Care of the Preterm Neonate with Congenital Heart Disease
What the Nurse Caring for the Patient with CHD Needs to Know

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Introduction: The risk of mortality and morbidity is significantly increased in premature infants as compared with full term infants. There are potential numerous complications from prematurity due to physiologic systems that are both structurally and functionally immature. The risk of complications increases with increased immaturity. Infants who are extremely premature, (born before 25 weeks gestation), have the highest risk of both morbidity and mortality.

Cardiovascular:
Overview: The preterm cardiovascular system is less physiologically and metabolically mature; there is an increased predisposition toward dysregulation and hemodynamic instability.

- Immature myocytes and calcium channels lead to greater sensitivity to afterload and reliance on extracellular calcium
- Immature sympathetic nervous system and potential altered response to endogenous catecholamines:
  - Increased vagal tone (preterm neonates up to 36 weeks) and risk for bradycardia
  - Immature response to baroreceptors and chemoreceptors
  - Reduced secretion and metabolism of endogenous catecholamines as compared with term newborns
  - In late preterm: 35-36 weeks gestation
    - Improving vasomotor tone when nearing term
    - Reduced cortisol and adrenocorticotropic hormone (ACTH) levels over time without increase in response to critical illness
- Abnormal peripheral vascular regulation leading to greater propensity toward decreased vascular tone, vaso-relaxation and decreased systemic vascular resistance (SVR); hypotension without evidence of shock is common
- Reduced vasoconstriction ability of Ductus Arteriosus (DA) leading to increased likelihood of remaining patent or re-opening following closure
  - In late preterm: 35-36 weeks gestation
    - Vasomotor tone maturing
• Maturing pulmonary vasculature leads to increased reactivity of pulmonary bed & predisposition to vasoconstriction and pulmonary hypertension (PHTN) of the newborn

• **Management strategies and Nursing Assessment Key Points:**
  o Monitor blood pressure (BP) closely
    ▪ Maintain mean arterial blood pressure (MABP) 5 points +/- gestational age
    ▪ May need to alter goals based on surgical repair or signs of shock
      • Monitor for elevated lactate, decreased peripheral perfusion (mild hypotension may not be an accurate indicator of shock state)
    ▪ Consider volume expansion as needed
      • Infuse slowly over at least 30 minutes to 1 hour if condition tolerates to avoid rapid swings in blood pressure
    ▪ Vasoactive medications with refractory hypotension and signs of shock
      • Dopamine:
        o Used commonly in gestational age <30 weeks to term neonate for hemodynamic and inotropic support
        o Adverse effects: increased pulmonary arterial (PA) pressure; inhibits thyrotropin, growth hormone, and gonadotropins
      • Epinephrine:
        o Limited data with use in pre-term neonates
        o Effective in increasing SVR; side effects in preterm population include hyperglycemia, tachycardia, increased lactate with increased dosing
      • Vasopressin:
        o Increased interest in use of hemodynamic support in preterm population
        o Preliminary trials demonstrate efficacy in supporting BP
          ▪ Minimal to no inotropic or chronotropic effects
          ▪ May cause pulmonary vasodilation
          ▪ Vasoconstrictive effects during hypoxia and severe acidosis
        o Monitor cortisol levels as indicated
          ▪ Consider drawing cortisol level, and hydrocortisone replacement for:
            • Severe refractory hypotension on vasopressor support
            • High vasopressor requirement
        o Maintain normalized electrolytes to optimize cardiac performance
          ▪ Ionized calcium
          ▪ Potassium may be elevated or decreased related to premature kidney function
          ▪ Magnesium

**Lesions Specific to the Pre-term Infant** (See Guidelines for specific CHD Defects)
  • Patent Ductus Arteriosus (PDA)
Normal fetal structure connecting the pulmonary artery to the aorta

Pulmonic origin of the duct typically located at the pulmonary artery bifurcation (just beyond in LPA) gently curving posteriorly and inferiorly to be inserted into the descending aorta beyond the origin of the left subclavian artery

During fetal life pulmonary vascular resistance (PVR) is high and ductal flow is right to left

Prematurity and PDA
- Patency maintained by low oxygen saturations and circulation of prostaglandins in the body in relation to lung disease and hypoxia
- Genetic factors preclude a higher incidence – Trisomy 21, Char syndrome, parental consanguinity; siblings of patients with a PDA have an increased incidence
- Congenital infections – rubella, sepsis in premature babies
- Medications – angiotensin converting enzyme (ACE) inhibitors

