenosis
    - Absent:
      - Pulmonary atresia, severe pulmonary stenosis
      - Aortic stenosis/atresia



- S<sub>3</sub>: due to increased flow across the AV valves from rapid, passive ventricular filling from the atria
  - Low-pitched, broad sound
  - Prominent when increased AV flow
    - Left to right shunts
    - Mitral valve insufficiency
- S<sub>4</sub>: occurs at final phase of ventricular filling and active atrial contraction during late diastole
  - Occurs just before S<sub>1</sub>
  - Low pitched
  - Rarely heard in neonate
  - Always pathologic → indicates decreased ventricular compliance
- Ejection clicks
  - Snapping sound just after first heart sound
  - Normal in first 24 hours of life, otherwise indicates cardiac disease
  - Associated with dilation of the great vessels or deformity of aortic or pulmonic valve
- Murmurs
  - Audible vibrations resulting from turbulence of blood flow
  - Noted in 50% of newborns
  - Due to:
    - Abnormal valves
    - Septal defects
    - Regurgitated flow through incompetent valves
    - High blood flow across normal structures
- Peripheral Pulses
  - Should be synchronous with equal intensity
  - Upper and lower extremity pulses should be palpated simultaneously and differences documented
  - Discrepancies (pulses > in upper extremities) suggest possibility of an abnormal aortic arch
  - Right brachial artery pulse should be compared with pulses in lower extremities because right subclavian artery is always preductal
  - Weak pulses indicate:
    - Left heart outflow obstructive lesions
    - Myocardial failure
    - Shock
  - Bounding pulses indicate:
    - PDA
    - Aortic insufficiency
    - Systemic to pulmonary shunts
  - Visible Precordial Impulse
    - After the first 12 hours of life indicates defect with volume overload
- Blood Pressure

- Mean arterial pressure estimated to be gestational age
- Hypertension: term: > 90/60; preterm: > 80/50
- Cuff width should be 25% greater than the width of the extremity
  - Too narrow → false high reading
  - Too wide → false low reading
- Peripheral edema
  - Rarely due to heart disease
- Liver
  - Palpable 2 – 3 cm below right costal margin midclavicular line
  - > 4 cm: CHF, hemolytic disease, liver disease
- Chest xray:
  - Evaluate cardiac size, shape and position
    - Cardiomegaly: defined as cardiac/thoracic ratio > .65
    - Position: midline
    - Size may be hard to estimate due to large thymus gland
    - Malpositioning: cardiac displacement, ambiguous rotation
    - Transient enlargement: polycythemia, perinatal anoxia or normally increased fluid present at birth
  - Rule out pulmonary parenchymal disease
  - Identify decreased vascular markings
    - Obstruction to right ventricular outflow
  - Identify increased pulmonary vascular markings
    - Increased blood flow to lung
    - Increased left sided heart pressure/volume
- Electrocardiography
  - Reflects abnormal hemodynamic burdens placed on the heart
  - Major diagnostic tool for evaluating arrhythmias and electrolyte imbalances on electrical conductivity
- Echocardiography
  - Rapid, noninvasive and painless evaluation of heart anatomy and flow using ultrasonic waves
  - Estimates pressures, measure gradients and evaluate heart function
- Magnetic resonance imaging
  - Three-dimensional, providing high-resolution images of the heart and great vessels.
  - Used in conjunction with echocardiograms and cardiac catheterization to evaluate pulmonary arteries and veins, and systemic veins
- Cardiac catheterization
  - Invasive procedure to obtain data for definitive diagnosis or preparation for surgery

- The focus of this invasive procedure has changed over the past 10 years from a diagnostic modality to an interventional procedure.

Signs and Symptoms of Cardiac Disease in the Neonate

- Cardiac disorders should be suspected in the presence of:
  - Congestive heart failure
  - Cyanosis
  - Heart murmurs
  - Dysrhythmias
- **Congestive Heart Failure**
  - A set of clinical symptoms that indicates the heart is not able to deliver an adequate cardiac output to meet the body’s metabolic requirements
  - Etiology:
    - Structural heart defects most common
    - Birth asphyxia, severe anemia, dysrhythmias and sepsis
    - Time of presentation of symptoms important—hints at the etiology

Causes of Congestive Heart Failure and Time of Onset	
Age at Onset of Symptoms	Underlying Cause
At birth	Hypoplastic left heart syndrome (HLHS) Severe tricuspid or pulmonary regurgitation Systemic arteriovenous fistula
In first week of life	Patent ductus arteriosus (PDA) in premature infants Transposition of the great vessels (TGV) Total anomalous pulmonary venous return (TAPVR) with pulmonary venous obstruction
1 to 4 weeks after birth	Coarctation of the aorta Critical aortic or pulmonary stenosis All other lesions listed above

Data from Park, M.K.: *Pediatric cardiology for practitioners* (4th ed.). St Louis, 2002, Mosby.

Verklan & Walden, 2015, p 567

- Noncardiac causes
  - Birth asphyxia: transient myocardial ischemia
  - Metabolic: hypoglycemia and hypocalcemia
  - Severe anemia
  - Overhydration
  - Sepsis
- Clinical Presentation
  - Tachypnea without increase in depth of respiration: first clinical sign of pulmonary edema
  - Tachycardia
    - Hyperactive precordium

- Poor perfusion
    - Pale, cyanotic or gray colouring
    - Poor capillary refill
    - Diaphoresis
  - Cardiomegaly on chest xray
    - Hypertrophic cardiomyopathy
    - Decreased or engorged pulmonary vasculature
  - Hepatomegaly
  - Fatigue or difficulty feeding
- Diagnosis
  - ABG:
  - Chest xray
  - ECG
    - Hypertrophy of one or more chambers.
    - Abnormal mean QRS axis.
    - Rhythm disturbances.
  - CBC with differential
    - Anemia or polycythemia
    - Decreased neutrophils and presence of left shift: sepsis Blood glucose: evaluate hypoglycemia as potential cause of cardiomyopathy
  - Electrolytes: Potassium and Calcium → alterations interfere with cardiac contractility
- Treatment Strategies
  - General support measures
  - Fluid and nutritional support
    - Acute phase: reduce volume intake to 2/3 maintenance levels
    - Use of glucose polymers (polycose), MCT oil to enhance caloric content
    - Increased IV infusions of fat emulsions up to 50% to increase caloric intake
  - Pharmacologic:
    - Digoxin
      - Achieve maximal CO
      - Use controversial in preterm and term newborns
      - Digitalize patient (dose depends on gestational age)
        - Observe for bradycardia (discontinue if HR < 100)
        - Arrhythmias or heart block
        - Hypokalemia
    - Diuretic Therapy to eliminate excess intravascular fluid
      - Furosemide (Lasix)
        - 1 – 2 mg/kg every 12 hrs IV or 1 to 3 mg/kg every 12 hr po
        - IV route preferable for fast action

- Hypokalemia and hypochloremia are side effects that can result in metabolic alkalosis
  - May cause hypocalcemia with urinary loss of calcium leading to nephrocalcinosis
  - Contraindicated in renal failure
  - Chlorothiazide (Diuril) – respiratory section
  - Spironolactone (Aldactone) -- respiratory section
  - Inotropes:
    - Severe CHF or cardiogenic shock
    - Dopamine, dobutamine, isoproterenol (respiratory section)
    - Milrinone
      - IV dose 0.3 to 1 mcg/kg/min.
      - Loading dose of 50 to 75 mcg/kg IV over 15 minutes if needed.
- Cardiac consultation: rule out/establish diagnosis of congenital heart lesion
- **Cyanosis**
  - Cyanosis observation depends on hemoglobin levels. At least 5 g of desaturated Hgb/dl necessary before cyanosis is apparent
  - Influenced by anemia/polycythemia
  - Peripheral cyanosis:
    - Due to sluggish movement of blood through the extremities with increased tissue oxygen extraction
    - Persists from birth
    - Does not involve mucous membranes
  - Central cyanosis:
    - Due to desaturated blood leaving the heart
    - Bluish discoloration of tongue and mucous membranes, reflecting arterial desaturation
  - Respiratory Pattern & Cyanosis
    - Tachypnea without dyspnea and no cyanosis → left to right shunt
      - If coupled with feeding difficulty and the baby has to stop feeding to breathe → CHF
    - Hyperpnea
      - Increased respiratory depth
      - Congenital heart lesions resulting in decreased pulmonary blood flow
    - Crying
      - Cyanosis evident due to increased oxygen consumption by the tissues
- **Shock**
  - Inadequate circulating blood volume, resulting in decreased perfusion and oxygenation to the tissues
  - Types:
    - Hypovolemic
      - Loss of blood due to placental abnormalities

- Acute blood loss postnatally
    - Plasma and fluid losses
  - Cardiogenic due to:
    - Myocardial failure
    - Congenital heart lesion
    - Cardiac arrhythmia
    - Restriction of function: tamponade, air leak, excessive PIP
    - Myocarditis
  - Distributive (septic shock)
    - Impaired peripheral arterial resistance due to release of toxins
    - Associated with gram-negative organisms, but gram-positive organisms may also be cause
- Clinical Presentation
  - Cardiopulmonary status changes
    - Tachycardia; Bradycardia
    - Increased work of breathing, tachypnea
    - Poor peripheral perfusion
    - Hypotension
  - Decreased urinary output
  - Metabolic disturbances
  - Evidence of coagulation defects
  - Indicators of blood volume
    - Changes in Hgb/Hct
    - Response to fluid challenge of 10 cc/kg of NS
    - Positive Betke-Kleihauer: indicates fetal-to-maternal transfusion in utero
  - Indicators for septic shock
    - Clinical signs of sepsis/positive cultures
    - Normal blood pressure with hypoperfusion
    - Edema from capillary protein and fluid leakage
    - Oliguria
    - Proteinuria
    - PPHN very common
- Treatment Strategies
  - Supportive care as mentioned above with CHF
  - Specific therapies
    - Increase blood volume and RBC mass
    - Treat sepsis
    - Maximize cardiac output
      - Inotropic agents should be started when there is evidence of oliguria, hypotension and acidosis

## **CONGENITAL HEART DISEASE**

- Incidence:
  - < 1% of all births (3-9 per 1000 live births)
    - Incidence in premature infants is 2 to 3 times that of term infants

- 85%: multifactorial causes
- 10 – 12%: chromosomal factors
- 1 – 2%: genetic factors
- 2%: exposure to environmental teratogens
- 14.5-66% are in conjunction with other structural anomalies.
  
- Genetic Factors
  - Trisomy 21: 50%
  - Trisomy 18: 90 – 100%
  - Trisomy 13: 90%
  - DiGeorge deletion 22q: 50%
  
- Environmental Factors and Teratogens
  - Associated with maternal ingestion of:
    - Anticonvulsants:
      - 2 – 3% of exposed fetuses will have pulmonary stenosis, coarctation, PDA
      - Phenytoin, Carbamazepine (Tegretol); Valproate, Trimethadione
    - Anticoagulants
      - Warfarin (Coumadin): no consistent pattern recognized
    - Antineoplastic medications
      - Aminopterin: dextrocardia
    - Lithium
      - 10% of exposed neonates: Ebstein anomaly, ASD, tricuspid atresia
    - Alcohol:
      - Fetal alcohol syndrome: VSD, coarctation, aortic regurgitation, ASD
    - Tobacco and smoking:
      - First-trimester smoking related topulmonary valve stenosis, TGV, ASD, right ventricular outflow tract defects, and PDA in term newborns
    - Maternal Disease/Infections
      - Diabetes mellitus, especially insulin-dependent: 5 times greater risk of cardiac anomalies
        - Hypertrophy of the septum and myocardium, VSD, double-outlet right ventricle, transposition, truncus, coarctation
      - Maternal lupus erythematosus: neonatal heart block
      - Rubella and CMV: viral illnesses that produces clinically significant heart disease: PDA, pulmonary stenosis, branch pulmonary stenosis, VSD and ASD
      - Maternal obesity
  
- Gender Preferences
  - Males
    - Coarctation

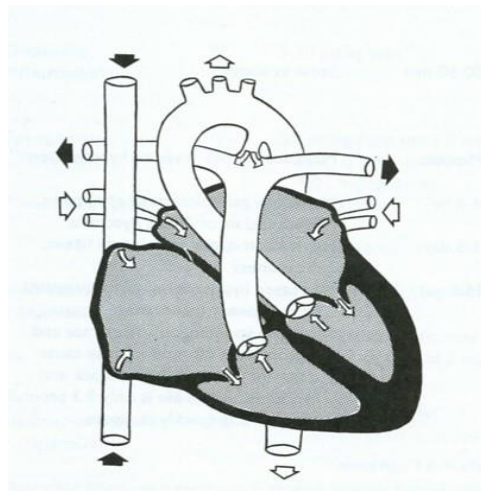
- Aortic stenosis
- Transposition
- Hypoplastic left heart syndrome
- Females
  - ASD
  - PDA

## **CONGENITAL HEART DEFECTS WITH INCREASED PULMONARY BLOOD FLOW**

### **Patent Ductus Arteriosus**

- 4<sup>th</sup> most common lesion
- Occurs 3 times more commonly in females than in males
- Isolated PDA in term babies 1:2000 live births
- Preterm:
  - Incidence inversely related to postmenstrual age
  - 30% of infants < 1500 g at birth
  - 40% of infants weighing 751-1000 g at birth
  - 50% of infants weighing 500-750 g at birth
- Persistent patency of the ductus arteriosus after birth
- Increased oxygen tension: potent stimulator of smooth muscle contraction and should close ductus. Premature neonate has immature response to oxygen.
- Hemodynamics
  - L → R shunt
    - PVR falls and SVR increases, blood is shunted from the aorta into the pulmonary artery
    - Increased pulmonary artery pressure and increased right ventricular pressure and volume lead to bilateral CHF
    - Despite increased CO, blood flow distribution is rearranged
      - Decreased blood flow to GI system
      - Implicated in IVH, NEC and BPD
  - R → L shunt
    - PVR greater than SVR blood is shunted from the pulmonary artery into the aorta and bypasses the lung
    - PPHN



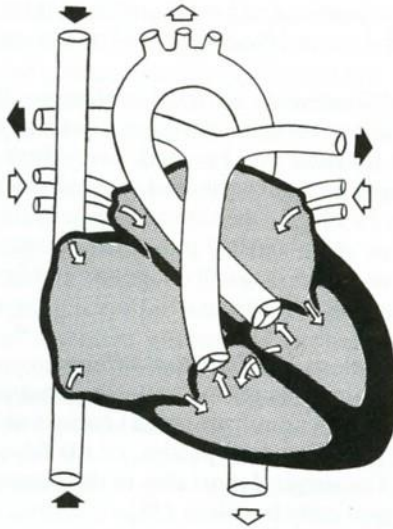


- Clinical Presentation
  - Presents at 4 – 7 days of life with inability to wean from ventilator or has increasing ventilatory and oxygen needs
    - Apnea and bradycardia if not on a ventilator
  - Increased pulmonary vasculature and cardiomegaly
  - Bounding peripheral pulses, Hyperactive precordium
  - Widened pulse pressures
  - Continuous murmur at upper left sternal border
  - Chest xray: mild cardiomegaly, pulmonary edema, increased pulmonary vascularity
  - Echocardiography: confirm shunting magnitude, blood flow patterns and anatomy of ductus
  - Clinical cardiovascular distress scoring
    - Score  $\geq 3$  indicates a hemodynamically significant PDA
      - Heart rate.
      - Peripheral arterial pulses.
      - Precordial pulsations.
      - Duration of murmur.
      - Cardiac silhouette on chest x-ray.
  - B-type natriuretic peptide
    - 70 and 100 pg/mL: symptomatic PDA
    - Specificity of 100% and sensitivity of 93% using a cutoff value of 132.5 pg/mL
- Treatment Strategies
  - Determine if hemodynamically significant
    - HR > 170-180, Tachypnea, Hepatomegaly, Bounding pulses
    - Increasing oxygen requirement/inability to wean from ventilator
  - Conservative intervention:
    - Fluid restriction
    - Diuretics
    - Positive end expiratory pressure
  - Indomethacin

- Initial dose is 0.2 mg/kg IV, followed by 2 doses 0.1 mg/kg IV every 12-24 hours for a total of 3 doses
  - Complications:
    - Transient decreased renal function
    - Increased incidence of GI bleeding
    - Inhibition of platelet aggregation for 7 – 9 days
  - Contraindications
    - Renal failure
    - NEC
    - Platelet count < 50,000 or active bleeding
    - Sepsis
- Ibuprofen lysine
  - Gained FDA approval in 2006 for treatment of clinically significant PDA in neonates weighing 500-1500g with a PMA  $\leq$  32 weeks at the time the medication is given
  - Initial dose: 10 mg/kg IV followed by 2 doses of 5 mg/kg at 24 and 48 hours after first dose
  - Safe and effective as indomethacin, with better maintenance of cerebral, mesenteric and renal blood flow that indomethacin
  - Does not decrease cerebral or mesenteric blood flow
  - Monitor: serum creatinine, BUN, platelet count and urine output
- Surgical treatment
  - Standard ligation
  - Placement of occlusion device
  - Minimally invasive thoracoscopic surgery

### **Ventricular Septal Defect**

- Abnormal opening in septum between right and left ventricle. Size ranges from pinhole to almost complete absence of ventricular septum
- Occurs in 2 per 1000 live births—most common CHD

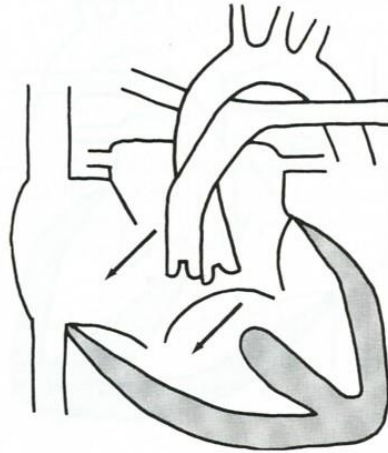


- Hemodynamics
  - Small defect: allows pressure differences between ventricles
  - Large defect: no resistance to flow. The systolic pressures in ventricles and great vessels are equal → shunting determined by SVR and PVR
  - When PVR decreases, there is a left to right shunt thru the defect → more blood ejected into pulmonary artery.
  - When pulmonary blood flow is about 3x > systemic flow, the left ventricle can't accommodate the load → signs of CHF
  - Excessive pulmonary artery blood flow eventually cause pulmonary artery hypertrophy and stenosis
- Clinical Presentation
  - Small VSD: asymptomatic
  - Moderate VSD:
    - Murmur along left sternal border
    - Fatigue with feeding
    - Recurrent respiratory infections.
  - Large VSD: as L→R shunting increases, signs of CHF develop
    - Presents about 1 – 2 months of age
    - Loud pansystolic murmur at left lower sternal border
    - Chest xray: cardiomegaly and increased pulmonary vascular markings
    - Echo: identify VSD, blood flow patterns
- Treatment Strategies
  - 50 – 75% of small defects close spontaneously
  - 20% of large defects become smaller
  - Mild CHF: treat with digoxin and diuretics
  - Surgery if failure to thrive or intractable CHF

### **Endocardial Cushion Defect**

- Endocardial cushions form the lower portion of the atrial septum, upper portion of the ventricular septum and septal portions of mitral and tricuspid valves
- Incidence: 1 per 9000 live births

- Hemodynamics:
  - Dependent shunting:  $PVR < SVR$ , the blood dependently shunts  $L \rightarrow R$  via ASD and VSD. Pulmonary blood flow increases  $\rightarrow$  left ventricle overloaded  $\rightarrow$  CHF
  - Obligatory shunting: higher pressures in left ventricle creates obligatory shunting from left ventricle  $\rightarrow$  mitral portion of A-V valve (atrioventricular regurgitation)  $\rightarrow$  L atrium  $\rightarrow$  ASD  $\rightarrow$  R atrium



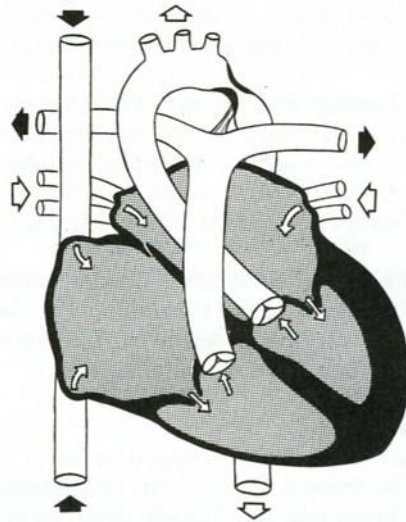
- Clinical Presentation
  - Related to A-V valve regurgitation
    - Severe: presents at 1 – 2 weeks with CHF
    - Competent valves: presents with CHF in first or 2<sup>nd</sup> month of life
  - Respiratory distress
  - Active precordium
  - Variable murmurs
  - Chest xray: cardiomegaly, bilateral atrial and ventricular hypertrophy, increased pulmonary markings
  - Echo: diagnose/demonstrate common AV valve; document valve regurgitation, blood flow patterns
- Treatment Strategies
  - Objective: prevent development of pulmonary vascular obstructive disease
  - Medical management of CHF
  - Palliative pulmonary artery banding: increases PVR and decrease pulmonary blood flow
  - Primary repair with closure of atrial and ventricular septal defects, and mitral and tricuspid valve reconstruction

## **OBSTRUCTIVE DEFECTS WITH PULMONARY VENOUS CONGESTION**

### **Coarctation of the Aorta**

- Most common CHD presenting in the 2<sup>nd</sup> week of life
- Males affected twice as often as females