Clinical features
- Signs of congestive heart failure (CHF) – tachypnea, poor feeding, poor growth
- Wide pulse pressure, bounding pulses, active chest wall (precordium)
- Pulmonary over-circulation
- Inability to wean from the ventilator or increase in ventilator requirements
- Acidosis

Management
- Optimizing hematocrit, fluid restriction, diuresis
- Indomethacin – non-steroidal anti-inflammatory drugs (NSAIDs) inhibit prostaglandin synthesis
- Surgical ligation – via left thoracotomy (more common approach), no cardiopulmonary bypass needed
  - For fragile Very Low Birth Weight infants (VLBW) the procedure may be done at bedside in NICU
- Catheter coil/device closure in the cardiac catheterization laboratory (cath lab)
  - Generally reserved for larger neonate / infants
    - Small, preterm neonate may be too small for arterial catheter/sheath required for catheterization

Prolonged use of PGE1
- Indications for use – to maintain patency of the PDA in lesions that require continuous flow to maintain life
  - Hypoplastic left heart syndrome (HLHS)
  - Aortic atresia
  - Critical aortic stenosis
  - Tricuspid atresia with severe pulmonary stenosis
  - Transposition of the great arteries (TGA)
  - Interrupted aortic arch
  - Severe coarctation of the aorta
  - Critical pulmonary stenosis

Side effects
- Apnea – may require intubation and mechanical ventilation
- Hypotension, edema, arrhythmias
- Seizures, hyperthermia
- Rash, erythema/flushed body
  - Risk for necrotizing enterocolitis from unbalanced circulation

- Palliative Procedures in preterm neonate
  - Pulmonary artery band (PAB)
    - Indications
      - Preferred initial palliation for those with a large left-to-right shunt and increased PA flow to limit pulmonary blood flow
      - Goal is to reduce pulmonary blood flow (PBF), balance circulation temporarily to allow for growth and maturation prior to staged or complete repair
        - Muscular ventricular septal defects (VSDs), multiple VSDs with coarctation of the aorta, single ventricle with increased pulmonary blood flow (tricuspid atresia type IIc)
    - Management
      - Monitor arterial saturation
        - Ideal oxygen saturation goal between high 70’s to 80’s
      - Assess for signs and symptoms of pulmonary over-circulation and CHF
      - Diuretics

- Modified Blalock-Taussig Shunt (mBTS)
  - Shunt from the systemic artery to the pulmonary artery
  - Advantages
    - Preservation of the circulation to the affected arm
    - Regulation of shunt flow by the size/length of mBTS
    - High early patency rate
    - Ease of shunt takedown
  - Indications – to provide PBF in cyanotic lesions that require prostaglandins for maintenance of ductal flow
    - Pulmonary Atresia with VSD
    - Severe Tetralogy of Fallot (TOF)
    - Double Outlet Right Ventricle (DORV) with pulmonary stenosis
    - TGA with pulmonary stenosis
    - Single ventricle with decreased PBF
  - Management
    - Assess for presence of shunt murmur
    - Inotropic medications to maintain adequate perfusion pressure of the shunt as indicated
    - Balancing the ratio of pulmonary to systemic perfusion (Qp:Qs)
      - Careful use of oxygen to avoid rapid drop in PVR
      - Use oxygen blender for manual ventilation of intubated patients
      - Afterload reduction may be required to optimize blood flow to systemic circulation
    - Aspirin may be indicated to avoid shunt thrombosis
Complications
- Risk for necrotizing enterocolitis (NEC) due to diastolic run off through the shunt, additionally at risk for decreased coronary artery perfusion
- Excessive pulmonary artery blood flow
  - Signs of CHF and pulmonary over-circulation
  - Elevated lactate
  - Failure to wean from mechanical ventilation
  - Increasing diuretic requirement

Neurologic System:
Overview: Preterm infants are at high risk for neurologic insult and dysregulation due to a variety of factors related to immaturity.

Intraventricular Hemorrhage (IVH):
- Common adverse event that may occur in preterm infants
- Incidence increased as gestational age and birth weight decreases
  - Preterm infants ≤33 weeks gestation highest risk
  - Late preterm infants 34-36 weeks gestation are still vulnerable to IVH and require careful monitoring
    - Cardiopulmonary bypass (CPB) and Deep Hypothermic Cardiac Arrest (DHCA) are a significant risk for pre-term population and a relative contraindication in the VLBW
    - Risk of IVH and mortality increases below 36 weeks gestation
    - Extracorporeal membrane oxygenation (ECMO) support is a relative contraindication in many institutions for patients <36 weeks gestation.
      - Patient <2kg in weight are a relative contraindication for ECMO support due to the technical challenges of peripheral cannulation
    - Evidence of IVH in preterm and term neonates necessitates a neurology consult prior to surgical intervention
      - Surgical intervention will usually remain on hold for a period of time determined by neurology team if IVH confirmed; these patients are higher risk for increased mortality & morbidity
- Severity of hemorrhage is based on whether the bleeding is confined to the germinal matrix region, or if it extends into the adjacent ventricular system or white matter (intraparenchymal)
- Grading system to define the extent of bleeding; grade I–IV
  - Each grade of IVH may be unilateral, or bilateral with either symmetric or asymmetric grades of IVH
    - Grade I (least severe) – Grade IV (most severe, involves white matter, and often hydrocephalus)
  - Hydrocephalus (complication of higher grade IVH)
    - Post-hemorrhagic hydrocephalus occurs in approximately 35 percent of preterm infants with IVH; risk increases with the severity of IVH
    - Hydrocephalus may be obstructive, communicating, or both; transient or sustained; and with slow or rapid progression; in some cases, shunt replacement is required
Management
- Daily head circumference measurement
- Serial head ultrasounds
- Neurology and neurosurgical consultation
  - Serial lumbar punctures to reduce intracranial pressure (ICP) as indicated
  - Direct ventricular taps may be indicated
  - Consideration for subgaleal or ventriculoperitoneal shunt, or endoscopic third ventriculostomy for long term treatment
  - Anticoagulation therapy may have impact on interventions performed
- Outcomes from IVH include cerebral palsy, sensory, cognitive, psychosocial or developmental impairment

Management strategies and Nursing Assessment Key Points:
- Avoid rapid fluctuations in blood pressure and hypertension
- Slow administration of fluid boluses
- Avoid hyperosmolar solutions if possible (i.e. sodium bicarbonate)
- Avoid fluctuations in pH; regulate pH for required cardiovascular hemodynamics
- Normalize coagulation factors, careful monitoring of anticoagulation if required
- Sedation to decrease effects of mechanical ventilation on cerebral blood flow fluctuations
- Monitor neurologic status and hematocrit closely
- Routine cranial ultrasounds at DOL 3, 7 and 30 or more frequent if indicated

Apnea of Prematurity
- Cessation of respiratory effort related to neurologic immaturity due to a blunted response of preterm infant to hypoxia and hypercarbia
  - Further risk factor includes use of Prostaglandins (PGE1) to maintain ductal patency
- Apnea leads to hypoxia and subsequent oxygen desaturation and bradycardia
- Apnea may be self-resolving or require tactile stimulation, oxygen, or bag mask ventilation (BMV)
  - Caffeine citrate to stimulate respiratory drive
    - Dose initially 10-20 mg/kg bolus PO/PG/IV
    - 5-10 mg/kg maintenance dose once daily 24 hours following load
    - Dose should be held if tachycardia develops (heart rate > 180)
    - Levels may be monitored

Pulmonary system:
Overview: Preterm neonates have an increased risk for respiratory distress syndrome (RDS), mechanical ventilation, and chronic lung disease due to system immaturity. Fetal lung development is separated into 5 distinct phases, with each phase having a specific role in development of the functional lung apparatus. Viable lung tissue and ability to perform gas exchange does not occur until approximately 23-24 weeks gestation, and at that time, at a very
limited capacity. Development of lung tissue, including alveoli and bronchial proliferation continues to develop well into age 3.

**Characteristics of the Preterm Lung:**

- Structural and functional immaturity
  - Capillary-alveolar interface or air-blood barrier
    - Immaturely formed at the end of 23-24 weeks
    - Breathing movements detectable by 23-24 weeks
  - Type II pneumocytes
    - Produce surfactant, a phospholipid responsible for reduction of surface tension in the alveolar bed
    - Begin to develop around 23 weeks
    - Do not become mature until approximately 36 weeks