- Constriction of the aorta distal to the left subclavian artery, usually at the site of insertion of the ductus
- Preductal coarctation associated with hypoplasia of the aortic arch.
- Up to 60% of infants with coarctation will have a bicuspid aortic valve.
- Hemodynamics:
  - Obstruction to left ventricular outflow → increased left ventricular, left atrial and pulmonary venous pressures. Pulmonary venous congestion develops
  - Severe coarctation: decreased blood flow to descending aorta → tissue hypoxia, acidosis, death when ductus closes

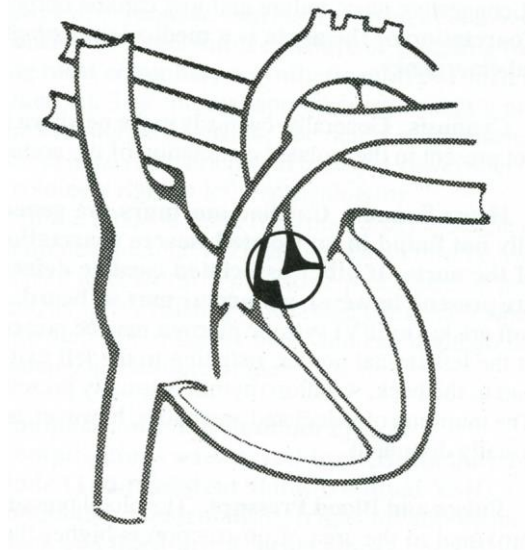


- Clinical Presentation:
  - CHF due to pressure overload on left ventricle
  - Decreased or absent pulses in lower extremities
  - BP higher in upper extremities > 15 mm Hg
    - Decreased BP left arm: left subclavian artery as site of coarctation.
    - Decreased BP right arm: right subclavian artery arises below coarctation (rare).
    - Pulses that “wax and wane”: increase or decrease in PDA blood flow.
  - Heart sounds: murmur depends on whether preductal or postductal
  - Chest xray: enlarged heart with congested pulmonary vascularity
  - Echo: diagnostic
- Treatment Strategies
  - Aggressive medical management of CHF
  - Prostaglandin E<sub>1</sub> (PGE<sub>1</sub>) to dilate ductus
  - Palliative balloon angioplasty in critically ill neonates less than 1000 g
  - Isolated postductal coarctation: control of CHF first, then surgical correction.
- Three common surgical repairs:
  - Balloon angioplasty to open the narrowing
  - Percutaneous stent placement

- Surgical correction: resection of abnormal segment with reanastomosis OR subclavian patch across area of obstruction.
- Prognosis
  - Long-term prognosis after coarctation repair is determined by the presence of residual or recurrent coarctation, persistence of pulmonary hypertension, and residual cardiovascular lesions
  - The most common complication is hypertension

### **Aortic Stenosis**

- 5 – 6% of all CHD
- Males affected 4 times more than females
- May be subvalvular, valvular, or supra-valvular
- Valvular stenosis is the most common, and usually has a bicuspid aortic valve



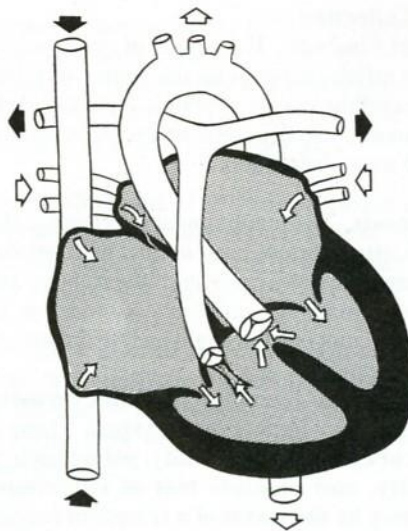
- Hemodynamics
  - Obstruction to left ventricular outflow leads to increased left ventricular pressures and hypertrophy
- Clinical Presentation
  - Usually asymptomatic at birth
  - Acrocyanosis
  - Heart sounds: harsh systolic murmur in upper right sternal border. Radiates to neck and lower left sternal border
  - CHF symptoms may not be evident for weeks
  - Chest xray: cardiomegaly with normal pulmonary vascular markings
  - If critical aortic stenosis—sudden deterioration when PDA closes
- Treatment Strategies
  - Medical management usually not successful
  - Initial: CHF treated with fluid restriction, diuretics, digoxin, acidosis management
  - If stenosis is critical, PGE<sub>1</sub> to prevent hypoxia

- Surgery: aortic valvotomy or valve replacement

## **OBSTRUCTIVE DEFECTS WITH DECREASED PULMONARY BLOOD FLOW**

### **Tetralogy of Fallot**

- Most common cyanotic heart lesion—10% of all defects
- Combination of four defects
  - VSD
  - Pulmonary stenosis
  - Right ventricular hypertrophy
  - Aorta overriding VSD
- Hemodynamics
  - Degree of pulmonic obstruction ranges from mild stenosis to complete atresia → accounts for the variability of presentation
  - Mild pulmonary stenosis: blood flows L → R via VSD → CHF
  - Severe pulmonary stenosis: blood flow R → L through VSD into the aorta → hypoxia and cyanosis

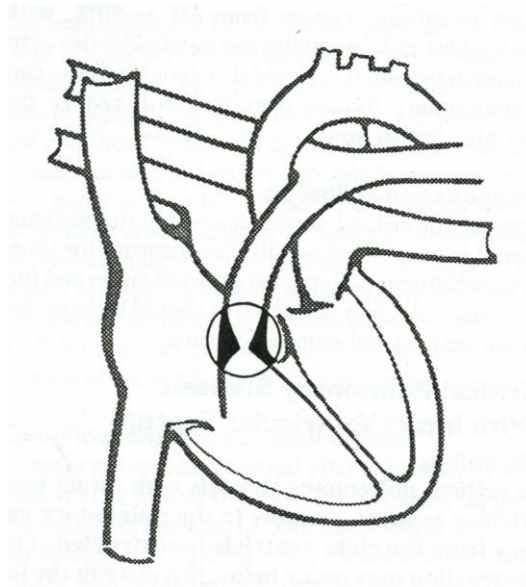


- Clinical Presentation
  - Mild pulmonary obstruction: mild cyanosis presents in first days of life
  - Severe pulmonary obstruction: presents in first days of life with severe cyanosis, hypoxia and dyspnea
  - Murmurs: mid to upper left sternal border
  - Chest xray: normal sized heart. Appears “boot” shaped. Pulmonary vascular markings are normal or decreased
  - Tetralogy “spells” (paroxysmal dyspnea and severe cyanosis) may present in the neonate
- Treatment Strategies
  - Pharmacologic: Propranolol drug of choice for treating hypercyanotic infants

- Severe presentation: PGE<sub>1</sub> to maintain patency of the ductus until taken to OR
  - Surgical correction
    - Closure of the VSD with a patch
    - Pulmonary outflow may be enlarged with a patch
    - Procedure done with the baby on cardiopulmonary bypass
    - If severe pulmonary stenosis or atresia, a Blalock-Taussig procedure is done with full correction at a later time (shunt that connects the subclavian artery to the pulmonary artery)

### **Pulmonary Stenosis**

- 5 – 8% of all CHD
- Anatomy: narrowed opening either in the pulmonary valve due to pulmonary valve cusp fusions, or above or below the valve due to tissue hypertrophy
- Hemodynamics:
  - In utero, right ventricular hypoplasia can develop depending on the degree of pulmonary valve stenosis and subsequent decrease in right ventricular blood flow
  - After birth, combination of right ventricular hypoplasia and severe pulmonary valve stenosis redirects blood flow R → L through the foramen ovale. Pulmonary blood flow depends on a L → R flow through the PDA
  - Mild stenosis: pulmonary blood flow is not severely restricted. Does not depend on the PDA.



- Clinical Presentation
  - Mild: loud systolic murmur at left upper sternal border is the only finding
  - Moderate to severe
    - Murmur less prominent
    - Cyanosis present, and increases when PDA closes
    - Hepatosplenomegaly

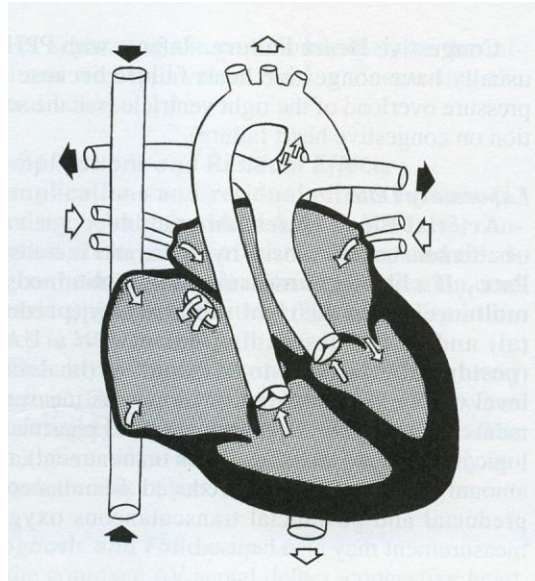


- CXR: mild cardiomegaly with bulging right heart border and decreased pulmonary vascular markings
- Treatment Strategies
  - Cyanosis present:
    - Oxygen, bicarbonate, and PGE<sub>1</sub>
    - Catheter-introduced balloon valvuloplasty or angioplasty
    - Surgical valvotomy
    - Tissue excision if valvuloplasty fails
  - No cyanosis
    - Conservative management
- Other defects: Pulmonary Atresia, Tricuspid Atresia

### **MIXED DEFECTS**

#### **Transposition of the Great Vessels**

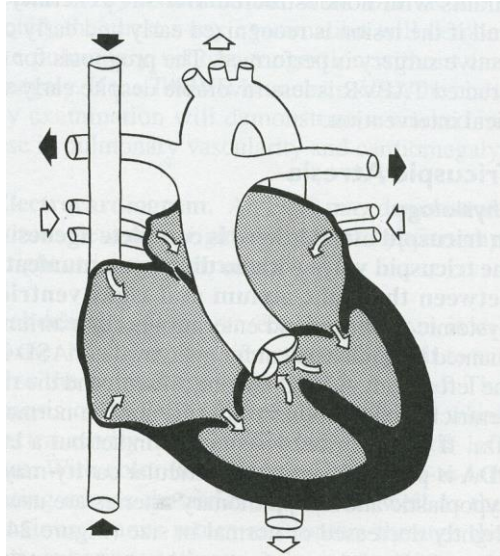
- Most common cardiac cause of cyanosis in neonates
- Incidence: 1:5000 live births
- The aorta arises anteriorly from right ventricle and the pulmonary artery arises posteriorly from left ventricle
- Hemodynamics
  - Oxygenated blood returns from the lungs into the L atrium → L ventricle → pulmonary artery → lungs
  - Unoxygenated blood returns from the body into the R atrium → R ventricle → aorta → body
  - Mixing occurs at the level of the ductus arteriosus (while patent)
  - PDA closes → eliminates obligatory shunting. Site of mixing is now the foramen ovale → inadequate → severe systemic hypoxemia



- Clinical Presentation
  - Generalized cyanosis within the first 24 hours of life. Become progressively more intense
  - Murmurs not common
  - Heart sounds normal
  - Chest xray: usually normal. May have an “egg-on-side” appearance
    - Pulmonary vascular markings may be increased or decreased
  - \*\*severely hypoxic neonate breathing comfortably with a normal physical examination, CXR and EKG → think TGA!
  
- Treatment Strategies
  - TGA is a cardiac emergency
  - Correction of metabolic acidosis/metabolic derangements
  - PGE<sub>1</sub> to maintain ductal patency until palliative surgery
  - Palliation of choice: balloon atrial septostomy
    - Increases PaO<sub>2</sub>s into 40’s and oxygen saturations into 80%’s
  - Corrective surgery
    - Arterial switch is the treatment of choice

### Truncus Arteriosus

- 1 – 2% of CHD
- Anatomy: single great artery arising from both ventricles, overriding a VSD
  - Type I: short pulmonary artery arising from base of the common trunk, then divides into the left and right arteries
  - Type II: right and left pulmonary arteries arise from the posterior surface of the common trunk
  - Type III: right and left pulmonary arteries have separate origins in the lateral walls of the common trunk



### Hemodynamics

- Both ventricles pump blood into the common trunk—supplies both the pulmonary and systemic circulation
- As PVR decreases, preferential shunting to the pulmonary circulations occurs
  - Increases blood flow to the lungs
  - Increased workload of the left ventricle

### Clinical Presentation

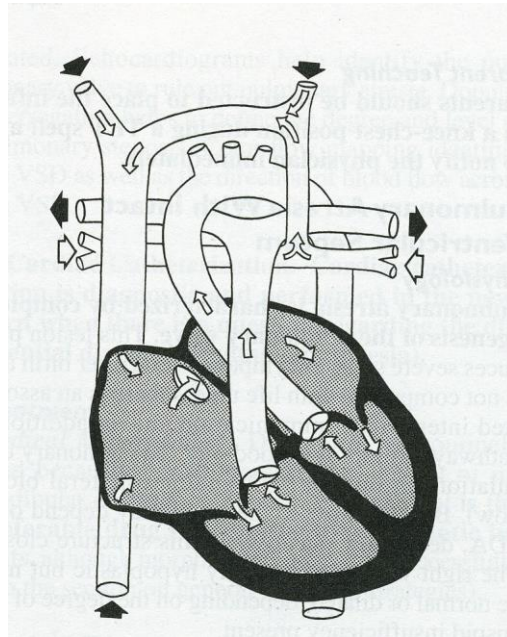
- CHF with bounding pulses and widened pulse pressure
- Intermittent cyanosis
- Harsh systolic murmur at mid- to lower left sternal border and systolic ejection click with single  $S_2$
- Cxray: cardiomegaly with increased pulmonary vascular markings
- Echocardiography: identify the number of truncal valve leaflets, presence of pulmonary stenosis, and evaluate the aortic arch

### Treatment Strategies

- Treatment of CHF
  - Diuretics, digoxin, angiotensin-converting enzyme inhibitors
    - Control pulmonary overload
    - Also decrease systemic resistance which leads to a decrease in pulmonary vascular resistance
- Surgical repair at a few days to 4 weeks
  - Homograft between the right ventricle and pulmonary artery
  - VSD closure using a patch
  - Separation of the pulmonary arteries from the truncus

## Total Anomalous Pulmonary Venous Return (TAPVR)

- Incidence: 1% of CHD
- Anatomy: Pulmonary veins drain into the right atrium, either directly or indirectly through a systemic venous channel
  - Patent foramen ovale or ASD needed for survival
  - Varying degrees of pulmonary venous obstruction occur



### Three types:

- Supercardiac: most common. Drainage is to the superior vena cava through the innominate vein
- Cardiac: pulmonary veins drain into the coronary, sinus or directly into the right atrium
- Infracardiac: the 4 veins join behind the heart, flow through the diaphragm and connect to the portal venous system

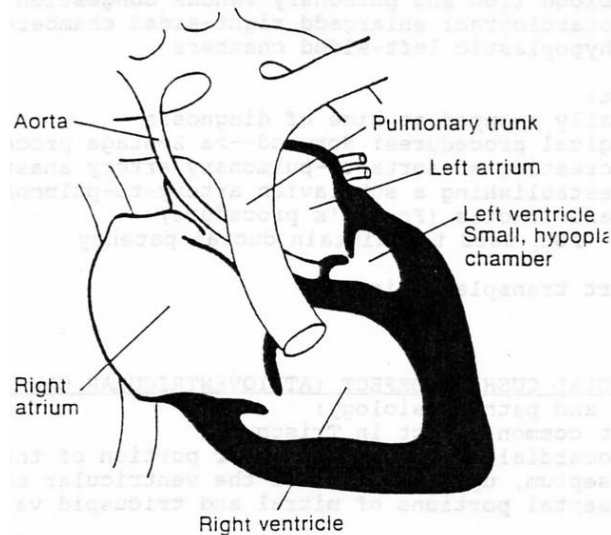
### Hemodynamics

- Oxygenated blood from the lungs drains into the right atrium → mixing with the systemic venous return
  - Part of this flow passes into the left atrium via the patent foramen ovale or ASD, into the left ventricle and out the aorta
  - As the PVR decreases, pulmonary blood flow will increase
- If obstruction to pulmonary venous return exists, the PVR will increase → pulmonary edema
  - Blood will flow from the pulmonary artery to the aorta thru the PDA
  - Closure of the PDA increases right to left atrial shunting
- Clinical Presentation
  - Non-obstructed:

- CHF
    - Mild cyanosis
    - Heart sounds: systolic murmur at upper left sternal border, diastolic rumble at lower left sternal border
    - Chest xray: right ventricular dilation, increased pulmonary vascular markings
  - Obstructed
    - Profound cyanosis
    - Respiratory distress
    - Chest xray: normal size with pulmonary edema
  - Echo: color flow mapping reveals an extra cavity behind the left atrium, right to left shunt across the atrial septum and the anomalous return as the blood enters the atrium, superior vena cava or coronary sinus.
- Treatment Strategies
    - Surgical treatment of obstructed TAPVR: emergency
    - Medical management of nonobstructed TAPVR: temporary measure to prevent or treat CHF
    - Surgery based on echocardiography
      - Anomalous veins are detached and transplanted to the left atrium
      - ASD is repaired

### Hypoplastic Left Heart Syndrome

- 2% of all cardiac defects; 28% have chromosomal abnormalities
- Most common cardiac cause of death in the first week of life
- Hypoplastic left ventricle, aortic arch and ascending aorta, with a dilated right ventricle and pulmonary artery
- Aortic and mitral valves may be atretic or hypoplastic



- Hemodynamics

- Right ventricle supports the circulation. Increasing pulmonary blood flow from the R ventricle leads to an increasing pulmonary venous return that can't exit through the left atrium into the L ventricle → pulmonary venous hypertension and pulmonary edema
- Blood supply to descending aorta, aortic arch and coronary arteries is PDA dependent
- PDA begins to close → decreased perfusion to systemic circulation → systemic and coronary ischemia
- Clinical Presentation
  - Asymptomatic at birth
  - Tachypnea and dyspnea
  - CHF presents at 24 – 48 hours of life
  - Closing PDA:
    - Severe mottling, gray pallor, markedly diminished pulses, cardiovascular collapse and shock
  - Chest xray: cardiomegaly with increased pulmonary blood flow and pulmonary edema
  - Echo: diagnosis
- Treatment Strategies
  - PGE<sub>1</sub> to maintain ductal patency and systemic circulation
  - Use of inhaled O<sub>2</sub> and nitrogen to keep FiO<sub>2</sub> < 21%
  - Treatment options
    - Comfort care: rarely done anymore
    - Multistaged surgical approach
      - Sano procedure for first stage includes placement of a conduit between the right ventricle and left and right pulmonary arteries.
        - Improved early survival, and improved coronary and systemic perfusion
      - “Hybrid” approach: involves placement of a stent in the ductus arteriosus along with bilateral pulmonary artery banding
        - Complications include narrowing of the ductus, which requires balloon dilation, and increased pulmonary blood flow.
  - Cardiac transplantation
    - ~23% of infants die waiting for a donor heart
    - Newer modalities to provide support while waiting for a heart include ECMO, and the Berlin Heart.
      - ~ 45% of the infants placed on ECMO will survive to transplantation

# METABOLIC DISORDERS

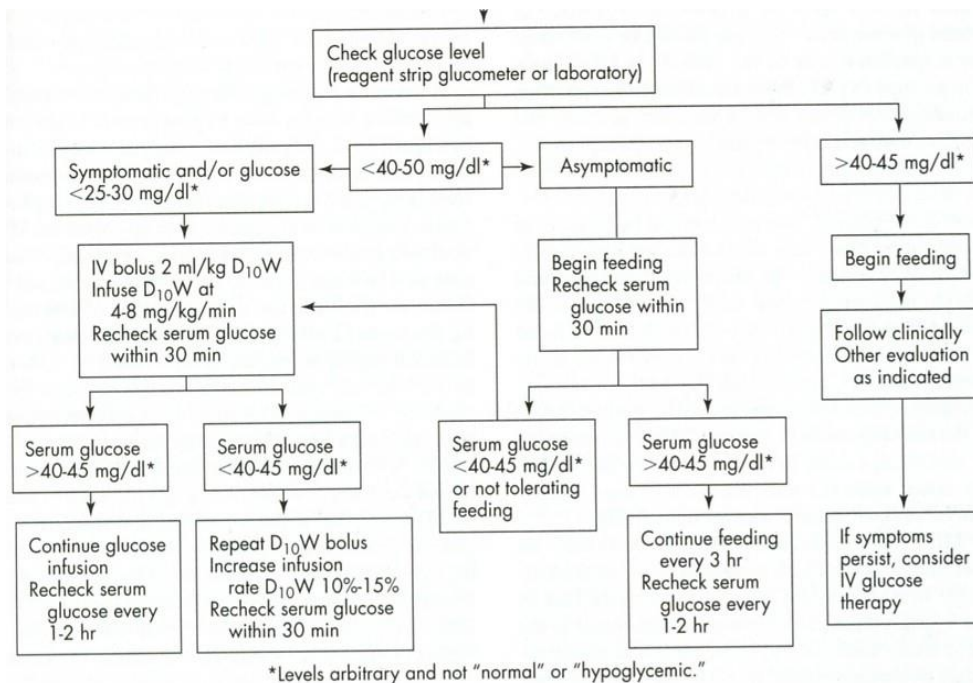
## Glucose Homeostasis

- Fetal glucose homeostasis:
  - Fetus is capable of glucose production → enzymes for gluconeogenesis are present by the 3<sup>rd</sup> month of gestation
  - Fetal glycogen synthesis begins about 9 weeks gestation
  - Major sites of glycogen deposition: liver, lung, heart and skeletal muscle
  - Energy also stored as adipose tissue during 3<sup>rd</sup> trimestre
  - Insulin: major stimulus for fetal growth
    - Present in the fetal pancreas by 8 – 10 weeks
    - Increases in late gestation
  - Glucose reaches fetus by facilitated diffusion across the placenta
    - Fetal levels ~ 70% of mother's
- Neonatal glucose homeostasis
  - Birth → loss of maternal source
  - Blood glucose concentration falls, reaching nadir at 1 – 2 hours of age
  - First postnatal hours, brain metabolizes lactate
  - At birth, catecholamine levels increase → induces synthesis of phosphoenolpyruvate carboxykinase (PEPCK)
    - Increased catecholamines stimulate lipolysis
    - Elevated glucagon and norepinephrine levels activate hepatic glycogen phosphorylase → induces glycogenolysis
    - Falling glucose concentration stimulates hepatic glucose-6-phosphatase activity → increased hepatic glucose release
    - Insulin secretion is suppressed and blood glucose levels increase ~ 3 – 4 hours
    - Hepatic glycogen is rapidly depleted if feeding is not established early
    - Becomes dependent on gluconeogenesis and lipolysis as primary modes of maintaining euglycemia. PEPCK rate limiting step.
- Hypoglycemia
  - Plasma glucose concentration of < 40 mg/dl
  - Pathophysiology
    - Immediate postnatal decrease in blood glucose concentration is physiologic
    - Failure to increase glucose concentrations after 4 hours is pathologic
    - Brain increases blood flow to improve glucose delivery
      - May predispose the brain to injury
    - When glucose consumption exceeds delivery, the brain uses alternate fuels
      - May contribute to neuronal damage
    - Lactic acid is elevated in late fetal and early postnatal life
    - Healthy term infants produce ketones effectively on days 2 and 3 of life
    - Preterm and SGA infant are very limited in mounting a counterregulatory ketogenic response
    - Prolonged hypoglycemia induces biochemical changes that damage the neuronal and glial cells in the brain