- RDS
  - Preterm infants ≤ 30 weeks up to 34 weeks gestation
    - Most common respiratory complication in this age group
  - Late Preterm infants 35-36 weeks gestation
    - Predisposed to RDS
    - Higher risk in insulin dependent diabetes mellitus (IDDM), cesarean delivery, twins
  - Disease of the immature lung due to surfactant characterized by
    - Lecithin–sphingomyelin (L:S) ratio <2:1
    - “White out” or reticulogranular, “ground glass” appearance on chest x-ray from diffuse atelectasis superimposed with air bronchograms
    - Increased work of breathing (WOB): tachypnea, grunting, retractions, nasal flaring, poor air movement and fine rales on auscultation
    - Decreased lung compliance and partial pressure of carbon dioxide (pCO₂) retention, respiratory / metabolic acidosis
    - Symptoms of RDS may be overshadowed in patients with severe CHD
    - RDS suspected if patient preterm and unresponsive to conventional management strategies
      - Elevated pCO₂ and positive inspiratory pressure (PIP) requirement on ventilator
      - Persistent acidosis and hemodynamic instability unexplained by current diagnosis
  - Long term outcomes of RDS
    - Chronic lung disease (CLD)
      - Premature infants
        - Requires positive pressure ventilation (PPV) in the first week of life
        - Still possess clinical signs of chronic respiratory disease, with oxygen requirement and abnormal chest x-ray at 28 days of life
        - Abnormal pulmonary outcome predicted by an oxygen requirement at 36 weeks gestation
- Majority results in bronchopulmonary dysplasia (BPD)
  - Stages
    - Acute lung injury: caused by combination of barotrauma, oxygen toxicity, cellular injury related to inflammatory response
    - Chronic phase: fibrosis and cellular hyperplasia, pulmonary fluid retentions, hyper reactive airways
  - Clinical presentation and effects on congenital heart disease (CHD)
    - Mechanical ventilatory requirements, persistent hypercapnia/ hypoxia, increased work of breathing (WOB), bronchospasm, pulmonary edema, CXR changes (areas of hyperinflation, atelectasis)
    - May lead to elevated PVR, right ventricular (RV) pressure, cardiomegaly, ventilation/perfusion (VQ) mismatch
      - High risk for right-sided failure
      - Significant hemodynamic effect on single ventricle physiology
      - Lesions with increased pulmonary blood flow may worsen CLD symptoms
- Management strategies and Nursing Assessment Key Points:
  - Requires increased positive end expiratory pressure (PEEP) to ventilate and prevent further alveolar collapse
  - Surfactant replacement
    - In preterm infants ≤ 30 weeks
      - Prophylactic therapy has been shown to be beneficial if given within 2 hours of delivery prior to symptom onset
    - Preterm > 30 weeks to 38 weeks (with risk factors)
      - Rescue dosing common once symptoms appear
        - Usually most effective if given within the first 48 hours following birth
        - Premature neonates begin to produce endogenous surfactant despite immaturity approximately 72 hours following delivery
  - Administered via endotracheal tube
  - Nursing considerations prior to administration
    - Always check endotracheal tube (ETT) placement prior to administration to ensure appropriate location
    - Suction ETT prior to administration and do not re-suction for several hours following administration unless indicated by clinical emergency
    - Monitor positive inspiratory pressure (PIP) and tidal volume (TV) following administration and be prepared to make quick adjustments once lung compliance improves
    - Transient oxygen desaturation during initial administration should resolve quickly with hand bag ventilation if it occurs
Monitor for complications of surfactant administration
  - Pulmonary embolism
  - Pneumothorax

Permissive hypercapnia (gentle ventilation)
  - Gentile ventilation strategies are gaining momentum in the management of premature lung disease
    - Benefits of permissive hypercapnia include:
      - Reduction in lung injury potential and incidence of severe broncho-pulmonary dysplasia (BPD)
      - Protective against brain hypoperfusion and reperfusion injury related to hypocapnia
      - Ideal partial pressure of carbon dioxide in arterial blood (PaCO₂) levels yet to be determined
    - Potential effects of permissive hypercapnia with ventilation strategies
      - Lower TV
      - Frequent synchronized inspired minute ventilation (SIMV) breaths
      - Maintenance of PEEP

Management of CLD
  - Careful use of oxygen
    - Oxygen delivery on blender to maintain saturation of peripheral oxygen (SPO₂) limits within range
    - Increase 10% above baseline for suctioning, as appropriate
  - Fluid restriction
  - Diuretics
  - Bronchodilators
  - May consider steroids in severe cases (after 1 month of age)

Renal System / Fluid and Electrolytes:

Overview: Premature infants have an increased risk for acute renal injury and chronic kidney disease; increased risk for fluid and electrolyte derangements due to immature renal tubules, reduction in renal blood flow and an immature integumentary system.
  - Nephrogenesis is complete by 34 weeks gestation in utero
  - In preterm infant from 25-34 weeks gestation, nephrogenesis in the preterm kidney is evident for up to 40 days post birth
  - In extreme prematurity of 23-24 weeks gestation, there is reduction in nephrogenesis until 36 weeks corrected gestational age