- Etiology:
  - Inadequate Substrate Supply
    - Most common etiology
    - Decreased fat and glycogen stores
      - Preterm infants
      - IUGR
    - Delayed or insufficient feedings; fluid restriction
    - Inborn errors of metabolism: galactosemia, amino acid disorders
    - Glycogen storage disease: inability to utilize stored glycogen as a result of enzyme deficiencies
    - Perinatal stress/hypoxia
  - Abnormalities of Endocrine Regulation: Hyperinsulinemia
    - Most common cause of persistent hypoglycemia
    - Increases glycogen synthesis and intracellular glucose uptake
    - Inhibits lipolysis, ketogenesis and glycogenolysis
    - **Infant of a diabetic mother:** increased transfer of glucose across the placenta from hyperglycemic mother → fetal pancreatic beta cells stimulated → increased insulin
      - After delivery, source of glucose abruptly removed
      - Hyperinsulinemia persists → hypoglycemia
      - Complications of IDM: polycythemia, hypocalcemia, macrosomia (dystocia/perinatal distress); congenital anomalies
    - Beckwith-Wiedemann syndrome: unknown cause
      - Hypoglycemia may be very profound
      - Characterized by oomphalocele, macroglossia, visceromegaly and hypoglycemia
    - Rh incompatibility
    - Tocolytics used in labor
  - Increased Glucose Utilization
    - Asphyxia/hypoxia: infant relies on anaerobic metabolism
      - Hypoxic-ischemic damage to liver impairs synthesis of gluconeogenic enzymes
    - Hypothermia: depletion of brown fat stores for nonshivering thermogenesis
    - Sepsis
    - Congestive heart failure, RDS, polycythemia/hyperviscosity
- **Hyperglycemia**
  - Blood glucose concentration of > 125 mg/dl or plasma glucose concentration > 150 mg/dl
  - Incidence: increases with decreasing gestational age/birthweight



- Pathophysiology
  - Hepatic glucose production continues even when hyperglycemic and in the presence of circulating insulin
    - Represents a failure of glucose autoregulation involving both the pancreas and the liver
  
- Etiology:
  - Highest risk: LBW infant (32 weeks < 1250 g) who can't tolerate an IV glucose infusion of > 6 – 8 mg/kg/min (ie D12.5W at 80 -100 ml/kg/day)
  - Gram-negative sepsis
  - IV lipid infusion given faster than 0.25 g/kg/hr
  - Methylxanthines
  - Surgical procedures
  
- **Clinical Presentation: Hypoglycemia**
  - Nonspecific and extremely variable
  - Asymptomatic
  - Abnormal cry, poor feeding, hypothermia, temperature instability
  - Neurologic signs: tremors, jitteriness, hypotonia, irritability, lethargy, seizures
  - Cardiorespiratory disturbances: cyanosis, pallor tachypnea, apnea
  - Whipple's triad must be met:
    - A reliable low blood glucose
    - Symptoms consistent with hypoglycemia must be evident
    - Symptoms resolve after euglycemia is achieved
  
- **Clinical Presentation: Hyperglycemia**
  - Asymptomatic
  
- **Treatment Strategies: Hypoglycemia**



Gardner, Carter, Enzman-Hines and Hernandez, 2016, p 352

- **Treatment Strategies: Hyperglycemia**

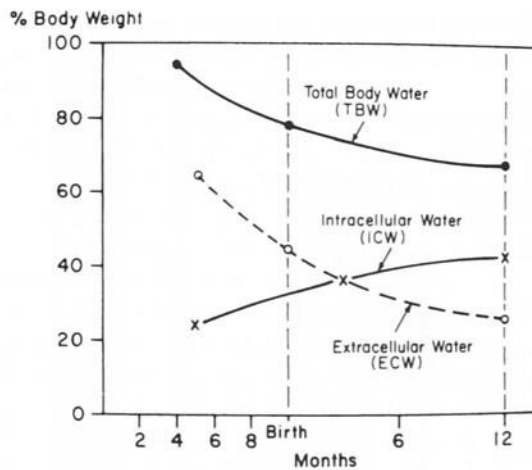
- Decrease glucose intake
- Monitor weight, urine output, fluid intake
- Glucose infusion rate:
 
$$\frac{[\text{Total ml/kg/day} \times \% \text{ dextrose (D10=0.1; D5=0.05)}] \times 1000}{1440 \text{ minutes/day}}$$
- Insulin infusion:
  - 0.2 to 0.8 mU/kg/min (0.01 – 0.05 units/kg/hr) for 12 – 24 hours
  - Start with a low infusion rate. Increase rate 10 – 20% every 60 – 90 minutes until glucose < 150 – 200 mg/dl
  - Monitor glucose levels every 15-20 minutes

## Fluid and Electrolyte Management

### Body Water Distribution

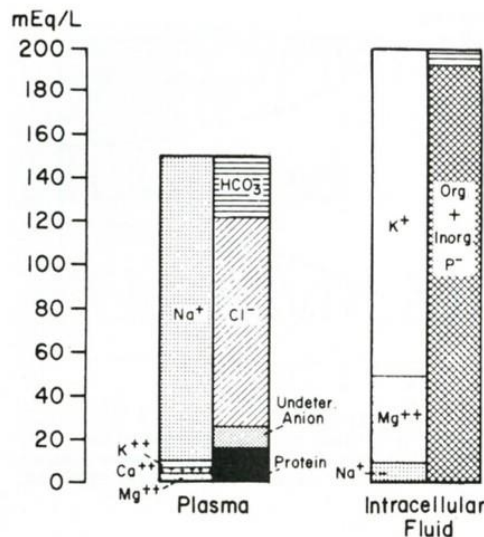
- 2 main compartments
  - Intracellular fluid (ICF)
  - Extracellular fluid (ECF)
    - Intravascular (plasma volume)
    - Interstitial space
- After birth, an acute increase in intravascular volume occurs

- Physiologic contraction of ECF volume occurs with diuresis in first week of life
  - Term: lose 5 – 10% of birth weight
  - Preterm: lose up to 20% of birth weight



MacDonald, Mullett and Seshia, 2005, p 363

- Amount and distribution of solutes/electrolytes is also redistributed
  - ECF
    - Main cation is sodium
      - Potassium, calcium, and magnesium
    - Main ion is chloride
      - Protein, bicarb and other anions
  - ICF
    - Main cation is potassium
      - Magnesium, calcium and sodium
    - Anions: organic and inorganic phosphates
      - Bicarbonate



MacDonald, Mullett and Seshia, 2005, p 364

- Regulation of Fluid Balance
  - Nephrons functional but immature until 34 weeks gestation
  - After birth, renal blood flow increases as renal vascular resistance decreases
  - Glomerular filtration rate increases:
    - Progressive increase in systemic blood pressure
    - Further decrease in renal vascular resistance
    - Gradual decrease in hematocrit
  - Both term and preterm can dilute urine, but when faced with a rapid fluid load the preterm has a delayed response, resulting in fluid retention
  - Reabsorption of sodium, bicarbonate and glucose is limited in the neonate
  - Antidiuretic hormone (ADH) released in response to hypotension and hyperosmolality
    - Influences water balance by stimulating the kidneys to conserve water
    - Neonates have decreased responsiveness to ADH—can't efficiently concentrate urine in response to fluid deprivation
  
- Fluid loss in Neonatal Period
  - Urine output
    - Initial diuresis: physiologic reduction of ECF
    - 1 – 4 ml/kg/hr
  - Stool losses
    - 5 – 10 ml/kg/day
  - Insensible Water Loss (IWL)
    - Free water loss occurring through passive evaporation from the skin and respiratory system
    - Major determinants of IWL
      - Environment
        - The lower the humidity level, the greater the evaporative gradient
      - Gestational age at birth
        - Mature infant has a well-cornified epithelial layer of skin
        - Subcutaneous fat envelops capillaries
      - Postnatal age
        - Skin matures very rapidly. IWL decreases 3 – 4 times by the end of the first week
        - Slows with decreasing gestational age
      - Relationship of body surface to size
        - Preterm has larger body surface area in relation to body weight, and much larger total body water content
      - Metabolic rate
        - Hyperthermia and an increased metabolic rate will increase IWL by increasing skin blood flow
        - With increased evaporative water losses, the infant loses body heat. 0.58 calories are lost for each cc of water evaporated at 37°
  - Assessment of Fluid Balance
    - Body weight: infant may not be stable enough to weigh

- Urine volume: collect before radiant warmer dries out diaper
- Specific gravity of urine
  - Indirect measure of urine osmolality (N: 100 to 300 mOsm/L).
  - Normal: 1.002 – 1.012
  - Unreliable if glucose, blood or protein present
- Physical assessment:
  - Skin turgor, mucous membranes, edema, anterior fontanelle (sunken)
- Hemodynamic assessment
  - Quality of pulses, blood pressure and perfusion
- Laboratory evaluation of hydration
  - Serum sodium, osmolality, blood urea nitrogen, creatinine, hematocrit

### **Fluid Depletion**

- Pathophysiology:
  - Fluid is lost from the body acutely or chronically.
- Etiology:
  - Extreme prematurity
    - Hyperosmolar hypernatremic dehydration
  - Acute blood loss
  - Diarrhea
  - Diabetes insipidus
  - Abdominal or pleural cavity exposure during surgery
  - Unreplaced losses from gastric suction
  - Medications that cause diuresis: caffeine; theophylline
  - Breast feeding malnutrition
- Clinical Presentation
  - Weight loss
  - Decreased urine output
  - Poor skin turgor, dry mucus membranes, sunken fontanelle/eyeballs
  - Tachycardia, peripheral vasoconstriction, pallor
  - Breastfed malnutrition: change in feeding behaviours
- Laboratory Data
  - Serum Na normal, low or high
  - BUN and creatinine elevated
  - Hematocrit value change from baseline
  - ABG's: metabolic acidosis
- Treatment Strategies
  - Minimize IWL
    - Supplemental humidity
    - Incubator rather than radiant warmer
  - Decrease respiratory losses using humidified gases
  - Fluids: 80 – 100 ml/kg/day with Na restriction
  - Treatment of hypovolemia with volume replacement and use of inotropes

- Complications
  - Electrolyte imbalance from slow excretion of daily solute load
  - Impaired excretion of drugs when urine output minimal
  - Renal failure and vascular thrombosis if severe dehydration

### **Fluid Excess**

- Edema: abnormal accumulation of ECF within the interstitial space, due to:
  - Low colloid osmotic pressure
  - Increased capillary permeability to water and protein
  - Increased hydrostatic pressure within the capillaries
  - Impaired lymphatic drainage of interstitial fluids and proteins
- Etiology
  - Impaired cardiac function
  - Excessive fluid intake
  - Perinatal asphyxia
  - RDS and BPD
  - Sepsis/NEC
  - Use of neuromuscular blocking agents
  - Renal failure
  - Syndrome of inappropriate antidiuretic hormone (SIADH)
    - Associated with CNS injury or meningitis
    - ADH secretion is inappropriate to usual osmotic and volume stimuli
    - Fluid retention with hyponatremia, low serum osmolality and high urinary sodium losses
- Clinical Presentation
  - Weight gain
  - Increased urine output if kidney can handle the load
  - Decreased urine output if renal failure
  - Edema: peripheral, generalized, pulmonary
  - Hemodynamic changes: depend on intravascular volume status
    - Symptomatic PDA, CHF
    - Tachycardia, increased pulses or pulse pressure
- Laboratory Data
  - Serum osmolality low (< 280 mOsm/L); urine osmolality normal
  - SIADH: urine output is low with increased specific gravity and sodium; serum has decreased sodium and osmolality
- Treatment Strategies
  - Fluid restriction and precise fluid management
  - Diuretics may be helpful
  - Improve cardiac function
- Complications
  - Third space losses
  - Worsening of RDS, development of BPD, symptomatic PDA and NEC

- Necrotic injury of skin—reposition frequently, protect skin from pressure with gel mattress

## **Electrolyte Balance and Disorders**

### **Sodium Homeostasis**

- Closely tied to water balance
- Cellular transport achieved by sodium-potassium pump
- Term infant efficiently absorbs sodium in proximal tubule
- Premature infant not capable of efficient reabsorption of sodium
  - High urinary losses of sodium
  - Not capable of increasing sodium excretion
    - Inefficient proximal tubule reabsorption
    - Distal tubule insensitive to aldosterone
  - Can not increase glomerular filtration rate
  - Requires more sodium to replace high baseline losses. CAUTION: any excess sodium will cause water and sodium retention

### **Hyponatremia**

- Low serum Na reflects either an excess of body water or a primary Na depletion
- Etiology
  - Prematurity
  - Conditions associated with a low intravascular volume – ex. Shock
  - Dilutional hyponatremia from excessive free water intake
  - Renal losses due to medications
  - Inadequate Na intake during period of rapid growth
  - SIADH
- Clinical Presentation
  - Usually asymptomatic
  - Serum Na < 130 mEq/L
- Treatment Strategies
  - Na supplementation after diuresis
  - Maintenance Na: 1 – 4 mEq/kg/day
  - Monitor weight, urine output, parameters of hydration, adequacy of intravascular volume
  - True SIADH: restrict fluid and monitor Na, osmolality and urine output
- Complications:
  - Acute hyponatremia can lead to a shift of fluid into brain cells and a cellular edema → apnea and seizures

### **Hypertatremia**

- Usually reflects deficiency of water relative to total body sodium content
- Etiology
  - Excessive IWL with insufficient fluid intake
  - High inadvertent Na intake
  - Diabetes insipidus
    - Deficiency of ADH, causing loss of water in excess of loss of Na

- Breast-feeding malnutrition in term infants
- Clinical Presentation
  - Signs of dehydration
  - Serum Na > 150 mEq/L
- Treatment Strategies
  - Gradually restrict Na to avoid sudden falls in plasma osmolality
  - Recalculate fluid intake
  - Reduce TEWL in the ELBW infant
  - Caution with saline solutions to maintain catheter patency
- Complications
  - Cell shrinkage

### **Potassium Homeostasis**

- Major cation in ICF compartment
- Regulated by the sodium-potassium pump
- Influenced by acid-base, insulin and glucagons
- Excretion depends on kidney function, GFR, urine flow rate and aldosterone sensitivity
- Hypokalemia
  - Decreased intracellular K infers inadequate cellular function
  - Etiology
    - Inadequate K intake
    - Increased GI losses from gastric suctioning
    - Metabolic alkalosis
    - Medications: bicarbonate, diuretics
    - Insulin: increases cellular uptake of K
  - Clinical presentation
    - Cardiac dysrhythmias
    - Hypotonia, abdominal distension, ileus
    - Serum K < 3.5 mEq/L
  - Treatment Strategies
    - K supplementation when urine output well established
    - Maintenance K 2 – 3 mEq/kg/day
  - Complications
    - Rapid administration of K can lead to fatal arrhythmias
    - Hypokalemia potentiates digitalis toxicity
- Hyperkalemia
  - Movement of K from the intracellular to the extracellular compartment.
  - Immature tubular function with poor response to aldosterone
  - Etiology
    - Extreme prematurity
    - Endogenous release of K from tissue destruction
    - Metabolic acidosis
    - Renal failure with decreased K clearance
  - Clinical presentation
    - Muscular weakness
    - Cardiac dysrhythmias



- Serum K > 6.5 mEq/L
- Treatment Strategies
  - Stop all K administration
  - Correct acidosis
  - Cation exchange resin (Kayexalate)
    - Na exchanged for K in intestine
    - Onset of action within 2 – 24 hours
  - Exchange transfusion
- Complications
  - Cardiac arrest
  - Kayexalate: hypocalcemia, hypomagnesemia, hypernatremia

### Calcium Homeostasis

- Functions:
  - Maintains cell membrane permeability
  - Activates reactions for muscle contraction, nerve transmission and blood clotting
  - Important for skeletal development
- Regulated by:
  - Parathyroid hormone (PTH)
    - Increases serum Ca by mobilizing Ca from bone and intestines
    - Decreases renal excretion of Ca
    - Stimulated by low serum Ca and magnesium levels
  - Vitamin D acts with PTH to increase absorption of Ca and phosphorus
  - Calcitonin decreases serum Ca which mobilizes effects of PTH
  - Phosphorus: inhibits absorption of Ca
- Serum Ca is transported in 3 forms
  - Protein-bound: accounts for 40% of total serum Ca
  - Inactivated Ca: combined with anions; accounts for 10% of total serum Ca
  - Free ionized Ca (iCa): physiologically active form; accounts for 50% of total serum Ca.
    - Acidosis increases iCa
- Hypocalcemia
  - Etiology
    - Prematurity: reduced Ca stores and relative hypoparathyroidism
    - Infant of a diabetic mother
    - Placental insufficiency
    - Perinatal asphyxia: precipitates a surge in calcitonin
      - Tissue damage and glycogen breakdown release phosphorus
    - Low Ca intake
    - “Late” occurs after 7 days
      - Hypomagnesemia
      - DiGeorge syndrome
      - High-phosphate formulas
        - Neonate can’t excrete excess phosphate
      - Intestinal malabsorption
  - Clinical Presentation

- Early: asymptomatic
      - Jitteriness, twitching
    - Serum total Ca < 7 mg/dl or ionized Ca < 4.4 mg/dl
  - Treatment Strategies
    - Monitor serum Ca of infants at risk
    - Early, mild hypocalcemia self resolving
      - Prevented by adding 200 mg/kg Ca gluconate to IV solutions
    - Late: correct underlying etiology
  - Complications
    - Rapid infusion of Ca can cause bradycardia or cardiac arrest
    - Tissue necrosis and calcifications can result from extravasated Ca
- Hypercalcemia
  - Etiology:
    - Iatrogenic
    - Hyperparathyroidism
    - Phosphate depletion: low dietary intake
  - Clinical Presentation
    - Hypotonia, weakness, irritability, poor feeding
    - Polyuria/dehydration
    - Bradycardia
    - Serum ca > 11 mg/dl; iCa >5.8 mg/dl
    - Xray: evidence of skeletal demineralization
  - Treatment Strategies
    - Hydrate infant and promote excretion of Ca
    - Restrict Ca and vitamin D intake
    - Increase phosphate intake
  - Complications
    - Nephrocalcinosis
    - Dysarrhythmias

### **Magnesium Homeostasis**

- Low neonatal Mag level directly related to maternal level prior to birth
- Acute decline stimulates PTH release
- Chronic Mg deficiency suppresses PTH → hypocalcemia
- Hypomagnesemia
  - Etiology
    - Decreased Mg supply: prematurity, placental insufficiency, IUGR, low dietary intake
    - Increased Mg losses: renal and intestinal disorders
    - Endocrine causes: neonatal hypoparathyroidism
  - Clinical presentation
    - Tremors, irritability, hyperreflexia, progressing to seizures
    - Failure to respond to therapy for hypocalcemia
    - Mg level < 1.5 mg/dl
  - Treatment Strategies

- Treat hypocalcemia
    - Magnesium sulfate given to relieve symptoms until Ca homeostasis achieved
  - Complications:
    - Hypotonia, respiratory depression, hypotension, cardiac arrhythmias
- Hypermagnesemia
  - Neonatal kidney unable to excrete excess
  - Etiology
    - Excessive Mg load: mother received MgSO<sub>4</sub> in labor
    - Reduced excretion: renal failure, Oliguria
  - Clinical Presentation
    - Respiratory depression, apnea
    - Lethargy, poor suck, loss of reflexes, flaccidity, hypotonia
    - GI hypomotility: abdominal distension
    - Serum Mg > 2.5 mg/dl
  - Treatment Strategies
    - Anticipate need for resuscitation if mother received large amounts of MgSO<sub>4</sub> during labor
    - Resolves with adequate hydration and urine output
    - Lasix can increase Mg excretion
    - Supportive care for signs of depression
  - Complications
    - Cardiac arrest and respiratory failure

## **General Principles of Fluid and Electrolyte Management**

### Day 1

- Calculate IWL based on gestational age, body weight and environment → replace this as free water
- Fluid requirements start at ~ 80 ml/kg/day
- Glucose infusion at rate of 4 – 8 mg/kg/min
- No sodium or potassium supplementation required
- Follow urine output, monitor electrolytes q 12 hrs
- Keep serum Ca 8 – 9 mg/dl
- Should lose 2 – 5% of birth weight

### Day 2-3

- Weight, serum electrolytes, urine output monitored
- Allow weight loss of 10 – 15% over first 3 – 7 days while maintaining normal serum electrolytes
- Increase fluids if weight loss > 5% in any one day, or 15% overall
- Decrease fluids if weight loss < 2% daily for first 3 days or < 7 – 10% overall
- Increase fluids if urine output < 0.5 ml/kg/hr in any 8 hour period **after** diuresis established (early Oliguria common)
- NaCl started: when fluid volumes need to be increase, or when Na < 135 mEq/l
  - Increase Na
    - If weight loss > 5%/day or 15% overall, and the serum Na is normal or low

- If there is hyponatremia ( $< 135$  mEq/l) and no weight gain to indicate fluid overload
  - Decrease Na
    - If no weight loss
    - If weight gain, unless there is also hyponatremia
- Potassium: add 1 – 2 mEq/kg/day when urine output established
- Glucose rate: remain fairly constant
- Increase fluids as tolerated

#### Day 4 – 7

- Nutritional intake gradually increased
- Monitor Cr levels, output, etc
- After diuresis, fluid therapy liberalized

### **Inborn Errors of Metabolism**

- Single gene disorders result in blocks in metabolic pathways
- Any metabolic pathway may be affected: carbohydrate metabolism, amino acid metabolism, organic acid metabolism, purine metabolism, errors in fatty acid oxidation, lysosomal storage diseases, errors of peroxisomes
- Can present any time; affect any organ system
- Treated as medical emergency
- Laboratory analysis dependent upon presenting symptoms
  - Electrolytes, ammonia, glucose, urine pH, urine-reducing substances, urine ketones are obtained prior to the initiation of treatment
- Characteristics
  - Hypoglycemia; ketonuria; seizures, parenchymal liver disease
  - Unusual odor, hyperammonemia
  - Acidosis with recurrent vomiting
  - Acidosis out of proportion with clinical picture
  - Family history/affected sibling
- Additional laboratory tests:
  - Serum and urine amino acids; urine organic acids
  - DNA testing available for some disorders
- Each State decides individually which disorders will be screened
  - Tandem mass spectrometry enables a single spot of blood to test for more than 40 inborn errors of metabolism
  - Hyperammonemias and lactic acidosis not tested by expanded newborn screen
- **Disorders of Carbohydrate Metabolism: Galactosemia**
  - Incidence: 1 in 40,000 live births
  - Etiology: deficiency of galactose-1-phosphate-uridyltransferase (GALT) prevents the conversion of galactose to glucose
  - Gene location: chromosome 9p13
  - Inherited as an autosomal recessive disorder
  - Clinical Presentation

- Appears normal at birth
    - Once milk feeding begins, galactose and other metabolites accumulate in blood and urine
    - Symptoms: vomiting, diarrhea, jaundice, failure to thrive, hepatomegaly, hypoglycemia.
    - Jaundice presenting in the first weeks of life, persisting.
    - Later signs: multiorgan toxicity, with liver disease that progresses to cirrhosis, portal hypertension, splenomegaly, ascites
    - *Escherichia coli* sepsis occurs as a complication in 50% of the affected infants
  - Associated findings:
    - Speech defects: especially expressive speech, delayed speech, language and learning disabilities.
    - Behavioral disorders, short attention span.
    - Infertility: ovarian failure and amenorrhea and hypogonadism.
    - Cataracts developing within 2 months of birth, reverse with treatment
  - Treatment.
    - Initiation of a lactose-free diet is essential
    - Parents must receive appropriate counseling
    - Galactose 1-phosphate levels in red blood cells are monitored.
    - With treatment, intellectual development may be normal or near normal
    - Communication problems continue throughout life despite speech therapy
- **Disorders of Amino Acid Metabolism: Phenylketonuria**
- Most common inborn error of amino acid metabolism that may result in mental retardation
  - Occurs in more frequently in whites, 1 per 10,000 live births
  - Gene location: chromosome 12q22-q24.1
    - Inherited as an autosomal recessive trait
  - Results from a deficiency of the liver enzyme phenylalanine hydrolase to convert phenylalanine to tyrosine
  - Presentation
    - Infant ingesting breast milk or formula will experience a gradual and persistent increase in plasma phenylalanine levels
    - Early symptoms: vomiting, poor feedings, hyperactivity, and irritability.
    - Untreated PKU: severe mental retardation, hyperactivity, and seizures.
    - After 6 months of age, developmental delays, seizures, infantile spasms, and musty-smelling urine
    - Untreated, the infant will demonstrate postnatal microcephaly.
  - Diagnosis
    - Standard newborn screening is done with the infant receiving a regular diet.
    - DNA sequencing and mutational analysis to identify carriers in families, and assist with family genetic counseling

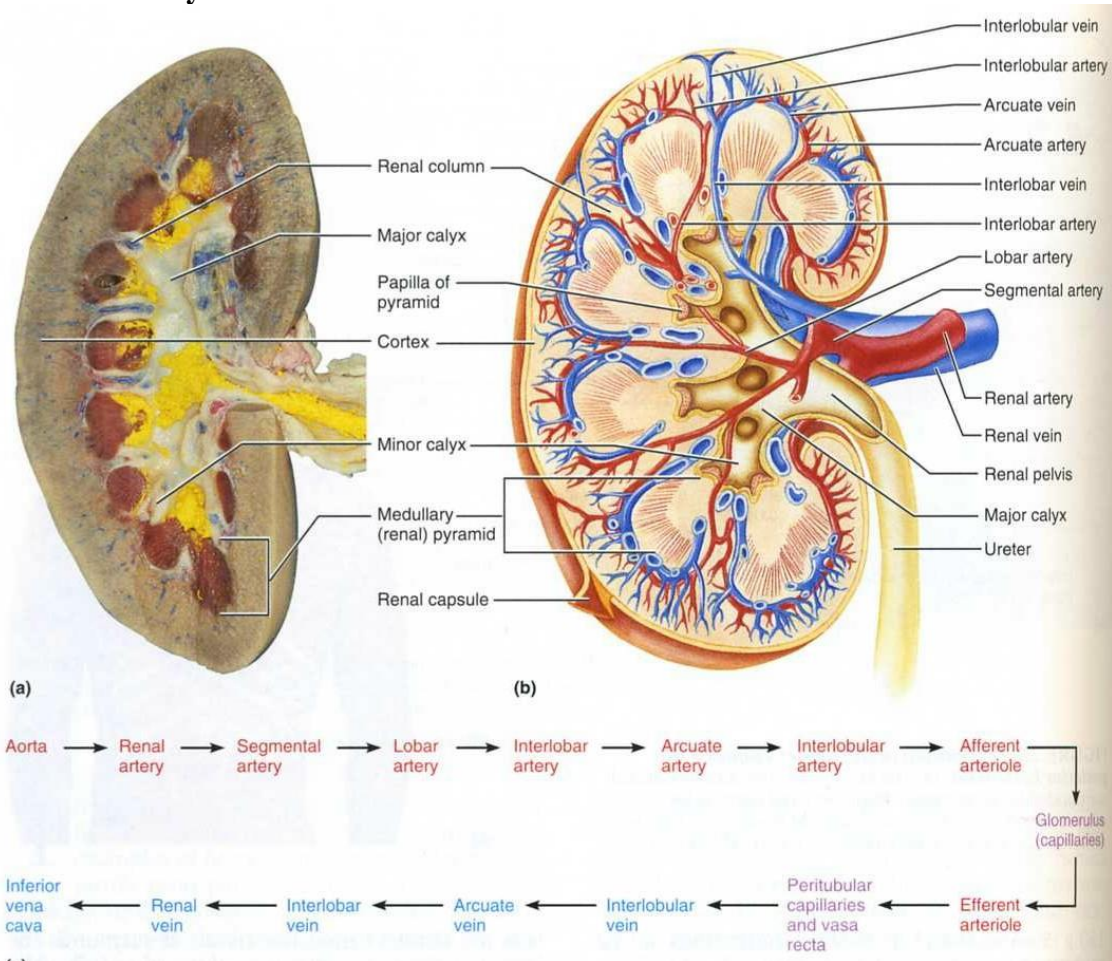
#### Treatment

- Low-protein diet and use of special amino acid-containing formula that does not have phenylalanine.
- Parents must be counseled to understand the importance of continued dietary restrictions.

- A phenylalanine exchange system that allows for normal daily utilization of foods containing phenylalanine while maintaining safe plasma phenylalanine levels is essential.

## DISORDERS OF THE RENAL SYSTEM

### Renal Anatomy:

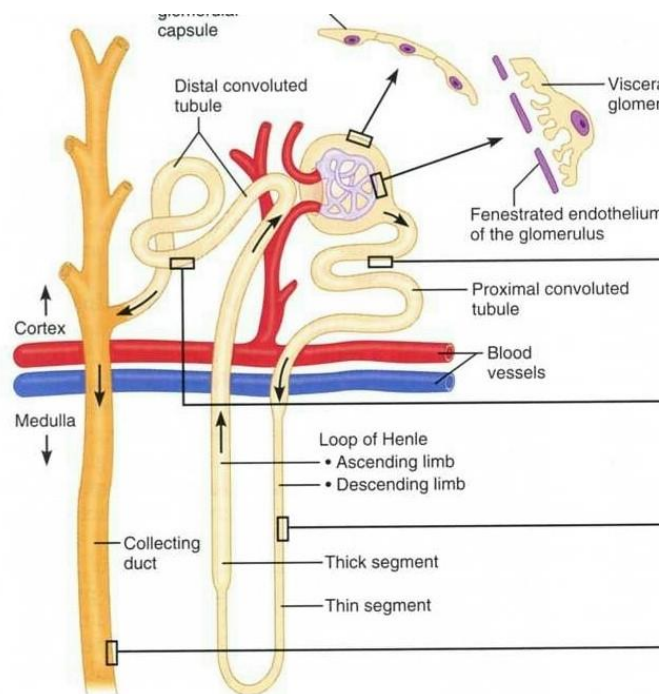


\*Marieb EN (2001). Human Anatomy & Physiology, 5<sup>th</sup> Ed. Benjamin Cummings: San Francisco. Pg 1006.

- Cortex: glomeruli, proximal and distal convoluted tubules and collecting ducts of the nephron
- Medulla: renal pyramids, straight portions of tubules, loops of Henle, vasa recta and terminal collecting ducts
- Renal sinus and pelvis: Renal sinus contains the uppermost portion of the renal pelvis and calyces, surrounded by fat in which renal vessels and nerves are imbedded
- Ureter: transports urine from the kidney to the bladder

## The Nephron

- Composed of glomerulus, Bowman capsule, and the tubules
- All nephrons present by ~34 weeks gestation



\*Marieb EN (2001). *Human Anatomy & Physiology*, 5<sup>th</sup> Ed. Benjamin Cummings: San Francisco. Pg 1006.

- Functional component of the nephron:
  - Glomerulus: formed by a capillary network
  - Bowman capsule: a membrane surrounding the glomerulus—serves as the filter mechanism
- Tubular system: proximal convoluted tubule, loop of Henle, distal convoluted tubule and collecting duct

## Renal Dynamics

- Renal Blood Flow
  - Comprises 4 – 6% of CO during first 12 hours of life; and 8 – 10% of CO during first week of life
  - Rate determined by CO, increasing systemic vascular resistance and decreasing renal vascular resistance
- Regulation of renal blood flow
  - Autoregulation
    - Ability of the kidney to maintain a relatively constant glomerular filtration rate (GFR) over a range of systemic blood pressures
    - Tubuloglomerular feedback mechanisms:

- Afferent arteriolar vasodilator
  - activated by decreased glomerular filtrate in the tubules → dilates afferent arteriole and increases GFR
- Efferent arteriolar vasodilator
  - feedback mechanism activated by decreased volume → stimulates renin release → constriction of the efferent arteriole to maintain the GFR.
- Hormonal regulation
  - Renin-angiotensin-aldosterone system
    - Major renal hormonal system
    - Responsible for regulation of systemic blood pressure, sodium, potassium, and regional blood flow

### **Renal Physiology**

- GFR doubles in first 2 weeks of life
- Fractional excretion of sodium decreases due to increasing tubular reabsorption
- Increasing ability to concentrate urine
- Renal vasoactive hormones are initially increased
- Renal vascular resistance decreases
- Renal blood flow increases
  
- Glomerular Filtration
  - Plasma is filtered through the glomerular capillary walls
  - Filtrate is collected in Bowman's space and enters the tubules where the composition is modified, until it is excreted as urine
  - 3 primary factors determine GFR:
    - glomerular capillary hydrostatic pressure
    - hydrostatic pressure in Bowman capsule
    - capillary colloid osmotic pressure
  - Factors decreasing GFR at birth:
    - Small glomerular capillary area available for filtration
    - Structural immaturity of glomerular capillary, associated with decreased water permeability
    - Decreased blood pressure
    - Increased hematocrit
    - Renal vasoconstriction, which results in decreased glomerular plasma flow
  
- Tubular Function
  - Components of the tubular system: proximal tubule, loop of Henle, distal tubule and collecting ducts
  - Proximal tubule is the major site of reabsorption
  - Important in the regulation of fluid and electrolytes
  - Altered in the neonate due to decreased renal blood flow and GRF
  - Tubular portions of the nephron are small and less functionally mature → altered ability to transport sodium, urea, chloride and glucose
  - Sites of urinary concentration and dilution



- Loop of Henle
    - Collecting ducts
  - Factors responsible for limited ability of the neonatal kidney to concentrate urine:
    - Anatomic immaturity of renal medulla
    - Decreased medullary concentration of sodium chloride and urea
    - Decreased responsiveness of the collecting ducts to arginine vasopressin
- Regulation of Acid-Base
  - Excreting acidic urine reduces the amount of acid in extracellular fluid, while excreting alkaline urine removes base from the extracellular fluid.
  - Kidneys regulate extracellular H<sup>+</sup> concentration through three processes
    - Secretion of H<sup>+</sup>
    - Reabsorption of filtered bicarbonate
    - Production of new bicarbonate.
- Laboratory Evaluation of Renal Function
  - Serum creatinine level
    - Most commonly used indicator of neonatal kidney function
    - Concentration immediately after birth reflects the maternal creatinine concentration, neonatal muscle mass, and GFR at the time of delivery.
    - Term infants: level gradually decreases from 1.1 mg/dL to a mean value of 0.4 mg/dL within the first 2 weeks of life.
    - Preterm infants: level does not fall steadily from birth but instead rises in the first 48 hours before beginning to fall to equilibrium levels
    - Failure of the serum creatinine level to fall or a persistent increase in serum creatinine suggests impairment of renal function.
      - Each doubling of the serum creatinine level represents an approximately 50% reduction in GFR
    - Blood urea nitrogen (BUN): indirect measure of kidney function
      - May be elevated as a result of increased production of urea nitrogen in catabolic states, sequestered blood, tissue breakdown, or increased protein intake
      - Renal insufficiency is suspected if the BUN is greater than 20 mg/dL or if it rises at a rate of 5 mg/dL/day or higher

### **Acute Kidney Injury**

- Characterized by a deterioration in kidney function leading to an inability to excrete waste products and maintain fluid and electrolyte homeostasis
- Defined as a serum creatinine of more than 1.5 mg/dL
- Oliguric acute kidney injury: urine flow rate of less than 1 mL/kg/hr.
- Nonoliguric acute kidney injury: urine flow rate is greater than 1 mL/kg/hr.
- Risk factors for developing acute kidney injury
  - Very low birth weight (<1500 g)
  - Low 5-minute Apgar score
  - Maternal drug administration (nonsteroidal antiinflammatory drugs and antibiotics)
  - Respiratory distress syndrome
  - Patent ductus arteriosus

- Neonatal medication administration (nonsteroidal antiinflammatory drugs, antibiotics, diuretics).
- Signs of acute kidney injury
  - Elevated serum creatinine and BUN
  - Hyperkalemia
  - Metabolic acidosis
  - Evidence of fluid overload or dehydration.
  - Half-life for medications excreted by the kidney may also be prolonged.
- The causes of acute kidney injury are multiple and can be divided into three categories: prerenal, renal, and postrenal

<b>Prerenal</b>
Dehydration
Hemorrhage
Sepsis
Necrotizing enterocolitis
Congestive heart failure
Drugs: angiotensin-converting enzyme inhibitors, nonsteroidal antiinflammatory agents, amphotericin, tolazoline
<b>Intrinsic</b>
Acute tubular necrosis
Renal dysplasia
Polycystic kidney disease
Renal vein thrombosis
Uric acid nephropathy
Transient acute renal insufficiency of the newborn
<b>Postrenal</b>
Posterior urethral valves
Bilateral ureteropelvic junction obstruction
Bilateral ureterovesical junction obstruction
Neurogenic bladder
Obstructive nephrolithiasis

Causes of Acute Renal Failure in the Neonate  
Fanaroff and Fanaroff, 2013, pg 419

- Prerenal AKI:
  - Due to hypoperfusion of normal kidney
  - Etiology: see table
  - Clinical Presentation
    - Oliguria, decreased urinary sodium losses, increased osmolality
- Intrinsic (parenchymal)
  - Most common etiology: perinatal asphyxia and sepsis (see table)
  - Severity ranges from mild tubular abnormalities to acute tubular necrosis, to infarction and corticomedullary necrosis with irreversible kidney damage
- Post-renal AKI
  - Due to disorders distal to the kidney that cause obstruction to urinary flow

- Etiology: see table
- Prognosis depends on degree of renal dysplasia, the frequency of urinary tract infections, and urinary stasis
- Clinical Presentation of AKI:
  - Oliguria: urinary output < 1 cc/kg/hour
    - ~ 33% of affected neonates have normal output
  - Serum creatinine > 1.5 mg/dL; or an increasing creatinine level  $\geq 0.3$  mg/dL per day
  - Polyuria, hematuria, proteinuria
  - Fluid overload, dehydration, vomiting, poor eating
  - Elevated serum medication levels
- Treatment Strategies
  - History and physical examination
  - Ultrasound of kidney/bladder
  - Voiding cystourethrography
  - Urinalysis/urine culture
  - Fluid challenge
  - Low-dose dopamine
  - Electrolytes, CBC and differential, glucose, ABGs
  - Monitor for development of congestive heart failure
  - Attention to nutrition to avoid a catabolic state

### **Hypertension**

- Assumed to have a specific secondary etiology
- Most common causes include renovascular anomalies and intrinsic renal disease

### *Vascular*

- Renal artery stenosis
- Renal artery thrombosis
- Coarctation of the aorta
- Hypoplastic abdominal aorta
- Renal vein thrombosis
- Idiopathic arterial calcification

### *Renal*

- Renal dysplasia or hypoplasia
- Polycystic kidney disease (autosomal dominant or recessive)
- Renal failure
- Obstructive uropathy
- Reflux nephropathy
- Pyelonephritis
- Glomerulonephritis

### *Tumors*

- Wilms' tumor
- Neuroblastoma

### *Endocrine*

- Adrenogenital syndrome
- Cushing disease
- Hyperaldosteronism
- Thyrotoxicosis

### *Other*

- Closure of abdominal wall defects
- Fluid overload
- Genitourinary surgery
- Hypercalcemia
- Increased intracranial pressure
- Medications
  - Phenylephrine
  - Corticosteroids
  - Theophylline
  - Deoxycorticosterone
- Seizures
- Chronic lung disease/bronchopulmonary dysplasia

Gardner, Carter, Enzman-Hines and Hernandez, 2011, p 734

- Ensure correct cuff size is used: small cuffs give falsely high values
- Clinical Presentation
  - Persistent elevation of blood pressure
    - Term: > 90/60
    - Preterm > 80/50
  - Nonspecific symptoms:
    - Feeding difficulties, tachycardia, lethargy, mottling of skin
    - Mild to moderate hypertension: asymptomatic
    - Life threatening hypertension: congestive heart failure

- Treatment Strategies
  - Renal ultrasound with Doppler flow study: rule out renovascular hypertension
  - Renal scan: renal thrombosis or correctable lesion
  - MRI or CT: tumors or masses
  - Treatment initiated when hypertension becomes severe: > 110 systolic
  - Goals: initial lowering of BP by 30% and determine cause
  - Treatment initiated when hypertension becomes severe: > 110 systolic

**Table 25-4 ANTIHYPERTENSIVE MEDICATIONS FOR USE IN THE NEONATAL PERIOD\***

MEDICATIONS	DOSE	SCHEDULE	ROUTE	COMMENTS
Propranolol	1-4 mg/kg/dose	bid-tid	PO	Contraindicated in heart failure, possibly in BPD, sedation
Hydralazine	0.025-1 mg/kg/dose	bid	IV	Tachycardia, sodium retention
	0.25-1.5 mg/kg/dose (max 4.5 mg/kg/day)	bid-qid	PO	
	0.1-0.5 mg/kg/dose with beta blocker	q6h	IV	
Captopril	0.4-0.8 mg/kg/dose (sole agent) 0.1-2.0 mg/kg/dose	tid	PO	Leukopenia, rash, proteinuria, hyperkalemia, acute renal failure, seizures
Enalapril	0.1-0.3 mg/kg/dose	qd-q12h	PO	Hypotension
Enalaprilat	0.005-0.05 mg/kg/dose	qd-q12h	IV	Hypotension
Diazoxide	1-5 mg/kg/dose	q4-24h	IV	Hyperglycemia, fluid retention, hyperuricemia
Sodium nitroprusside	0.5-10 µg/kg/min	Continuous infusion	IV	Keep covered in foil, careful observation for infiltration of IV or varying rate of administration

\*No reported experience in the newborn with nifedipine, clonidine, labetalol, or verapamil. Furosemide and thiazides are not antihypertensive medications but are used for volume overload.  
BPD, Bronchopulmonary dysplasia.