Characteristics of Preterm Renal Function and Fluid / Electrolyte Homeostasis:
  - In utero glomerular filtration rate (GFR) is low but increases rapidly following birth as a result of increased renal blood flow
    - Preterm renal blood flow may be less than half that of term neonate and will gradually increase over time
Fluid homeostasis in pre-term neonate

- Pre-diuresis stage – oliguric stage occurring immediately after birth up to 36 hours of life
- Diuretic stage (day 2-4 of life): significant loss of extracellular water despite fluid restriction
- Post diuresis: urine output stabilizes based on intake

- Creatinine clearance maturation is slower
- Predisposition for metabolic acidosis particularly during first week of life
- Immature renal tubules lead to limited ability to excrete or effectively retain sodium simultaneously; difficulty concentrating urine; increased free water loss
- Reduced response of adrenal gland to aldosterone; renin-angiotensin-aldosterone system is not maximally inhibited, predisposing to risk of sodium overload with aggressive sodium replacement

**Management strategies and Nursing Assessment Key Points:**

- Fluid management: anticipate phases of fluid balance and manage intake accordingly
  - Pre-diuresis: restricted fluids for first 24-48 hours post delivery
    - 60-80 ml/kg/day based on anticipated water losses; may restrict further if acute kidney injury is suspected
  - Diuresis: advance fluids based on daily weights and serum sodium levels
    - Requirements may vary between 100-120 ml/kg/day or higher based on cardiovascular effects, estimated fluid losses and nutritional requirements
    - Serum sodium requirements may be unreliable if diuretic therapy is required for the stabilization of CHF
  - Post-diuresis: maintain fluid administration at level required to provide cardiovascular homeostasis and nutritional gains

- Humidity
  - The use of humidification within a closed isolette has been shown to improve insensible water loss and fluid requirements in very low birth weight infants, less than 30-32 weeks gestation
    - Initial humidity is generally set at 60-70% relative humidity (RH) but may be increased to 80% if patient condition warrants
    - Therapy is continued for approximately 10-14 days until preterm epidermis matures
    - Refer to institutional infection control standards with humidification, and weaning guidelines

- Electrolytes
  - Anticipate electrolyte derangements within the first few weeks of life in the preterm neonate, particularly for <34 weeks gestation
    - Utilize sodium supplementation cautiously, monitor serum or whole blood sodium 2-3 times daily to determine hydration status
    - Hyperkalemia and hypocalcemia are common; monitor levels at least 2-3 times daily, or more frequently as indicated
Predisposition to hyperkalemia and hypocalcemia may have significant impact on cardiac function of pre-term neonate

- Metabolic acidosis is common in the first few weeks of life
  - Manage metabolic acidosis carefully
  - Negative outcomes associated with bicarbonate administration in the pre-term population particularly in relation to incidence of IVH
    - Avoid sodium bicarbonate administration
    - If no alternative, utilize “neut” (diluted) bicarbonate of 0.5 mEq/ml; AVOID USE of sodium bicarbonate 1 mEq/ml due to risk of IVH
  - Registered dietician consult for recommendations to slowly correct metabolic acidosis
  - Renal immaturity and drug metabolism
  - Higher risk for overdosing due to immature renal function
    - Dose adjustments are needed to avoid toxicity
    - Many medications utilized in pre-term infants are off-label use
    - NEOFAX is drug reference specifically formulated for use in the pre-term population

Gastrointestinal System:
Overview: Preterm infants are born with limited nutrient reserves, immature metabolic pathways and gastrointestinal (GI) function, and increased nutritional demands. Medical and surgical complications associated with both prematurity and cardiovascular disease alter nutritional requirements and complicate delivery of adequate caloric intake.

Characteristics of Preterm Gastrointestinal System (GI) and Nutritional Homeostasis:
- GI system of the preterm infant is characterized by:
  - Reduced gastric and bile acid secretions, protease cascade, and intestinal lactase activity that may predispose to feeding intolerance
  - Intestinal dysmotility in infants < 34 weeks gestation
    - May persist beyond 34 weeks
    - Predisposition to bacterial overgrowth
  - Esophageal tone is reduced in < 30 weeks gestation
  - Mesenteric blood flow dysregulation may occur, predisposing preterm infants to necrotizing enterocolitis (NEC)
- NEC is the most common surgical disorder of this patient population
  - Factors related prematurity and low flow states associated with CHD create increased risk
  - Cardiac lesions and repairs associated with increased pulmonary shunting (mBTS), and decreased systemic output (HLHS, single ventricle physiology with decreased systemic output, coarctation of aorta and low cardiac output syndrome), are at highest risk
  - Histologic examination suggests the disease consists of ischemia, gradual tissue compromise, proliferation of colonizing bacteria with release of endotoxins and
cytokines, bacterial invasion and fermentation with gaseous distention and inflammation