Gardner, Carter, Enzman-Hines and Hernandez, 2011, p 736

- Complications
  - Congestive heart failure
  - Left ventricular hypertrophy

### Potter Syndrome (Oligohydramnios Syndrome)

- Also known as “prune belly syndrome” because of the appearance of the abdomen
- Spectrum of abnormalities characterized by abdominal wall deficiency and hydronephrosis
- Males affected 10 times more than females
- Etiology:
  - Thought to be related to obstructive uropathy and mesenchymal dysplasia
- Clinical Presentation
  - Potter facies: blunted nose, micrognathia, low-set ears, wide spaced eyes, depressed nasal bridge
  - Lax, floppy abdominal wall, flattened diaphragm with flaring of ribs
  - Massively dilated upper urinary tract and bladder
  - Severe cases: pulmonary hypoplasia
- Clinical Assessment
  - Urine output

- Anomalies
- Symptoms of respiratory distress
- Perinatal history of Oligohydramnios
- Palpate abdomen: presence of kidneys
- Diagnostic Testing:
  - Renal ultrasound: assess renal parenchyma
  - VCUG should not be done—knowing if there is reflux will not change management
- Treatment Strategies
  - Administer antibiotics for UTI prophylaxis
  - Vesicostomy: decompress urinary tract
- Complications
  - Associated with ARF and RDS
  - Palliative care /support for family. The kidneys are often dysplastic, which will determine the prognosis.
    - Most affected will die in the neonatal period
    - May not develop end stage renal failure until much later in life
    - Reconstruction of the urinary tract and plication of the abdominal wall may improve the outcome in some survivors

### **Polycystic Kidney Disease**

- Cysts are present, without evidence of renal dysplasia
- Etiology:
  - Autosomal recessive polycystic kidney disease
    - Typically bilateral
    - Kidney enlarged with proliferation of renal tubules and dilated collecting tubules
  - Autosomal dominant polycystic kidney disease
    - Cyst formation in nephron, Bowman's space, liver
    - Mean onset at age 57
- Clinical Presentation (recessive)
  - History of oligohydramnios
  - Bilateral flank masses
  - Oliguria, renal insufficiency
  - Abdominal distention from massively enlarged kidneys
  - Respiratory distress, pneumothorax
  - Hypertension
- Treatment Strategies
  - Renal ultrasound: shows symmetrically enlarged hyperechoic kidneys with loss of corticomedullary junction
  - Genetic counseling for parents
  - Monitor renal function
  - Supportive care
    - Monitor electrolytes: hyperkalemia, hyperphosphatemia, hypocalcemia
    - Treat hypertension, congestive heart failure
    - Adequate nutrition to support growth and development
- Complications

- Renal failure
- Hypertension
- Congestive heart failure
- Portal hypertension and hepatic failure

### **Hydronephrosis**

- Dilation of the pelvis and calyces of one or both kidneys, resulting from obstruction of urine flow
- Etiology
  - Unclear; congenital obstruction is commonly at the site of the ureteropelvic junction.
  - Also known as congenital megaureter.
  - More common in males: posterior urethral valves major cause of urethral obstruction. If severe, the obstruction will lead to bladder hypertrophy, hydroureter and hydronephrosis.
- Clinical Presentation
  - No physical findings unless bladder/kidney palpated on physical exam
  - Palpable abdominal mass
  - Stigmata of Potter syndrome
  - Urinary tract infections – recurrent may lead to renal damage
- Diagnostic Testing:
  - Renal ultrasound: kidney and bladder should be done between 2 – 5 days of age.
  - Voiding cystourethrogram (VCUG): detect posterior urethral valves
  - Evaluate BUN and creatinine levels
- Treatment Strategies
  - No immediate treatment for mild to moderate unilateral obstruction: monitor
  - Surgical correction for obstruction at uteropelvic an/or uterovesical junctions
    - Uteropelvic/uterovesical junction obstruction:
      - Pyeloplasty: stenotic segment removed and ureter reattached
    - Posterior urethral valves
      - Catheterize to provide urinary drainage
    - Vesicoureteral reflux:
      - Antimicrobial prophylaxis: Amoxicillin
      - 95% of neonates have complication-free corrections

### **Renal Vein Thrombosis**

- Etiology
  - Any condition resulting in decreased renal blood flow
    - Hyperviscosity
    - Hypovolemia
    - Hypercoagulable states
- Clinical Presentation
  - Hematuria, flank mass and thrombocytopenia
  - Hypertension
  - Oliguria
- Treatment Strategies

- Renal ultrasound: enlarged kidney
- Doppler flow study: thrombosis
- Treat underlying etiology
- Supportive care: correct electrolyte disorders, fluid imbalance, coagulation disorders

### Urinary Tract Infections

- Etiology
  - Abnormalities of urinary tract
  - Sepsis
    - *E. coli*: responsible for 75% of UTIs
  - Occurs more frequently in males than females
- Clinical Presentation
  - May be asymptomatic
  - Symptomatic: nonspecific presentation
- Diagnostic Studies:
  - Urine culture
  - Urinalysis
  - Blood culture
  - CBC with differential
  - Ultrasound: rule out urologic abnormalities
  - Voiding cystourethrogram (VCUG) to rule out reflux
- Treatment Strategies
  - Antibiotics given for 10 days:
    - Ampicillin and aminoglycoside
    - Vancomycin and aminoglycoside if Nosocomial
  - Prophylaxis coverage if abnormal urinary tract
  - Sterilization of urine should be documented post-treatment
  - VCUG should be done as soon as the infection has resolved to assess for vesicoureteral reflux

### Hypospadias

- Urethral meatus located on ventral surface of penis
- Varies in severity: slightly malpositioned meatus still within the glans and without chordee  
→ extreme genital ambiguity with hypoplastic phallus, bifid scrotum and scrotal or perineal meatus
- Etiology
  - Delay or arrest in normal sequence of development
- Clinical presentation
  - Urinary meatus located on undersurface of penis
  - Deviation of urinary stream
- Clinical Assessment
  - Observe external genitalia:
    - Variable chordee
    - Assess for associated anomalies

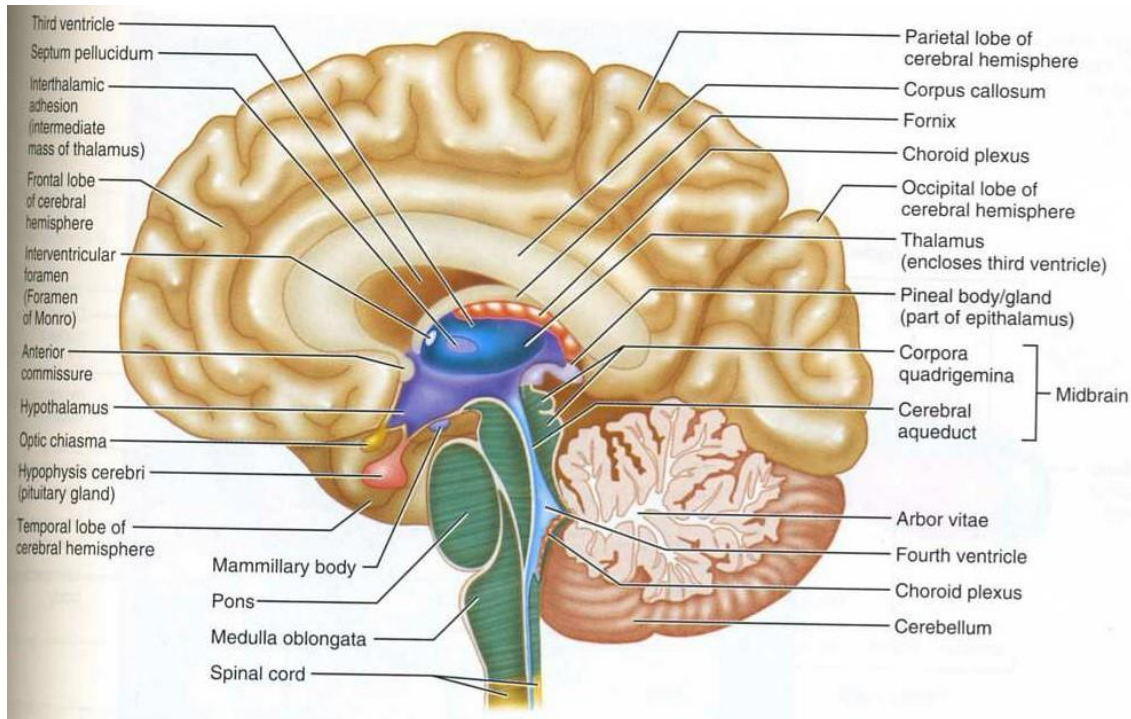


- Inguinal hernia
  - Cryptorchidism
- Treatment Strategies
  - Avoid circumcision\*\*
  - Genotypic evaluation if only one gonad palpated
    - Congenital adrenal disease must be ruled out if no gonads are present
  - Surgical repair
    - Move meatus distally
    - Straighten curved penis
    - Single stage repair at about 6-12 months of age

### **Exstrophy of the Bladder**

- Bladder is exposed and protruding onto the abdominal wall
- All male infants have an associated epispadias
- Remainder of the urinary tract is normal
- Etiology
  - Abnormal development of the cloacal membrane
- Clinical Presentation
  - External presentation of the bladder
  - Associated anomalies
  - Palpate:
    - Descent of testes
    - Inguinal hernias
    - Widening of symphysis pubis
- Treatment Strategies
  - Cover with plastic wrap only
  - Prepare for surgical closure
  - Antibiotic therapy for 7 days postoperatively

## REVIEW OF THE NEUROLOGICAL SYSTEM

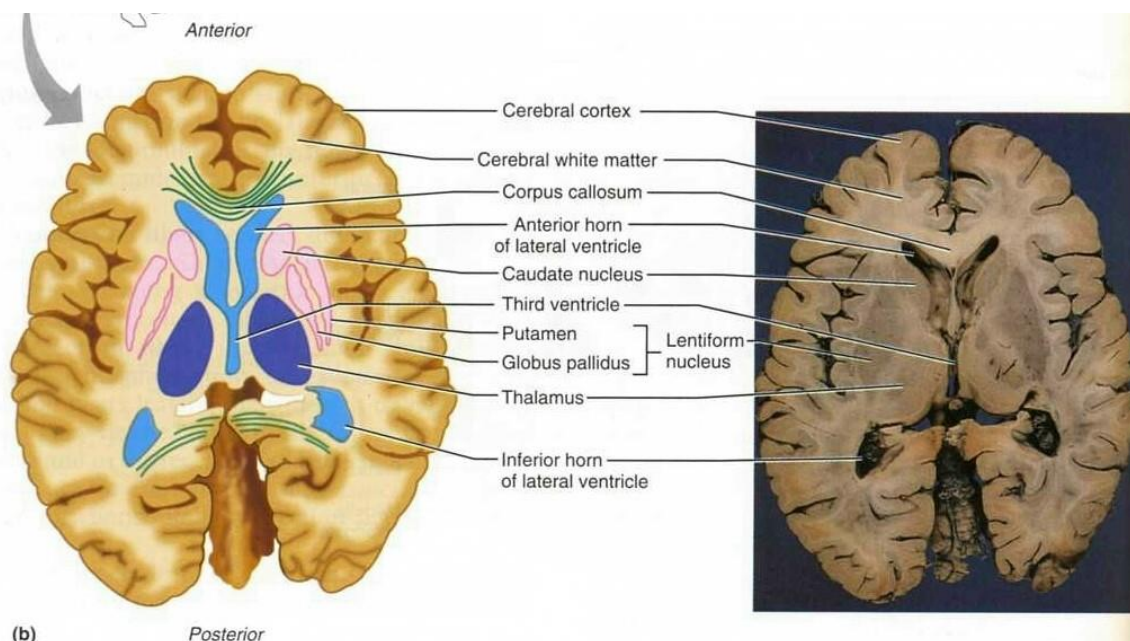


Marieb EN (2001). Human Anatomy & Physiology, 5<sup>th</sup> ed. San Francisco: Benjamin Cummings, pg. 444.

### Anatomy

- Cerebellum
  - Promotes integrative muscle function
  - Maintains balance
  - Enables smooth, purposeful movements
- Cerebrum
  - Contains 4 lobes
    - Frontal lobes: concerned with decision making
    - Parietal lobes: hearing, understanding speech and forming an integrated sense of self
    - Occipital lobes: vision
    - Temporal lobes: center for smell, with association areas for memory and learning
  - Corpus callosum: fiber bundles connecting the cerebral hemispheres
  - Cerebral cortex
    - Encompasses the mind
  - Gray matter
  - Lateral ventricles
  - Third ventricle
  - Thalamus: integrates sensory input
  - Hypothalamus: regulates body temperature
- Brainstem

- Relays input and output signals between higher brain centers and spinal cord
- Three main components
  - Medulla oblongata
    - Implicated within cranial nerves VIII, IX, X, XI and XII
    - Controls areas of the abdomen, thorax, throat and mouth
  - Pons
    - Carries information between the brainstem and the cerebellum
  - Midbrain: eye movements



(b) Posterior  
 Marieb EN (2001). Human Anatomy & Physiology, 5<sup>th</sup> ed. San Francisco: Benjamin Cummings, pg. 444.

### Physiology

- Glucose Metabolism
  - Glucose is transported from blood to brain by a glucose transporter found in capillaries
  - Brain depends on adequate circulation to supply both oxygen and glucose to create enough energy for normal growth and metabolism
  - Glycogen stores are minimal or nonexistent in the premature baby
  - 38 molecules of ATP are generated for each molecule of glucose oxidized under aerobic conditions
  - Under anaerobic conditions:
    - Lactate results → only gives off two molecules of ATP
    - Glycolysis is increased as much as ten-fold
    - Concomitant increase in the net uptake of glucose from the blood
    - Inefficient anaerobic metabolism continues to excessively consume glucose such that glucose delivery cannot meet the demand
    - As a result, ATP and brain glucose levels fall within minutes

- Ischemia further compounds the hypoxia because the impaired circulation rapidly increases lactate and tissue acidosis
    - A “normal” chemstrip or blood glucose reading may have little relationship to the brain glucose value under anaerobic conditions.
  - Neonatal brain is glucose dependent. CNS is quickly and significantly affected by hypoglycemia. Blood glucose levels < 30 are associated with significant decreases in cerebral blood flow
- Cerebral blood flow
  - Brain increases cerebral blood flow to maintain glucose and oxygen
  - Cerebral blood flow increased:
    - Decreasing pH
    - Increasing potassium
    - Hypoxemia
    - Increasing osmolarity
    - Decreasing calcium
    - Blood glucose < 30 mg/dl
- Autoregulation
  - Maintains steady-state cerebral blood flow over a broad range of perfusion pressures
  - Normal arterial blood pressure in the preterm at or near the lower autoregulatory limit
    - Increased vulnerability to ischemic brain injury with modest hypotension
  - Cerebral vasculature vasodilates maximally in response to hypoxemia, hypercapnia and acidosis
  - Hypotension leads to ischemia
    - Ischemia damages blood vessels and surrounding structures supporting blood vessels
    - Blood flow to cerebral white matter restored only after reperfusion of other brain regions
    - Once adequate blood supply resumes, hemorrhage can occur into ischemic areas
  - Hypertension leads to hemorrhage

### **Neurologic Assessment**

- History
- Observation
  - Undisturbed state
  - Determine behavioural state

**TABLE 24–1. Neonatal State Classification Scale**

STATE	CHARACTERISTICS
Quiet sleep	Regular breathing, eyes closed; spontaneous activity confined to startles and jerky movements at regular intervals. Responses to external stimuli are partially inhibited, and any response is likely to be delayed. No eye movements, and state changes are less likely after stimuli or startles than in other states.
Active sleep	Irregular breathing patterns, sucking movements, eyes closed but rapid eye movements can be detected underneath the closed lids. Infants also have some low-level and irregular motor activity. Startles occur in response to external stimuli and can produce a change of state.
Drowsiness	While the newborn is semidozing, eyes may be open or closed; eyelids often flutter; activity level variable and interspersed with mild startles. Drowsy newborns are responsive to sensory stimuli but with some delay, and state change frequently follows stimulation.
Alert inactivity	A bright alert look, with attention focused on sources of auditory or visual stimuli; motor activity is inhibited while attending to stimuli.
Active awake	Eyes open, considerable motor activity, thrusting movements of extremities, and occasional startles set off by activity; reactive to external stimulation with an increase in startles or motor activity. Discrete responses are difficult to distinguish due to general high activity level.
Crying	Intense irritability in the form of sustained crying, and jerky limb movement. This state is difficult to break through with stimulation.

(Data from Brazelton, T. B.: Neonatal Behavioral Assessment Scale, 2nd ed. London. Heinemann. 1984.)

- Evaluate posture and muscle tone
  - Term: flexed
  - Preterm: open, extended position
  - May reflect intrauterine positioning initially

**NEUROMUSCULAR MATURITY**

	-1	0	1	2	3	4	5
<b>Posture</b>							
<b>Square Window (wrist)</b>	>90°	90°	60°	45°	30°	0°	
<b>Arm Recoil</b>		180°	140°–180°	110°–140°	90–110°	<90°	
<b>Popliteal Angle</b>	180°	160°	140°	120°	100°	90°	<90°
<b>Scarf Sign</b>							
<b>Heel to Ear</b>							

- Minimal, absent or asymmetric movements indicate a need to rule out neurologic abnormalities
    - Quality of movements: jitteriness, seizures, tremors, hypertonic/hypotonic
  - Respiratory Activity
    - Signs of respiratory distress
    - Hypoventilation (apnea)
    - Quality of the cry
      - Vigorous and sustained, easily elicited
      - High-pitched, shrill cry, weak and unsustained indicate probable neurologic abnormalities
      - Stridor
  - Inspect skin
    - Lesions: note number, size, shape, colour and texture
      - Café-au-lait spots: neurofibromatosis
      - Port-wine facial hemangioma: Sturge-Weber syndrome
      - Areas of depigmentation
    - Abrasions, lacerations, bruises and forceps marks
- Physical Examination
  - Note head shape, symmetry, hair whorls, fontanelles, sutures
  - Measure occipital frontal circumference
    - < 10<sup>th</sup> percentile: symmetric vs asymmetric compared with total body growth; microcephaly
    - > 10<sup>th</sup> percentile: compare with body growth; macrocephaly
  - Examine facial structures
  - Spine
  - Reflexes
    - Check grasp, Babinski, Moro, gag, suck, root and tonic neck
    - Evaluate symmetry and strength of response
    - Abnormal Moro: consider clavicular or humeral fractures; brachial plexus injury

## **Neurologic Disorders:**

### **Anencephaly**

- Partial absence of skull bones, with absent cerebrum, most commonly involving the forebrain and variable amounts of upper brainstem
- Etiology: failure of anterior neural tube closure
- Clinical presentation
  - Exposed neural tissue with little definable structure
  - Anomalous skull has froglike appearance from en face view
- Management strategies
  - Identified by prenatal ultrasound
  - Provide comfort care measures
  - Support the grieving process

### **Posterior Neural Tube Defects**

- Due to failure of posterior neuropore closure

- **Spinal Bifida Occulta**
  - Mildest form of NTDs
  - Skin covers the opening of the spinal column
  - Defect
    - Dermal sinus between adjacent vertebrae
      - Hairy patch or birthmark may be above the defect
    - Bulge under the skin as the spinal cord ends terminate in fatty tissue
      - Vertebral involvement along with a fatty area, hairy patch or dimpled skin increase suspicion of later bowel, bladder or motor problems
- **Meningocele**
  - Spinal column develops normally but bulges through incompletely developed vertebrae
  - Neurologic function is often normal
  - Minor muscle paralysis or incontinence can result if nerves protrude into the sac
- **Myelomeningocele**
  - Characterized by herniation of the meninges and spinal cord at the site of the defect
  - Usually are “exposed” lesions on the back without vertebral or dermal covering
    - May be leaking or sealed
  - 4 times more common than meningoceles
  - Occur in the lumbar or lumbosacral region
- **Associated Problems**
  - Arnold-Chiari II malformation
    - Occurs in 95% with lumbar lesion
    - Results in hydrocephalus and brainstem dysfunction
      - Brainstem is forced downward and obstructs the fourth ventricle with compression of the upper cervical spinal cord.
      - Hydrocephalus arise from compression of the 4<sup>th</sup> ventricle or obstruction of CSF outflow through the foramen magnum
  - Hydrocephalus
    - Very common complication in 70—90%
    - Evaluate for hydrocephalus with CT scan and head ultrasound after birth
  - Chronic bladder infections and subsequent kidney deterioration
  - Clubfeet
  - Dislocated hips
  - Kyphosis at birth, scoliosis later in childhood
  - Mental retardation: 30% of myelomeningocele
- **Treatment Strategies**
  - Diagnostic evaluation
    - Radiographic
    - Spinal ultrasound
    - MRI
  - Cover lesion with sterile gauze moistened with warm sterile normal saline
  - Maintain in prone kneeling position
  - Immediate neurosurgical and urology consultation
  - Observe for signs of hydrocephalus
  - Orthopedic consultation: maximal function of lower extremities
- **Outcome:**

- Survival in 90%, with 80% having normal intelligence
- 95% ambulatory with or without special aids
  - Lesions below first sacral vertebra: walk unaided
  - Lesions between 4<sup>th</sup> and 5<sup>th</sup> lumbar vertebrae: walk with crutches or braces
  - Lesions above 2<sup>nd</sup> lumbar vertebrae: wheelchair dependent
- Optimistic outlook for meningocele because of normal spinal cord

## **Hydrocephalus**

- Excessive cerebrospinal fluid in the ventricles of the brain
- 70% of CSF produced from choroid plexus
- Etiology
  - Excessive CSF production
  - Inadequate CSF absorption secondary to abnormal circulation
  - Excess ventricular CSF secondary to aqueductal outflow obstruction
    - Causes obstructive, noncommunicating hydrocephalus
    - Most common in neonate
  - Excess ventricular CSF with flow between the lateral ventricles and the subarachnoid space
    - Results in communicating, nonobstructive hydrocephalus
- Congenital hydrocephalus
  - Aqueductal stenosis
  - Dandy-Walker cyst
  - Myelomeningocele with Arnold-Chiari malformation
  - Congenital masses or tumors
  - Congenital infection
- Clinical presentation
  - Large head, increasing FOC
  - Widened sutures
  - Full and tense fontanelles
  - Vomiting, lethargy, irritability
  - Setting-sun eyes
- Treatment Strategies
  - Thorough physical examination
  - Serial head ultrasounds
  - Neuroimaging techniques: CT, MRI
  - Decrease noxious stimuli
  - Use of gel pillows to decrease skin breakdown
  - Ventriculoperitoneal shunt placement



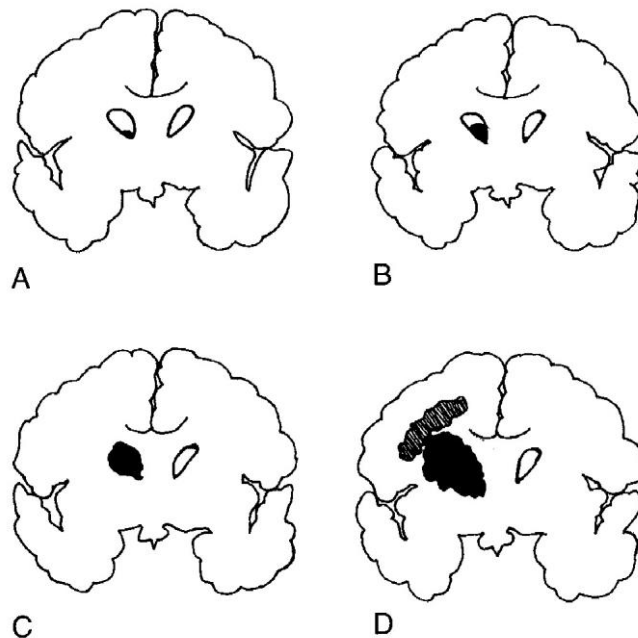
**Box 26-1 POSTOPERATIVE VENTRICULOPERITONEAL SHUNT CARE**

- I. Positioning
  - A. Place on unaffected side (may position on shunt side with "dough" over operative site once incision has healed). Keep head of bed flat (15 to 30 degrees) to prevent too-rapid fluid loss.
  - B. Support head carefully when moving infant.
  - C. Turn q 2 hr from unaffected side of head to back.
- II. Shunt site
  - A. Use strict aseptic technique when changing dressing.
  - B. Pump shunt if and only as directed by neurosurgeon.
  - C. Observe for fluid leakage around pump.
- III. Observe and document all intake and output. Watch for symptoms of excessive drainage of CSF:
  - A. Sunken fontanel
  - B. Increased urine output
  - C. Increased sodium loss
- IV. Observe, document, and report any seizure activity or paresis.
- V. Observe for signs of ileus:
  - A. Abdominal distention (serially measure abdominal girth)
  - B. Absence of bowel sounds
  - C. Loss of gastric content by emesis or through oro-gastric tube
- VI. Perform range-of-motion exercises on all extremities.
- VII. Observe and assess for symptoms of increased intracranial pressure (shunt failure):
  - A. Increasing head circumference (measure head daily)
  - B. Full and/or tense fontanel
  - C. Sutures palpably more separated
  - D. High-pitched, shrill cry
  - E. Irritability and/or sleeplessness
  - F. Vomiting
  - G. Poor feeding
  - H. Nystagmus
  - I. Sunset sign of eyes
  - J. Shiny scalp with distended vessels
  - K. Hypotonia and/or hypertonia
- VIII. Observe and assess for signs of infection:
  - A. Redness or drainage at shunt site
  - B. Hypothermia and/or hyperthermia
  - C. Lethargy and/or irritability
  - D. Poor feeding and/or weight gain
  - E. Pallor
- IX. Parent teaching (see Figure 26-1)
  - A. Demonstrate and receive return demonstration of drug administration.
  - B. Teach parents side effects of medications.
  - C. Document on NICU's routine discharge teaching checklist with routine care.

Gardner, Carter, Enzman-Hines and Hernandez, 2011, p 753

**Periventricular-Intraventricular Hemorrhage**

- Originates in the subependymal germinal matrix
  - Arterial supply derived from anterior and middle cerebral arteries, as well as anterior choroidal artery
  - These arteries feed an elaborate capillary network of thin-walled vessels that terminate in the vein of Galen
  - Terminal, choroidal and thalamostriate veins course anteriorly to form the internal cerebral vein, which courses posteriorly to join the vein of Galen, leading to a U-shaped turn in the direction of blood flow
- Occurs when a subependymal germinal matrix hemorrhage extends into the lateral ventricles
  - Grade I: localized at the Foramen of Monro (underneath ventricles above 3<sup>rd</sup> ventricle)
  - Grade II: partial filling of lateral ventricles without ventricular dilatation
  - Grade III: IVH with ventricular dilatation
  - Grade IV: extension of blood into the cerebral tissue itself



**FIGURE 64-1.** Illustration of intraventricular hemorrhage (IVH) grades as determined by degree of hemorrhage (see Table 64-2). **A**, Grade I hemorrhage involves less than 10% of the ventricular volume in the lateral ventricles; **B**, grade II hemorrhage involves 10% to 50%; **C**, grade III involves greater than 50% of the ventricular volume and is often associated with some ventricular dilatation; and **D**, grade IV (Papile et al, 1978) or unclassified (Volpe, 2001) is associated with parenchymal echodensities on head ultrasound study, indicating parenchymal infarction.

Tausch, Ballard and Gleason, 2005, p 966

- Risk factors
  - Preterm has a pressure-passive state due to lack of autoregulation of cerebral blood flow in the cerebral arterioles
  - Germinal matrix is highly vascular with a lack of a supporting basement membrane
  - Increased amount of fibrinolytic activity in germinal matrix region
  - Extravascular tissue pressure decreases over first few days of life
    - Elevated venous pressure or fluctuations in cerebral blood flow velocity can lead to IVH
  - Common risk factors are the preterm baby < 34 weeks who develops RDS and requires ventilatory assistance
  - Associated with
    - Perinatal asphyxia
    - Hypotension/hypertension
    - Rapid administration of sodium bicarbonate
    - Rapid volume expansion
    - Pneumothorax
    - Ligation of PDA

- Pathophysiology:
  - Occurs when the subependymal germinal matrix hemorrhage extends into the lateral ventricles
  - Parenchymal intracerebral hemorrhage
    - Most extensive periventricular-intraventricular hemorrhage
    - Involves bleeding into the intracerebellar white matter
    - May also precipitate a cerebral infarction
    - Occurs in 10-15% of hemorrhages
- Incidence:
  - 40-60% of very low birth weight neonates.
  - <28 weeks PMA have 3 times higher risk than 28-31 PMA
    - Primary site of bleeding germinal matrix in the subependymal area next to the caudate nucleus
  - 3.5 to 4.6% of term infants have a periventricular-intraventricular hemorrhage.
    - More than half of these hemorrhages originate at the choroid plexus of the lateral ventricles
- Timing of onset:
  - 50% occur by 24 hours
  - 80% by 48 hours
  - 90% by 72 hours
  - By 7 days, 99.5% have occurred
  - 20-40% exhibit progression of hemorrhage over 3-5 days
  - extension of the hemorrhage may occur over the first few days secondary to events leading to alterations in cerebral blood flow
- Clinical Presentation
  - Varies from asymptomatic to sudden and catastrophic deterioration
    - Full fontanel, decreased hematocrit, hyperglycemia, hyperkalemia, hypotension and bradycardia very typical
  - Common presentation: gradual clinical deterioration with an altered level of consciousness, hypotonia, abnormal extremity movements, abnormal eye movements
- Diagnostic testing
  - Routine screening of all neonates < 30 weeks gestation between 7 and 14 days of age, with repeat head ultrasound at 36 – 40 weeks postmenstrual age
  - If IVH present, repeat head ultrasound in 2 weeks unless earlier testing warranted
  - MRI for ELBWI at 36 – 40 weeks if suspicion of parenchymal brain injury
  - Grading of IVH:

**TABLE 64-2****Grading of Intraventricular Hemorrhage (IVH) by Cranial Ultrasound Findings**

Papile	Grading System	Volpe	Grading System*
I	Subependymal hemorrhage with minimal or no intraventricular hemorrhage	I	Germinal matrix hemorrhage <10% IVH
II	Definite intraventricular hemorrhage without distention of the ventricles	II	IVH 10%-50%
III	Enlargement of the ventricles secondary to distention with blood	III	IVH >50%, usually with distention of lateral ventricle
IV	Extension of the hemorrhage into the parenchyma along with intraventricular hemorrhage and enlargement	Separate notation	Periventricular echodensity signifying parenchymal lesion

\*By cranial ultrasound

IVH, intraventricular hemorrhage

Tausch, Ballard and Gleason, 2005, p 967

- Treatment Strategies
  - Prevent perinatal asphyxia and birth trauma
  - Promote in-utero transport
  - Provide efficient, expedient intubation
  - Minimal handling/developmental care strategies
  - Avoid events associated with wide swings in arterial/venous pressures
    - Excessive motor activity
    - Pneumothorax
    - Apnea; overventilation
    - Give volume replacement slowly
    - 2 people for endotracheal suctioning
    - avoid acidosis
- Complications/Outcome
  - Small hemorrhage
    - Neurodevelopmental disability similar to that in premature infants without hemorrhage
    - Major neurodevelopmental disability in 10%
  - Moderate hemorrhage
    - Major neurodevelopmental disability in 40%
    - Mortality rate 10%
    - Progressive hydrocephalus < 20%
  - Severe hemorrhage
    - Major neurodevelopmental disability in 80%
    - Mortality rate 50 – 60% with hydrocephalus common in survivors

**Seizures**

- Repeated seizures associated with hypoventilation and apnea, which may result in cardiovascular disturbances and ischemic brain injury
- Hypercapnia, in combination with increased lactate and an adaptive rise in systemic blood pressure, may abruptly increase cerebral blood flow, and precipitate IVH
- Etiology
  - Excessive simultaneous electrical discharge or depolarization of neurons
- Risk factors:

- Metabolic encephalopathies
  - Decreased production of ATP
    - Ischemia, hypoxemia, hypoglycemia
  - Electrolyte imbalances
    - Hyponatremia/hyponatremia
    - Hypocalcemia
    - Hypomagnesemia
  - Inborn errors of metabolism
- Structural
  - IVH
  - Trauma
  - Hypoxic ischemic encephalopathy
- Sepsis
  - Group B strep meningitis
  - *E. coli* meningitis
- Familial (genetic)
  - Onset 2<sup>nd</sup> and 3<sup>rd</sup> days of life
  - Otherwise appears well
  - Self-limiting: stops within 6 months
  - Autosomal dominant inheritance
- Clinical Presentation

Seizure Type	Major Clinical Manifestations
Subtle	Repetitive blinking, eye deviation, staring Repetitive mouth or tongue movements Apnea Bicycling–rowing movements
Tonic (i.e., generalized or focal)	Tonic extension of limb or limbs Tonic flexion of upper limbs, extension of lower limbs
Clonic (i.e., multifocal or focal)	Multifocal, synchronous, or asynchronous limb movements Repetitive, jerky limb movements Nonordered progression Localized repetitive clonic limb movements with preservation of consciousness
Myoclonic (i.e., generalized, focal, multifocal)	Single or several flexion jerks of upper limbs (common) and lower limbs (rare)

MacDonald, Mullett and Seshia, 2005, p 1385

- Treatment Strategies
  - Determine underlying etiology
  - Rule out jitteriness
  - Review history for any predisposing etiology
  - Diagnostic testing
    - Serum glucose level
    - Electrolytes
    - ABGs
    - Cultures: blood, urine, ? CSF

- Head ultrasound
- Medications
  - Phenobarbital
    - Load: 20 mg/kg slow IV over 15 minutes
    - Maintenance: 3 mg/kg/day beginning 12 – 24 hours after loading dose
    - Therapeutic range: 15 – 30 mcg/ml
  - Phenytoin or Fosphenytoin (Fosphenytoin 1 mg = phenytoin 1 mg)
    - Load: 15 – 20 mg/kg over 30 minutes (10 minutes for fosphenytoin)
    - Maintenance: 4 – 8 mg/kg/day
    - Therapeutic range: 6 to 15 mcg/cc first weeks; increasing to 10 – 20 mcg/cc (due to changes in protein binding)
- Outcome
  - Related to underlying etiology

### **Hypoxic-Ischemic Encephalopathy**

- Risk Factors
  - Antepartum: severe pregnancy induced hypertension, fetal growth restriction, socioeconomic status
  - Acute intrapartum events
    - cord accident
    - uterine rupture
    - intrapartum hypoxia
- Incidence:
  - Term infants: 2-4%
  - ~ 60% of very low birth weight infants
  - Timing of the insult
    - Antepartum: 20%
    - Intrapartum: 30%
    - Antepartum-intrapartum: 35%
    - Postpartum (Neonatal Period): 10%
      - Congenital heart disease
      - Severe pulmonary disease
      - Severe recurrent apnea
      - Large patent ductus arteriosus
      - Preterm neonate
- 
- Pathophysiology
  - Brain is subjected to hypoxia, ischemia and hypercarbia, leading to metabolic acidosis
  - Increased blood flow to the brain in an attempt to compensate → cerebral edema and circulatory circumstances
  - Loss of cerebral vascular autoregulation occurs → pressure-passive cerebral blood flow
  - Asphyxia persists → decreased cardiac output, hypotension, marked decrease in cerebral blood flow → tissue necrosis and cerebral edema → multiorgan failure

- Brain pathology follows: cystic degeneration (cavities) in the white matter (cystic encephalomalacia)
  - Periventricular leukomalacia
    - Bilateral necrosis
    - Hemorrhage into ischemic area as a result of subsequent reperfusion
- Criteria for HIE
  - Profound metabolic or mixed acidemia with a pH < 7.0 in umbilical cord blood
  - Persistence of a Apgar score of 0 to 3 for longer than 5 minutes
  - Neonatal neurologic sequelae
  - Multiorgan system dysfunction
- Clinical presentation
  - Stage I (mild encephalopathy)
    - Hyperalert state
    - Normal muscle tone, active suck, strong Moro, normal grasp
    - Increased tendon reflexes
    - Myoclonus present
    - Hyperresponsiveness to stimulation
    - Dilatation of pupils, reactive
  - Stage II (moderate encephalopathy)
    - Lethargy, hypotonia, weak suck
    - Increased tendon reflexes, myoclonus
    - Weak suck, incomplete Moro
    - Frequent seizure activity
    - Pupils constrictive and reactive
    - Critical period: infant either improves or deteriorates
      - Signs of deterioration
        - Development of seizures, cerebral edema, abnormal EEG
  - Stage III (severe encephalopathy)
    - Obtunded to stuporous to comatose
    - Mechanical ventilation necessary to sustain life
    - Apnea/bradycardia
    - Seizures appear within first 12 hrs
    - Severe hypotonia, flaccid
    - Absent Moro, grasp, suck
    - Survivors improve within several days to months
      - Feeding difficulties common due to abnormalities of suck and swallow
      - Generalized hypotonia common
      - Severe neurologic disabilities possible
- Treatment strategies
  - Prompt resuscitation
  - Correct fluid, electrolyte, acid-base disorders
  - Monitor blood volume; avoid swings in blood pressure
  - Treat seizures/neurology consult
  - Diagnostic testing
    - EEG
    - Head ultrasound

- CT/MRI
- Stabilization of body systems
- Consideration of hypothermia
  - Total body cooling
  - Selective head cooling

■ ■ Comparison of Brain Cooling Trials		
Parameter	CoolCap	Body Cooling
Mode of cooling	Head and systemic	Systemic only
Equipment	Cooling cap and radiant warmer	Cincinnati Sub-Zero Hyper-Hypothermia System
Target core: temperature	34° to 35°C	33.5°C
Target core: site	Rectum	Esophagus
Temperature control method at core site	Servo control of abdominal skin temperature 36.8° to 37.2°C; manual control of CoolCap to achieve target core temperature at rectum	Servo control of esophagus
Age at therapy initiation	<6 hours	<6 hours
Time to achieve target core temperature	2 hours	Approximately 1.5 hours
Duration of cooling therapy	72 hours	72 hours
Rate of rewarming after therapy cessation	0.5°C/hour	0.5°C/hour

Verklan & Walden, 2015, pg 777

- Goal of hypothermia:
  - Maintain the brain's energy phosphorylated metabolites
  - Improve coupling between cerebral blood flow and oxidative metabolism
  - Decrease release of excitatory transmitters
  - Decrease nitric oxide production
  - Decrease apoptosis
    - Necrosis: passive process of cell swelling, disrupted cytoplasmic organelles, loss of membrane integrity and eventual lyses of neuronal cells and activation of the inflammatory process
    - Apoptosis: active process of cell shrinkage, nuclear pyknosis (loses density), chromatin condensation and genomic fragmentation (destroying genetic material). The inflammatory response is not involved.
- Complications
  - Based on severity of brain insult; selective neuronal necrosis



## IMMUNOLOGIC SYSTEM REVIEW

### Immune System

- Functions
  - Defense
  - Homeostasis
  - Surveillance
- Humoral Immunity
  - Specific antibody-mediated response
  - Functions most effectively if there has been prior exposure
  - Antibodies are derived from B cells, which have been activated by T-cells
  - Functions of antibodies
    - Recognize bacterial antigens
    - Neutralize or opsonize foreign substances, making them susceptible to phagocytosis
  - Types of immunoglobulins
    - Immunoglobulin G (IgG)
      - Major immunoglobulins of serum and interstitial fluid
      - Effective against bacterial and viral pathogens
      - Transported across placenta: majority in 3<sup>rd</sup> trimestre
    - IgM
      - Does not cross the placenta
      - Detectable at 30 weeks gestation
      - Levels may increase with intrauterine infection
      - Serum levels rapidly increase after birth
    - IgA
      - Most common immunoglobulins in GI tract, respiratory tract
      - Secreted in colostrums and breast milk
      - Does not cross placenta
    - IgE
      - Present in very small amounts in serum and secretions
      - Major role in allergic reactions
      - Cellular immunity
- Cellular Immunity
  - Specific cellular immunity mediated by T lymphocytes, which enhance the efficiency of phagocytic responses
  - T lymphocytes activated by antigens to which they have become sensitized ==> memory or activated T cells
  - 3 types of activated T cells
    - cytotoxic: kill foreign or virus-infected cells
    - helper: enable B or T cells to respond to antigens and activate macrophages
    - suppressor: repress responses of specific T and B lymphocytes to antigens
  - T lymphocytes modify behaviour of phagocytic cells, produce cytokines and increase their antimicrobial activity

- Non-specific cellular immunity
  - An inflammatory response involving phagocytosis
  - Includes neutrophils, monocytes and complement
  - Neutrophils
    - Are phagocytes
    - First line of defense against bacterial infection
    - Neutrophil storage pool is present that exceeds the circulating pool.
  - Monocytes
    - Important in the defense against fungal and bacterial infections
    - Found primarily in connective tissue
  - Complement
    - Proteins that interact or mediate a cascade of synthesis of other proteins responsible for chemotaxis, opsonization and cell lysis
      - Classic pathway: activated by antibody-dependent mechanism
      - Alternative pathway: activated by antibody-independent mechanism
    - Purposes
      - Increase neutrophil mobilization from bone marrow
      - Attracts neutrophils to the site of infection
      - Opsonize bacteria for improved phagocytosis

#### Clinical Assessment of Immune System

- Risk factors
  - Maternal
    - Antepartum:
      - Inadequate prenatal care, nutrition
      - Substance abuse
    - Intrapartum
      - Prolonged rupture of membranes
      - Group B streptococcal colonization
      - Chorioamnionitis
      - Prolonged/difficult labor
      - Premature labor
      - Urinary tract infection
  - Neonatal risk factors
    - Prematurity
    - Low birth weight
    - Difficult delivery, perinatal asphyxia, meconium
    - Congenital anomalies
    - Male
    - Multiple births
  - Environmental
    - Hospital admission
    - Invasive procedures
    - Common use of broad-spectrum antibiotics

- Clinical Presentation
  - Variable
  - Thermoregulatory instability
  - Neurologic
    - Lethargy, jitteriness, irritability
    - Seizures, high-pitched cry
    - Hypotonia/hypertonia
  - Respiratory
    - Most common
    - Grunting, retractions, cyanosis
    - Apnea, tachypnea
  - Cardiovascular
    - Tachycardia, arrhythmias
    - Hypotension
    - Decreased peripheral perfusion/vasoconstriction
  - Gastrointestinal
    - Poor feeding, vomiting, increasing residuals
    - Diarrhea, abdominal distention
  - Skin
    - Rash, pustules, petechiae
    - Jaundice, pallor
    - Vasomotor instability
  - Internal organ manifestations
    - Hepatomegaly, splenomegaly
  - Metabolic disturbances
    - Glucose instability
    - Metabolic acidosis
  
- Hematologic Evaluation
  - Complete blood count
    - Normal: 5000—30,000 / mm<sup>3</sup>
    - Leukocytosis: elevated count
    - Leukopenia: depressed count
      - Due to sepsis or PIH
  - Differential

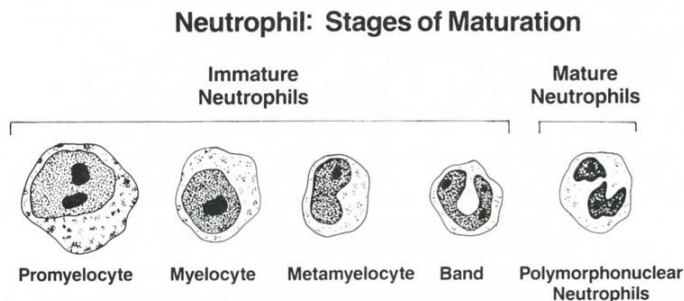


FIGURE 31-3 ■ Neutrophils represent a percentage of the total white blood cell count and are reported as the differential on a complete blood cell count.