- Early identification of infants at risk and initiation of treatment is the most important factor associated with outcome

- Clinical signs include:
  - Change in clinical exam: respiratory distress, apnea, bradycardia, lethargy, temperature instability, feeding intolerance
  - Changes in abdominal exam: abdominal distension, tenderness, elevated gastric aspirates, vomiting, bloody stools
  - Laboratory findings: hyponatremia, thrombocytopenia and metabolic acidosis
  - Radiologic findings
    - Kidney-ureter-bladder x-ray (KUB) may reveal abnormal gas pattern consistent with ileus
    - Cross-table or left lateral decubitus: mass appearance, fixed loops of bowel and bowel wall edema, pneumotosis
    - “Free air” in the peritoneum, portal venous air, or pneumoperitoneum indicate intestinal perforation and represent a surgical emergency

- **Management strategies and Nursing Assessment Key Points:**
  - Frequent abdominal assessment including visual inspection and abdominal girth
  - Assess for blood in stool (heme testing)
  - Gastric aspirates – may or may not be useful; concern arises if bloody or bilious gastric secretions
  - Medical management
    - Bowel rest, gastric decompression, and administration of broad spectrum antibiotics
    - Close observation and serial abdominal exams including KUB
  - Surgical management
    - Peritoneal drainage: Less invasive and may be used for infants who are too unstable for an operative procedure
    - Laparotomy: for perforated NEC or spontaneous intestinal perforation (SIP)

**Hepatic/ Hyperbilirubinemia:**

**Overview:** Neonatal jaundice is caused by increased bilirubin production, decreased bilirubin clearance and increased enterohepatic circulation. Many types of jaundice are considered normal in neonates; risks vary related to gestational age, total bilirubin level and prematurity. Management of Hyperbilirubinemia is based on patient, gestational age, birth weight and bilirubin level.

- **Classifications of Hyperbilirubinemia:**
  - Physiologic hyperbilirubinemia: most common; shorter neonatal red blood cell (RBC) life span increases bilirubin production
  - Breastfeeding jaundice: occurs in 1/6th of breastfed infants; increased entero-hepatic circulation of bilirubin in neonates with poor enteral intake within the 1st week of life
Breast milk jaundice: occurs after first 5 to 7 days; peaks at ~ 2 weeks of life; increased concentration of β-glucuronidase in breast milk, causing an increase in the deconjugation and reabsorption of bilirubin

Pathologic hyperbilirubinemia (in term infants)

Management strategies and Nursing Assessment Key Points:

- Phototherapy
  - Fiber optic phototherapy blankets and/or lights
  - Preterm infants with rapidly rising bilirubin level may need maximum phototherapy (up to 3 lights) with maximum skin exposure
  - Eye protection must be utilized with all forms of phototherapy
  - Fluid and electrolyte assessed closely due to increased insensible losses; will require an increase in total fluids to compensate
  - Assess for re-bound bilirubin 12 – 24 hours following discontinuation of therapy

- Exchange transfusion for rise in bilirubin of greater ≥ to 1mg/dl/hour despite maximum phototherapy
  - Blood for exchange transfusion should be less than 7 days old with hematocrit of 45-50
  - Infants blood volume is ~ 80ml/kg; exchange is usually double volume (160 ml/kg)
  - Push-pull technique in 5-20 ml aliquots via umbilical or other central venous catheter utilized
  - Monitoring during exchange transfusion includes:
    - Signs of hypocalcemia, hypomagnesemia, hypoglycemia, acidosis, hyperkalemia, thrombocytopenia
    - Other risks: bleeding, hemolysis, thrombosis, arrhythmias, volume overload, sepsis

Glucose metabolism:
Overview: At birth the neonate loses maternal source of glucose and must respond by glucogenolysis of hepatic stores and metabolize exogenous sources from feedings. Glucose levels fall in the first 2 hours of life and then stabilize around 4 hours of life at ~ 60-70 mg/dl.