- Neutrophil count
  - Absolute neutrophil count (ANC) =  $WBC \times (\% \text{ immature neutrophils} + \% \text{ mature neutrophils}) \times 0.01$
  - Neutropenia:  $< 1500/mm^3$ 
    - Most accurate predictor of sepsis
  - Neutrophilia
    - May be elevated at birth due to birth stress, increased neutrophil production
    - Elevated with Trisomy 21, hemolytic disease
  - Immature/Total neutrophil (I/T) ratio
    - Increase also known as “left shift”
    - $\frac{\% \text{ Bands} + \% \text{ immature forms}}{\% \text{ Mature} + \% \text{ Bands} + \% \text{ Immature forms}}$
    - I/T ratio  $> .20$  is suggestive of infection
  - Platelet count
    - Normal:  $150,000 - 400,000/mm^3$
    - Thrombocytopenia
      - $<100,000/mm^3$  associated with sepsis
- Diagnostic Evaluation
  - CRP (C-Reactive Protein)
    - Non-specific acute-phase reactant that is synthesized in response to IL-6 which appears in the blood during the inflammatory process.
    - Best done every 12 hours when sepsis is suspected. There is a latency period of 6 – 8 hours and a stabilization time of 1 – 2 days once therapy is begun.
    - CRP is elevated in more than half of infected neonates, but it has a low positive predictive value—it is more useful in determining the effectiveness of treatment, resolution of sepsis and duration of antibiotic therapy.
  - Culture
    - Blood
      - Central or peripheral sample
      - May be falsely negative if mother received antibiotics during labor
    - Cerebrospinal fluid
      - Reserved for those with CNS signs or proven bacteremia
      - Positive culture: repeat CSF tap every 24-36 hours until sterile

Table 22-5 NORMAL CEREBROSPINAL FLUID VALUES IN NEONATES				
	WHITE BLOOD CELLS	POLYMPHONUCLEAR NEUTROPHILIC (LEUKOCYTES)	PROTEIN (MG/DL)	GLUCOSE (MG/DL)
<b>Premature Infants</b>				
Reported means	2-27		75-150	79-83
Reported ranges	0-112		31-292	64-106
<b>Term Infants</b>				
Reported means	3-5	2-3	47-67	51-55
Reported ranges	0-90	0-70	17-240	32-78

Modified from Remington JS, Klein JO, eds: *Infectious diseases of the fetus and newborn infant*, ed 2, Philadelphia, 1983, WB Saunders.

- Urine
  - Obtain sample by sterile catheterization or supra-pubic needle aspiration
- Follow-up:
  - To document sterilization when a positive culture has been obtained
  - Persistent bacteremia caused by:
    - Resistance to antibiotics
    - Incorrect administration of antibiotics
    - An occult site of infection that may require surgical intervention
    - Central venous or peripherally inserted central catheters left in place during treatment for bacteremia
- Therapy
  - Antibiotic Therapy
    - Choice depends on likely organisms
    - Ampicillin used in combination with an aminoglycoside for initial broad-spectrum treatment of suspected or confirmed bacterial infection
    - Meningitis: ampicillin and Cefotaxime until specific organism isolated
    - Third generation cephalosporins
      - increased antimicrobial activity against gram-negative bacilli
      - enhanced penetration across the blood-brain barrier over gentamicin
    - Duration of therapy 10 –14 days for proven sepsis; 21 days for meningitis
    - If cultures are negative, discontinue after 48 – 72 hours
  - Intravenous immune globulin (IVIG)
    - May be effective in decreasing mortality from Nosocomial infections
    - Neutralizes virus, promotes phagocytosis, increases opsonization and enhances polymorphonucleocyte migration

### Sepsis

- Early onset
  - *E. coli*, group B strep, *L. monocytogenes*, *H. influenzae*, *Enterobacter*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *S. aureus*
- Nosocomial
  - Coagulase-negative staphylococci, *S. aureus*, *candida albicans*, *K. pneumoniae*, *P. aeruginosa*, *Serratia marcescens*
- Clinical Presentation
  - Nonspecific
  - Subtle signs of temperature instability, lethargy, poor feeding and glucose instability

### Meningitis

- Major pathogens: GBS and *E. coli*
- Acquisition:
  - Direct invasion

- Contamination between CSF space and integumental surfaces
- Bacterial dissemination from infected structures
- Clinical presentation
  - General symptoms of sepsis
  - Specific CNS symptoms: increased irritability, alteration in consciousness, poor tone, tremors, seizures
  - CSF culture
    - Positive culture must be repeated 24 – 36 hours after initiation of treatment to ensure adequate therapy
- Antibiotic therapy
  - Duration dependent on pathogens and clinical response
  - Use for 14 – 21 days

### **Pneumonia**

- Transmission
  - Vertical
    - Onset within first 72 hours of life
    - GBS most common pathogen
  - Horizontal
    - Onset after 72 hours of life
    - Due to human contact/contaminated equipment
- Clinical presentation
  - Specific symptoms of respiratory distress
- Diagnosis
  - Chest xray: asymmetric densities and pleural effusion
  - Pulmonary granularity present in GBS-related pneumonia

### **Urinary Tract Infections**

- Most common pathogen: *E. coli*
- 30% association between UTI and septicemia
- Clinical presentation
  - Variable, as discussed above
- Follow-up
  - Repeat urine culture should be sterile within 36 – 48 hours after initiation of antibiotics
  - If UTI documented, voiding cystourethrogram should be done

### **Bacterial Infections – Group B Streptococci**

- Gram-positive bacteria
- Organism in maternal cervix, vagina, anus and urethra
- Colonization with GBS in 15 – 35% of women
- Early-onset sepsis
  - Fulminant presentation, typically within 24 hours of life
  - Most common presentation is pneumonia and/or meningitis

- Acquired by vertical transmission
- Clinical presentation: respiratory distress, hypotonia, lethargy, tachycardia, pallor, hypothermia, shock
- Late-onset sepsis
  - Insidious presentation after 72 hours of age
  - Meningitis is common complication
  - Horizontal transmission
  - Clinical presentation: fever, lethargy
- Treatment:
  - Antibiotic therapy
  - Fluid management
  - Volume expansion
  - Seizure control
  - Monitoring of electrolytes, fluid balance status, weight, intake and output
  - NICU supportive care

### **Bacterial Infection: *E. Coli***

- Most common gram-negative organism causing sepsis and meningitis
- Found in female genital tract
- High incidence of colonization in the neonate
- Nosocomial acquisition from person to person; nursery environmental sites
- Colonization of human GI tract soon after birth
- Symptoms
  - Fulminant infection:
    - Respiratory distress, cardiovascular collapse, meningitis, multiorgan failure, death
  - Localized infection
    - Cellulitis pneumonia, septic arthritis, urinary tract infection, otitis media
- Treatment
  - Sensitive to aminoglycoside and third-generation cephalosporins

### **Fungal Infection: Candidiasis**

- Pathogen: *C. albicans*, significant neonatal pathogen
- Mucocutaneous candidiasis
  - Most common form of candidiasis
  - Acquired during passage thru birth canal or from mother during breast feeding
  - Clinical presentation
    - Pearly, white material on buccal mucosa, dorsum and lateral areas of tongue, gingivae and pharynx
  - Treatment Strategies
    - Oral nystatin oral suspension (100,000 units/cc) each side of mouth every 6 hours for 3 days after symptoms have subsided
- Cutaneous candidiasis
  - Strongly associated with the presence of oral *Candida*
  - Clinical presentation
    - Appears initially as erythematous and vesiculopapular lesions

- Then develops into fine white, scaly collarettes
  - Treatment strategies
    - Use of topical agents such as nystatin four times a day, continue 2 to 3 days after the rash has cleared
    - Keep area free from moisture and stool
    - Simultaneous treatment with oral nystatin to minimize risk of recurrence
- Acute Disseminated (systemic) candidiasis
  - Serious nosocomial infection occurring in VLBW infants
  - Common sites of infection: lungs, kidney, liver, spleen and brain
  - Risk factors
    - Prematurity
    - Total parenteral nutrition and fat emulsions
    - Prolonged use of broad spectrum antibiotics
  - Clinical presentation
    - Respiratory deterioration, apnea, acidosis
    - Abdominal distention, carbohydrate intolerance
    - Hypotension
    - Skin abscesses
    - Temperature instability
    - Erythematous rash
    - Fungus in urine can lead to UTI
  - Treatment strategies
    - Cultures: blood, urine, CSF
    - Renal ultrasound
    - Ophthalmologic examination
    - Amphotericin B
      - Initial dose 0.1 mg/kg IV over 20 – 60 minutes
      - Maintenance dose: 0.25 – 1 mg/kg/day every 24 hours over 2 – 6 hours
      - Close monitoring of hematologic and renal function
    - Flucytosine
      - 50 – 100 mg/kg in 2 divided doses for 3 – 4 weeks
      - Used in combination with amphotericin B, especially if severe infection or CNS involvement

### **Viral Infections – Herpes Simplex Virus (HSV)**

- Types:
  - HSV-1
    - Non-genital type
  - HSV-2
    - Genital type
    - Causes 75% of neonatal disease
- Transmission
  - 85- 90% acquired at time of delivery
  - > 75% of neonates who acquire neonatal HSV have been born to women who had no history of clinical findings suggestive of active HSV infection during pregnancy



- Greatest risk to neonate is with mother who has a primary infection at birth
  - Transmission is ~ 50%
- Reactivation of disease: transmission occurs in < 5% of deliveries
- Clinical Presentation
  - Congenital transmission
    - Early vesicular rash, SGA
    - Chorioretinitis
    - Diffuse brain damage, microcephaly, intracranial calcification
  - Intrapartum/Postpartum transmission
    - Vesicular lesions, thermal instability
    - Respiratory distress, cyanosis
    - Poor feeding, vomiting
    - If CNS involvement: irritability, seizures
- Treatment strategies
  - Culture vesicular lesions, blood, CSF
  - Polymerase chain reaction (PCR) is more sensitive than cultures
  - Systemic infection
    - Acyclovir 10/mg/kg every 12 hours for premature; every 8 hours for term, for 14 – 21 days
  - Ocular involvement
    - 3% vidarabine in addition to parenteral therapy
- Isolation precautions
  - Mothers with HSV infections need to use strict handwashing techniques prior to touching their baby
  - Infants born to mothers with active lesions should be physically separated from other infants and managed with Transmission Precautions in addition to Standard Precautions
  - Infants with HSV infection should be isolated and managed with Contact Precautions
  - Infants born to mother with a history of infection but without lesions at time of delivery do not require isolation

## **Hepatitis B**

- Transmission: vertical
  - Virus found in any bodily secretion, including breastmilk
  - If mother is hepatitis B surface antigen (HBsAg) positive there is no added risk to baby of acquiring HBV infection
    - Breastfeeding not contraindicated if immunoprophylaxis recommendations are followed
- Presentation:
  - Infected in utero: asymptomatic at birth
  - Infected at delivery or after birth—will not have HBsAg present for 2—5 months
- Prevention:
  - Routine screening for all pregnant women
  - Universal screening of all infants
  - Routine neonatal immunization
    - Hepatitis B vaccine

- Engerix-B 10 mcg
  - Recombivax HB 5 mcg
  - Term infant immunized at discharge, 2 months and 6 months of age
  - Preterm immunized at discharge if weight > 2 kg or at 2 months of age
- Treatment
  - If born to a HBsAg-positive mother, treatment is 85—95% effective in preventing the development of hepatitis B carrier state
  - Initial bath to remove blood/secretions that may be contaminated
  - Administration of hepatitis B immunoglobulin (HBIG) 0.5 ml IM as soon as possible within 12 hours of birth, in addition to a hepatitis vaccine
  - Isolation: Standard Precautions

## G A S T R O I N T E S T I N A L   S Y S T E M   R E V I E W

### Functions of the GI tract

- Absorption and digestion of nutrients
- Maintenance of fluid and electrolyte balance
- Elimination of waste products
- Protection from toxins and pathogens

### Parenteral Nutrition

- Indications
  - Surgical GI disorders
  - Short bowel syndrome
  - Serious acute GI diseases
  - Congenital anomalies
  - Renal failure
  - Birthweight < 1500 g and gestational age < 32 weeks
  - Cardiopulmonary disease
- Peripheral Route
  - Dextrose concentrations limited to 12.5% to prevent irritation to veins
- Central Route
  - Dextrose concentrations not restricted
  - Increased risk of
    - Mechanical complications
    - Sepsis
    - Thrombosis of large vessels
  - Percutaneous catheters more commonly used
  - Surgically placed central venous catheters
    - Long term use
    - More stable than percutaneous lines
    - Risks of surgery and anesthesia

## Enteral Feeding Methods

- Minimal enteral feedings or Trophic Feedings
  - Before 2 weeks of age
  - Given simultaneously with parenteral nutrition
  - Used to encourage functional development of the gut
  - Benefits
    - Shorter time to achieve full enteral nutrition
    - Lower incidence of feeding intolerance
    - Possible decrease in NEC
    - Improvement in metabolic status
    - Colonization of the gut with normal flora
- Initiation of oral feeds
  - Free of symptoms of respiratory distress
  - Demonstrates suck-swallow-breathe coordination with an intact gag reflex
  - Oral feeds route of choice for >34 weeks
  - Advantages of oral feedings
    - Facilitates the infant's total digestive capacity
    - Allows for self-regulation of feeds
    - Social behaviour states are promoted, especially if parents involved
- Gavage feedings
  - Used for infants < 32 weeks who are unable to orally feed with safety
  - Size 5F – 8F inserted by standard technique
  - Administer feeds by gravity or pump over 15 – 30 minutes
  - Observe for intolerance: oxygen desaturations, emesis, bradycardia, apnea
  - Continuous:
    - 4-hour feeding volume should be aseptically prepared
    - human milk: tubing changed every 4 hours. Syringe placed vertical to facilitate fat delivery (rises to the surface of the milk)
- Transpyloric feedings
  - Not recommended routinely: feedings bypass the stomach and may result in fat malabsorption
  - Recommended for severe gastroesophageal reflux
    - Minimizes risk of aspiration because end of tubing is beyond the pyloric sphincter
- Gastrostomy feedings
  - Indications: congenital anomalies requiring surgical intervention
  - Inability to suck and swallow due to severe neurologic insult
  - Need for long-term gavage feeds
  - Gastrostomy site requires regular assessment for leakage around the tube

## Feeding Intolerance

- Residuals
  - Feeding tube aspirated every 2 – 4 hours, before a feeding
  - Normal: incompletely digested aspirates of 2 – 4 cc/kg or a 1 hour volume if continuous feeds
  - Increasing residuals are a sign of intolerance

- Decrease feeding volume
  - Decrease rate of delivery
  - Slow rate of feeding advance
  - Presence of blood or bile in the aspirate warrants investigation for NEC
- Emesis
  - Etiology
    - Overdistended stomach
    - Gastroesophageal reflux
    - Poorly positioned feeding tube
    - Gastric irritation from enterally administered medications
    - Sepsis
    - Obstruction
    - Metabolic disorders
    - Increased intracranial pressure
    - Overstimulation
  - Treatment strategies
    - Allow feeding to flow more slowly
      - Use a smaller gavage tube
      - Slow rate of feeding/place over longer period of time
      - Decrease feeding volumes
      - Prone positioning
      - Modify stressful environment
- Gastroesophageal Reflux
  - Suspect in infant with irritability, emesis, apnea, bradycardia, respiratory deterioration, refusal to eat
- Abdominal Distention
  - With or without palpable/visible loops
  - Variations in abdominal circumference up to 1.5 cm normal if no other signs of illness
  - Persistent
    - Xray
    - Abdominal girth measured every 4 to 8 hours
- Diarrhea
  - May indicate transient lactase deficiency
  - Culture for bacterial or viral pathogens if sepsis suspected
- Apnea and/or Bradycardia
  - Occurs frequently during and after feeds
  - Symptoms vagally mediated by:
    - Gavage tube
    - Gastric distention
    - GER
    - Compromise of lung volumes or airway obstruction
- Danger Signs
  - Bile: sign of significant ileus or obstruction
  - NEC: blood, tense or tender abdomen, abdominal wall erythema
  - Feedings should be held and parenteral nutrition begun

- Diagnostic investigation

### **Abdominal Wall Defects**

- **Gastroschisis**
  - Herniation of the abdominal contents through an abdominal wall defect, usually to the right of the umbilicus
  - Etiology
    - Unclear
  - Clinical presentation
    - No sac covers intestinal contents
    - Includes large and small intestine
    - Intestines may be thickened, edematous and inflamed
    - Umbilical cord is intact
    - Associated conditions:
      - Intestinal malrotation and atresia
      - Majority are premature and small for gestational age
- **Omphalocele**
  - Herniation of abdominal contents into the umbilical cord
  - Usually covered by peritoneal sac
  - Umbilical arteries and veins insert into apex of defect
  - 50 – 70% have associated anomalies
    - cardiac defects
    - chromosomal anomalies
  - Etiology
    - Unclear
  - Clinical presentation
    - Large defects: stomach, liver, spleen, bladder, ovaries
    - Small defect: umbilical cord that is unusually fat
    - Sac may rupture prior to or at time of delivery
- **Treatment Strategies for neonate with abdominal wall defect**
  - Prevent hypothermia, maintain sterile environment and maintain perfusion to eviscerated contents
  - At time of delivery, place infant in bowel bag from feet to axilla
    - If not available, cover defect with sterile normal saline dressings
  - Place on side to support the defect with small roll
  - Minimal handling
  - Supportive NICU care
  - NPO with OG tube to low-intermittent wall suction
  - IV fluids and antibiotic therapy
    - Fluids increased due to high losses through bowel wall
  - Pre- and post-operative care

### **Esophageal Atresia (EA) and Tracheoesophageal Fistula (TEF)**

- Esophageal atresia: interruption in the esophagus

- TEF: abnormal communication between the esophagus and trachea
- EA and TEF may occur commonly in association with each other
- Associated defects
  - Low birth weight
  - Cardiac defects
  - GI anomalies
  - EA: frequent component of VACTERL or VATER association
    - Should have cardiac evaluation, renal ultrasound and skeletal xrays
    - Also common with CHARGE syndrome
- Etiology
  - Incomplete elongation and separation of esophagus and trachea during 4<sup>th</sup> week of gestation
- Types:

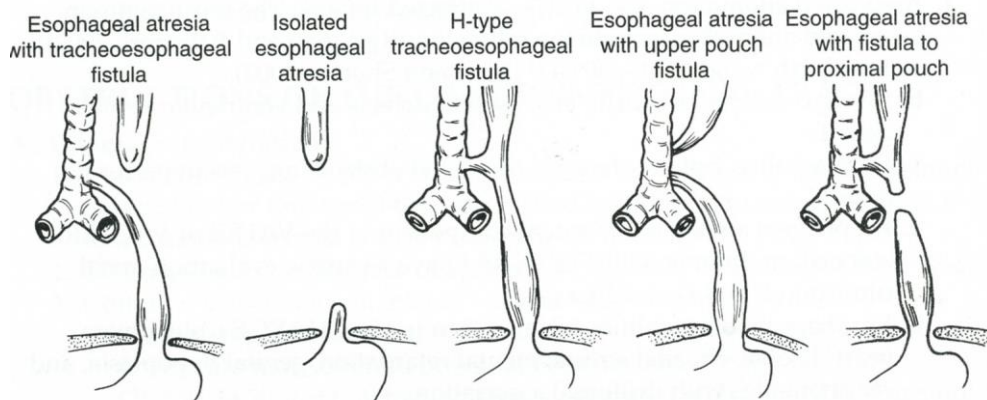


FIGURE 28-3 ■ Esophageal malformations.