Hypoglycemia
- Etiology of hypoglycemia
  - Increased utilization/hyperinsulinism associated with infants of diabetic mothers, LGA infants, genetic or metabolic disorders, maternal drug exposure including beta-blockers, and malposition of umbilical artery catheters
  - Decreased production/stores related to prematurity, intra-uterine growth retardation (IUGR)
  - Increased utilization associated with acute illness and perinatal stress, sepsis, shock, hypothermia, exchange transfusion, metabolic or endocrine disorders, polycythemia
- Clinical signs and symptoms of hypoglycemia are non-specific and may include poor feeding, tremors, jitteriness, seizures, lethargy, apnea, weak or high pitched cry

Management strategies and Nursing Assessment Key Points:
Normal neonatal blood glucose levels are usually between 70-100 mg/dl
- Treatable hypoglycemia cutoff considered at 40mg/dl although many practitioners would consider 55-70 mg/dl treatable
- Glucose should be measured in the first 1-2 hours after birth
- Any infant with serum glucose < 40 should be treated with glucose
- Glucose levels < 40 at any time requires close monitoring
  - Within 24 hours of life goal should be > 45mg/dl
  - After 24 hours of life, goal should be > 50mg/dl
- Close monitoring is required if the glucose level remains low, does not increase with feedings, or if clinical signs of hypoglycemia are present
  - Premature infants may not be protected from central nervous system (CNS) compromise due to hypoglycemia
  - Development of clinical symptoms may be a late sign of hypoglycemia
- IV glucose therapy should be considered if:
  - Infant cannot be fed
  - Symptomatic
  - Oral feeds to not maintain glucose > 45mg/dl
  - Initial or follow-up glucose level < 25mg/dl
- Treatment with IV glucose in neonates usually begins with 2 ml/kg of D10%
- Continuous treatment with IV dextrose 10% to give 6-8 mg glucose/kg/minute as a baseline; glucose infusion rate (GIR) may be calculated:
  - [(Concentration, g/100 mL) x (infusion rate, ml/hr) x (1000 mg/g) ÷ (weight, kg)] x (60 min/hr)
  - Preterm neonates with co-morbid diagnoses may require a higher GIR
- Glucose levels assessed every 20-30 minutes after initiation of IV infusion, then every hour until stable

Hyperglycemia
- Less common than hypoglycemia in preterm neonates
- Defined as plasma glucose > 145 mg/dl
- Hyperglycemia in premature infants is associated with:
  - Medications such as steroids
  - Exposure to exogenous glucose
  - Sepsis and depressed insulin release
  - Persistent exogenous glucose production due to catecholamines and other stress hormones related to illness, painful procedures
- Management strategies and Nursing Assessment Key Points:
  - Insulin infusion is generally indicated when glucose level is > 250 mg/dl
  - Neonates are very sensitive to insulin; when infusion is started, glucose levels should be checked at least every 30 minutes
  - Glucose levels must be decreased slowly to avoid rapid fluid shifts

Integumentary system:
Overview: The integument of the preterm neonate is physiologically and structurally immature predisposing the infant to increased risk for heat loss, insensible water loss, infection and systemic absorption of toxins. Preterm neonates have underdevelopment and fewer outer layers
of skin (stratum corneum) depending on their gestational age. The premature dermal layer has reduced elastin fibers and collagen, predisposing preterm infant to edema; there is diminished cohesion between the dermal and epidermal layers at the dermo-epidermal junction. The skin acid mantle has not developed within the first few days of life. Epidermal maturation occurs within 10-14 days following birth.

- Maturational issues predispose premature infants to:
  - Lack of protection against infection, toxin absorption and increased insensible water loss
  - Increased risk for necrotic injury in relation to edema and pressure areas; risk of epidermal stripping injuries

- **Management strategies and Nursing Assessment Key Points:**
  - Avoid insensible water loss
    - Utilize isolette to reduce evaporative water loss
    - Humidification – see fluid and electrolytes
    - Emollients (ie. Eucerin / Aquafor)
      - Useful for drying effects of environment
        - Careful use on non-intact skin
        - Water based, single patient, single use is recommended to avoid bacterial growth
        - There are little evidence that emollients improve insensible water loss from immature skin
      - Benefits versus risk of infection must be weighed
  - Protect against infection
    - Bathing
      - Every other day for infants > 32 weeks
      - Not more than every 4 days for infants < 32 weeks
        - Utilize pH neutral cleansers
        - Water only for infants < 32 weeks
        - Use cotton balls or soft cloths to avoid skin irritation
        - Immersion baths are acceptable if clinically stable and within recommendations of institutional infection control department
      - Skin disinfectants
        - Weigh risk versus benefit due to risk of systemic absorption
          - Alcohol may be used for procedural preparation: risk for drying and skin irritation
          - Chlorhexidine bath
            - Off label use in preterm population
            - Used in some institutions in the pre-term population > 28 weeks once epidermis has matured (after 2 weeks of age)
          - Betadine not recommended due to risk of systemic absorption and effects on thyroid
  - Prevention of skin tears
    - Do not use adhesive removers due to increased risk of systemic absorption
Avoid use of skin bonding agents due to risk of increased adhesion and epidermal stripping
- Pectin based skin barriers (ie. Duoderm, Hollihesive) may be helpful if placed between the skin and adhesives
- Minimize tape and band aid use; double back tape or use cotton to reduce the adhesive quality of the tape