Verklan and Walden, 2015, p 594

- Blind proximal pouch (EA) with distal TEF
- Isolated EA
- H-type: isolated TEF without EA
- EA with fistula between upper pouch and trachea
- EA with fistulas between upper pouch and lower pouches and trachea
- Clinical presentation
  - Depends on the type of anomaly
  - Accumulation of oral secretions in mouth; drooling
  - Inability to pass gastric tube
  - Coughing, choking, cyanosis with feeds
  - Abdominal distention if fistula between distal esophagus and trachea
  - Recurrent pneumonia: isolated TEF without EA
  - Diagnostic testing
    - History of polyhydramnios
    - Gastric tube stops in the esophageal pouch
    - Xray: gastric tube appears coiled in upper esophageal pouch
      - Gasless abdomen: indicates an isolated EA

- Treatment strategies
  - Preoperative care
    - Head of bed elevated to 30 – 45 degrees
    - Replogle tube in pouch with low-intermittent wall suction to remove oral secretions
    - Comfort measures to prevent crying
  - Post-operative care
    - Pain management
    - Suction endotracheal tube only the length of the ETT to avoid damage to tracheal suture line
    - Gastrostomy tube care
    - NICU supportive care
  - Post-operative complications
    - Leaking at site of anastomosis
      - commonly occurs at days 2 –6 postop
    - Stricture at site of anastomosis
      - Investigate if feeding difficulties after 3<sup>rd</sup> week postop
    - Dysmotility of lower esophageal segment
    - Pneumonia/sepsis
    - Tracheomalacia, severe enough to require tracheostomy
    - TEF cough: stridor, brassy cough and bronchospastic airway symptoms. Caused by deformation and softening of tracheal cartilages from compression of posterior trachea by enlarged proximal esophageal pouch
    - GER common

### **Necrotizing Enterocolitis**

- An acquired disease that affects the GI system, most often in the premature infant
- Etiology: unclear and multifactorial
- 3 mechanisms suggested
  - Intestinal ischemia:
    - Redistribution of blood flow occurs in response to asphyxia or hypoxia
    - Shunting of blood away from mesenteric, renal and peripheral vasculature beds
    - Conditions:
      - Asphyxia/hypoxia
      - Hypotension/hypovolemia
      - Hypothermia
      - Umbilical lines
      - Polycythemia
      - PDA
  - Bacterial colonization of the intestinal tract
    - Delayed in those who have been NPO
    - Organisms associated with NEC: *Klebsiella*, *E. coli*, *Clostridia* species
  - Enteral feeds
    - 90 – 95% have had enteral feeds
    - formula may provide a substrate for bacterial proliferation

- feeding increases intestinal oxygen demand during nutrient absorption
    - Increase of > 20 ml/kg/day associated with NEC
  - onset between 3 and 10 days of life
  - distal ileum and proximal colon most commonly affected
- Incidence:
  - up to 10% of all admissions to the NICU
  - Approximately 90% of cases occur in preterm infants
- Clinical presentation
  - Occurs sporadically and in clusters
  - Occurs within first week of life to several weeks after birth.
  - Abdominal distention; visible loops of bowel
  - Gastric residuals
  - Bilious vomiting
  - Bloody stools
  - Lethargy
  - Abdominal tenderness
  - Apnea, bradycardia, hypoperfusion, hypotension
  - Temperature instability
  - Laboratory findings
    - Leukocytosis/leukopenia
    - Electrolyte imbalances
    - Metabolic acidosis, hypoxemia, hypercapnia
    - Disseminated intravascular coagulation

**Modified Bell's Staging Criteria for Necrotizing Enterocolitis**

Stage	Systemic Signs	Intestinal Signs	Radiologic Signs	Treatment
I: Suspected				
A	Temperature instability, apnea, bradycardia	Elevated pre-gavage residuals, mild abdominal distention, occult blood in stool	Normal or mild ileus	NPO, antibiotics × 3 days
B	Same as for IA	Same as for IA, plus gross blood in stool	Same as for IA	Same as for IA
II: Definite				
A: Mildly ill	Same as for IA	Same as for I, plus absent bowel sounds, abdominal tenderness	Ileus, intestinal pneumatosis	NPO, antibiotics × 7-10 days
B: Moderately ill	Same as for I, plus mild metabolic acidosis, mild thrombocytopenia	Same as for I, plus absent bowel sounds, definite abdominal tenderness, abdominal cellulitis, right lower quadrant mass	Same as for IIA, plus portal vein gas, with or without ascites	NPO, antibiotics × 14 days
III: Advanced				
A: Severely ill, bowel intact	Same as for IIB, plus hypotension, bradycardia, respiratory acidosis, metabolic acidosis, disseminated intravascular coagulation, neutropenia	Same as for I and II, plus signs of generalized peritonitis, marked tenderness, and distention of abdomen	Same as for IIB, plus definite ascites	NPO, antibiotics × 14 days, fluid resuscitation, inotropic support, ventilator therapy, paracentesis
B: Severely ill, bowel perforated	Same as for IIIA	Same as for IIIA	Same as for IIB, plus pneumoperitoneum	Same as for IIA, plus surgery

Tausch, Ballard and Gleason, 2005, p 1126

- Xray findings



- Diffuse gaseous distention of intestines early, nonspecific sign
- Asymmetric bowel gas pattern
- Persistently dilated loop of bowel
- Pneumatosis intestinalis
- Pneumoperitoneum
- Medical management
  - NPO and gastric decompression
  - Pain management
  - Antibiotics
  - Serial xrays every 6 – 8 hours
  - Circulatory support
  - Respiratory/ventilator support
  - Blood glucose monitoring
  - NICU supportive care –see Bell’s staging criteria
- Surgical management
  - Pneumoperitoneum: absolute indication
  - Relative indications
    - Progressive clinical deterioration
    - Portal vein gas
    - Persistent fixed dilated loop of bowel
  - Principles of surgery
    - Decompress bowel, resect necrotic bowel and divert proximal fecal stream
    - Placement of peritoneal drains without surgery has had some success with the initial management of critically ill, extremely low birth weight infants with perforated NEC or isolated intestinal perforation
- Postoperative care

### **Gastroesophageal Reflux**

- The retrograde movement of gastric contents into the esophagus and above.
- Is not well defined in neonates
- Regurgitation can be a sign of GER, but GER can occur without regurgitation.
- Incidence: 3 – 10% of preterm neonates < 1500g
  - 40% to 50% of infants regurgitate more than once a day
- Etiology
  - There is a transient relaxation of the lower esophageal segment
  - Delay in esophageal clearance of contents
  - Air entry into stomach during swallowing
  - Excessive swallowing
  - Delayed gastric emptying
  - Decreased esophageal motility
- Associated Conditions
  - Prematurity
  - Perinatal asphyxia with developmental delay
    - ECMO babies at high risk because of the acute status requiring ECMO
  - GI tract anomalies or conditions

- TEF/esophageal atresia
    - Pyloric stenosis
    - Gastroschisis/Omphalocele
  - Chronic lung disease
  - Medications
    - Xanthines,
    - Betamimetics
    - Prostaglandin
    - Dopamine
- Diagnosis
  - Clinical presentation
    - Feeding difficulties
      - Regurgitation most common presentation
      - Gagging
      - Feeding refusal
      - Aspiration
      - Failure to thrive
    - Fussiness, irritability, back arching with feeding
    - Respiratory difficulty
      - Apnea: most commonly occurs after feeding with the infant supine or seated
- Diagnostic Studies
  - Upper GI series
  - Esophageal pH probe
    - Detects acid reflux only
  - Endoscopy
- Medical management
  - Interventions to minimize simple regurgitation
    - Thicken feedings: increases viscosity and caloric density
    - Feed slowly
    - Small frequent feedings
    - Position at 45 – 60 degree angle during feeding
  - Minimize/eliminate provoking factors
    - Suctioning
    - Xanthine and betamimetic agents → increase lower esophageal sphincter relaxation
- Pharmacologic management
  - Prokinetics
    - Increase gastric motility
    - Bethanechol, metoclopramide
  - H<sub>2</sub> antagonists
    - Decrease gastric acid
    - Rantidine, famotidine
- Surgical management
  - Nissen fundoplication

- Stomach is wrapped 360 degrees around the lower esophageal sphincter.
- Procedure most commonly performed

#### Prognosis

- Resolves in almost all infants by 12 – 18 months of age.
- Prognosis depends on complications: respiratory disease, esophagitis (occurs in 60-85% with significant reflux) and hematologic (anemia from chronic bleeding)

#### Meconium Ileus

- A mechanical obstruction of the distal ileum due to an accumulation of thick, inspissated meconium within the lumen
- Predominant finding in neonates with cystic fibrosis
- Etiology: unknown. Hyposecretion of pancreatic enzymes plays a role, or abnormal viscid secretions from the mucous glands of the small intestine
- Incidence: unknown. Cystic fibrosis occurs in 1:2000 live births of white infants—10-15% have meconium ileus
- Associated conditions
  - Cystic fibrosis
  - Hepatobiliary disease
- Types of meconium ileus
  - Simple meconium ileus
    - Most common
    - Distal segment of the small bowel is obstructed with thick, tar-like, tenacious meconium and the proximal segment is dilated
    - Presentation is typically within 48 hours
  - Complicated meconium ileus
    - Volvulus
    - Intestinal necrosis and perforation
    - Meconium peritonitis
    - Clinical presentation typically within 24 hours
- Diagnosis:
  - Abdominal distention
  - Bilious vomiting
  - Failure to pass meconium within 12-24 hours
  - Palpable, rubbery loops of bowel
  - Complicated form: present with signs of sepsis and respiratory distress
  - Family history of cystic fibrosis. Definitive diagnosis of CF based on sweat chloride iontophoresis or chromosome analysis
  - Radiographic studies
    - Plain xray: soap bubble or ground glass appearance of distal intestine
    - Distended bowel loops without air-fluid levels
    - Complication forms: Scattered calcifications due to intrauterine intestinal perforations
    - Contrast xray: may show microcolon
- Management pre-nonsurgical procedure/preoperatively
  - General GI decompression

- Evaluate for associated conditions: volvulus, atresia, perforation, peritonitis
- The baby must be ready to go to the OR during nonsurgical procedure in case complications arise
- Non-surgical procedure:
  - Hypertonic contrast water-soluble enema: dislodges the meconium by drawing fluid into the intestine and allowing for normal intestinal activity
    - Successful in about 60%: meconium pellets passed quickly, followed by liquid meconium for 24 hours
- Surgical repair of uncomplicated meconium ileus: T-tube inserted into the ileum, which is irrigated postoperatively with *N*-acetylcysteine (Mucomyst) or pancreatic enzymes
- Surgical repair of complicated meconium ileus
  - Always requires surgery
  - Compromised intestine is resected
  - Bowel viable: end-to-end anastomosis is done
  - Bowel necrosis: compromised intestine is resected and an ostomy is placed at the proximal and/or distal segments
- Post-operative care
  - Typical NICU care, pain management, etc
  - Fluids at one and one-half times maintenance. Hypovolemic shock can occur secondary to rapid fluid shifts resulting from hypertonic solutions used for the enema
  - Monitor: urine output, urine and serum osmolality, blood urea nitrogen, creatinine.
  - Assess for intestinal perforation: can occur up to 48 hours after the enema
  - NPO, gastric decompression until normal bowel function is restored
  - Irrigation of distal stoma or T-tube with *N*-acetylcysteine or pancreatic enzymes about post-op day 3
  - Observe for postop complications
    - Volvulus
    - Gangrene
    - Perforation
- Patient Management
  - Prevent infection: antibiotics, chest physiotherapy, Mucomyst, supplemental humidity: to prevent atelectasis and pneumonia with infants with CF are prone to develop
  - Nutrition: TPN until ready for enteral intake. Feeding begun with elemental formula or breast milk, and supplemented with pancreatic enzymes
  - Parental education
    - Genetic counseling
    - Pulmonary hygiene, prevention of infection, nutritional supplements

## Hyperbilirubinemia

- Bilirubin levels  $> 5 - 7$  mg/dl
- Bilirubin synthesis
  - Produced from the breakdown of heme-containing proteins
- Bilirubin transport
  - Binds to albumin for transport in the blood to the liver
  - Binding of albumin to bilirubin is reversible. Factors decreasing albumin-bilirubin binding
    - Metabolic derangements
    - Hypothermia
    - Sepsis
    - Free fatty acids
  - Bound bilirubin does not cross blood-brain barrier
  - When available albumin binding sites are saturated, unconjugated bilirubin circulates as free bilirubin and can cross the blood brain barrier
- Liver uptake, conjugation, excretion
  - In liver, bilirubin detaches from albumin and enters the hepatocyte
  - Converted to glucuronic acid → conjugated, is measured as direct bilirubin and is water soluble
  - Conjugated bilirubin excreted into bile, into intestine and excreted
  - In the intestine, bilirubin may be converted back to unconjugated form → enterohepatic circulation
- Factors influencing bilirubin levels
  - Race: higher in Asian, Native American, Greek
  - Perinatal events:
    - Delayed cord clamping
    - Bruising
    - Asphyxia: inability of liver to process bilirubin
    - Early feedings: increasing gut motility and decreases reabsorption
- Physiologic jaundice
- Visible when bilirubin reaches  $5 - 7$  mg/dl
- Manifestation of normal hyperbilirubinemia
- Diagnosis of exclusion
- Due to a combination of
  - Increased bilirubin load to liver
  - Defective conjugation secondary to decreased glucuronyl transferase activity
  - Decreased excretion of bilirubin
  - Levels peak on day 3 of life in full term and  $5 - 6$  in preterm
- Breastfeeding and Jaundice
  - Breastfeeding jaundice:
    - Early onset, days 2 – 4 of life
    - Related to inadequate frequency of breast-feeding during early days of lactation
    - Can be avoided by frequent breast feeding and avoiding glucose water supplementation

- Breastmilk jaundice
  - Late onset, day 4 – 7 of life
  - Occurs in 10 – 30% of breastfed newborns in weeks 2 – 6 of life
  - Bilirubin levels can reach 12 – 20 mg/dl and remain elevated for up to 2 months
  - Recognized as prolonged physiologic jaundice
- Treatment strategies
  - AAP does not encourage interruption of breastfeeding in healthy term infants
  - Observe, continue breast feeding, start phototherapy
  - Supplement breast feeding with bottle feeding, with or without phototherapy
  - Temporarily discontinue breast feeding
    - Bilirubin levels should decrease rapidly
- Pathologic Unconjugated Hyperbilirubinemia
  - Criteria
    - Jaundice that appears in the first 24 hours of life
    - Total serum bilirubin that increases > 5 mg/dl per day
    - Total serum bilirubin level that exceeds 12.9 mg/dl in term or 15 mg/dl in preterm
    - Direct serum bilirubin level > 2 mg/dl
    - Jaundice lasting for more than 1 week in a term, or 2 weeks in preterm
  - Etiology
    - Hemolysis
      - ABO/Rh incompatibilities
      - Bacterial and viral sepsis
      - Inherited disorders of RBC metabolism
        - RBC enzyme defects
      - Inherited disorders of bilirubin metabolism
    - Extravasation of blood
      - Cephalohematoma
      - Cerebral hemorrhage
    - Increased enterohepatic circulation
      - Delayed feeding
      - Intestinal obstruction
    - Decreased hepatic function and perfusion
      - Hypoxia, anoxia
      - Spies
    - Inborn errors of metabolism
      - Galactosemia
      - Cystic fibrosis
- Kernicterus
  - Acute bilirubin encephalopathy
  - Bilirubin staining of neurons and neuronal injury, especially in basal ganglia
  - Etiology
    - Unbound bilirubin crosses blood brain barrier, stains and injures brain cells
  - Infants at risk for developing severe hyperbilirubinemia

- Jaundice in first 24 hours
    - Visible jaundice prior to discharge
    - Near term infant
    - Exclusive breast feeding
    - Bruising, Cephalohematoma
  - Clinical presentation
    - Initial phase: slight lethargy, hypotonia, paucity of movement, poor suck, high-pitched cry
    - Intermediate phase: moderate lethargy with irritability, increased tone, backward arching of neck (retrocollis) or back (opisthotonos), fever
    - Advanced phase: deep stupor to coma, pronounced retrocollis/opisthotonos, no feeding
  - Treatment strategies
    - No treatment for kernicterus
    - Chronic bilirubin encephalopathy: hearing loss, cerebral palsy, gaze abnormalities, developmental delay
- Management of unconjugated hyperbilirubinemia
  - Any infant who is jaundiced before 24 hours requires a measurement of serum bilirubin
    - If elevated, required evaluation for hemolytic disease
  - Phototherapy
    - Most effective in decreasing nonhemolytic hyperbilirubinemia
    - Mechanism of action
      - Photo-oxidation
        - Bilirubin oxidized to water-soluble products excreted in urine
      - Photoisomerization
        - Major mechanism

**Guidelines for the Management of Hyperbilirubinemia Based on Birth Weight and Relative Health of the Newborn**

Birth Weight	Serum Total Bilirubin Level (mg/dL)			
	Healthy		Sick	
	Phototherapy	Exchange Transfusion	Phototherapy	Exchange Transfusion
<b>Premature</b>				
<1000 g	5-7	Variable	4-6	Variable
1001-1500 g	7-10	Variable	6-8	Variable
1501-2000 g	10-12	Variable	8-10	Variable
2001-2500 g	12-15	Variable	10-12	Variable
<b>Term</b>				
>2500 g	15-18	20-25	12-15	18-20

Tausch, Ballard and Gleason, 2005, p 1247

- Conversion of bilirubin to water soluble structural and configurational isomers that can be excreted by liver without conjugation
  - Increased hepatic excretion of unconjugated bilirubin and increased bowel transit time also due to phototherapy
- Effectiveness influenced by
  - Energy output of phototherapy unit
  - Spectrum of light
  - Amount of infant's body surface area exposed to the light
- Delivery methods
  - Banks of fluorescent lights
  - Fiberoptic blankets
  - Tungsten-halogen lamps: danger of burns if placed too close
- Management of phototherapy
  - Fluorescent lights should be placed 45 – 50 cm from the neonate
  - Bank of lamps should be covered with plexiglass to protect from UV light
  - Fluorescent lights should be placed at least 2 inches from top of incubator
  - Expose as much skin surface as possible
  - Turn frequently to allow all areas of skin to be exposed
  - Temperature control important—use of servo control optimal
  - Monitor fluids carefully
    - Increases insensible water losses
    - May cause diarrhea
  - Monitor bilirubin levels after phototherapy discontinued—rebound of 1 to 2 mg/dl
  - Side effects
    - Diarrhea
    - Hyperthermia
    - Dehydration
    - Skin rashes
    - Lethargy



## **Certification Websites**

- American Association of Critical Care Nurses Certification Corporation: [www.certcorp.org](http://www.certcorp.org)
  - Critical Care Registered Nurse Neonatal
  
- National Certification Corporation: [www.nccnet.org](http://www.nccnet.org)

## **Test Questions**

1. Potential effects of pregnancy-induced hypertension on the maternal-placental-fetal unit would include:
  - a. maternal hyporeflexia, fetal hyperproteinemia, and polyuria in the neonate
  - b. maternal hyperglycemia, placental previa, and respiratory distress in the neonate
  - c. maternal seizures, abruptio placentae and fetal distress during labor
  - d. maternal hypercalcemia, placental previa and meconium aspiration in the neonate
  
2. The fetal pathway connecting the pulmonary artery and the aorta is the
  - a. ductus venosus
  - b. ductus arteriosus
  - c. foramen ovale
  - d. foramen of Munro
  
3. Cold stress can lead to:
  - a. anemia
  - b. hypertension
  - c. increased oxygen consumption
  - d. decreased carbon dioxide production
  
4. Anaerobic metabolism as a result of hypoxia contributes to:
  - a. decreased glucose utilization and alteration of cardiac function
  - b. increased insulin production and storage of fats
  - c. decreased insulin production and hemolysis
  - d. increased lactic acid production and decreased pH
  
5. Persistent pulmonary hypertension of the newborn is associated with:
  - a. congenital anomalies
  - b. perinatal asphyxia
  - c. neonatal anemia
  - d. maternal analgesia
  
6. After the neonate receives surfactant replacement therapy, the nurse should anticipate and respond to:

- a. improved chest expansion
  - b. hypercapnia
  - c. intraventricular hemorrhage
  - d. pneumatosis intestinalis
7. The diuretic that is the most  $\text{Ca}^{++}$  sparing is
- a. Aldactone
  - b. Diuril
  - c. Lasix
  - d. Furosemide
8. Compensated metabolic acidosis is characterized by
- a. hyperventilation
  - b. hypoventilation
  - c. increased renal excretion of  $\text{HCO}_3$
  - d. decreased renal excretion of  $\text{HCO}_3$
9. A decrease in pulmonary blood flow occurs with
- a. coarctation of the aorta
  - b. ventricular septal defect
  - c. truncus arteriosus
  - d. Tetralogy of Fallot
10. One important factor in assessment of the thrombocytopenic infant includes:
- a. determination of the mother's Rh antigen status
  - b. maternal history of low platelet count
  - c. evaluation of the hemoglobin/hematocrit values
  - d. timing of administration of Vitamin K

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**Answers to Test Questions**

1. c
2. b
3. c
4. d
5. b
6. a
7. b
8. a
9. d
10. b