Eye Development:
Overview: Vascularization of the retina occurs by 40 weeks gestation. The developing retinal capillaries are susceptible to injury and over vascularization in preterm infants. Retinopathy of prematurity (ROP) is a disease related to the disruption of normal vascularization, overgrowth of retinal capillaries, and in severe cases can lead to blindness from retinal detachment and scarring. Excessive exposure to oxygen is seen as the causative agent in the development of the disease.
- **Management strategies and Nursing Assessment Key Points:**
  - Monitor of oxygen saturation – ideal levels remain unknown
    - Maintain minimal oxygen requirement to achieve desired oxygen saturation
      - 100% saturation in neonate with non-cyanotic CHD lesion may be too high
      - If physiologically able, maintain oxygen saturation between 88-94%
  - Vitamin A supplementation
    - May provide antioxidant protection from oxygen free radicals, and has shown some promise in the reduction of ROP
  - Eye exams by a pediatric ophthalmologist; *(timing may vary based on institution)*
    - All infants < 1500 grams and/or < 32 weeks should have 1st examination at 3-6 weeks of life
    - First eye exam by gestational age
      - 26 weeks or less: 6 weeks from birth
      - 27-28 weeks: 5 weeks from birth
      - 29-30 weeks: 4 weeks from birth
      - 31 weeks and >: 3 weeks from birth

Developmental and Growth Issue in the Preterm Neonate:
Overview: Growth impairment during early infancy, especially in preterm infants, can have detrimental effects that may persist into adulthood. Due to a high risk of poor growth during the neonatal intensive care unit (NICU) stay, and even after discharge, it is important to closely monitor nutritional status and weight gain. Normative growth data are available for healthy term infants. However, data are limited for preterm infants during both hospitalization and after discharge. In preterm survivors, there is a high risk of short and long term neurodevelopmental impairment and chronic health problems. These problems often require additional health care and resources.

Growth Curve comparison
- Term infants:
  - Weight gain norms for full term infants:
- In utero: after 28 weeks gestation = 208 grams (g) per week
- 30 g/day until 3 months of age
- 20 g/day between 3 and 12 months of age
  - Length gains:
    - In utero: 1.1 cm/week from 28 to 40 weeks gestation
    - 0.75 and 0.5 cm/week for the first 3 and the following 2 to 3 months, respectively
  - Head circumference gains:
    - In utero: 0.75 cm/week during the last trimester
    - 0.5 cm/week from birth to three months of age
    - 0.25 cm/week after 3 months of age

- Preterm infants:
  - Growth Curves used to track growth of preterm infants have been based upon intrauterine standards or upon small numbers of preterm infants
    - Usually lead to inadequate growth (most have weights below 10th percentile at time of discharge)
  - Once birth weight regained, growth goals include:
    - Weight – 15 g/kg per day
    - Length – 1 cm/week
    - Head circumference – 0.7 cm/week
  - Corrections for gestational age should be made for weight through 24 months of age, for stature through 40 months of age, and for head circumference through 18 months of age

- Nutritional requirements for adequate growth:
  - Challenges in Preterm infant
    - Immature GI function limits the advancement of enteral feedings
    - Poor tolerance of intravenous lipids and glucose limits the use of parenteral nutrition leading to inadequate caloric and protein intake
  - Deficits increase with decreasing gestational age
    - Are most severe in extremely low birth weight (ELBW) infants (birth weight < 1000 g)

- Parenteral Nutrition (PN)
  - Indications
    - Often indicated for very low birth weight (VLBW) infants (birth weight of less than 1500 g)
    - Pre-term infants who are unable to achieve adequate caloric intake from enteral feedings
    - Pre-term infants with severe medical problems associated with prematurity and/or CHD
    - Nutritional requirements of VLBW infants or preterm infants with CHD are rarely met by enteral feeds in the first two weeks after birth
  - Benefits of early use of adequate PN
    - Minimizing weight loss, correction of in-utero growth restriction and prevent growth failure
    - Improvement of neurodevelopmental outcome
    - Reduce the risk of mortality and later adverse outcomes, such as NEC and
bronchopulmonary dysplasia

**Enteral Feeding**
- Preterm infants struggle to maintain adequate enteral caloric intake due to a variety of causes including:
  - Poor oral feeding related to developmental or neurologic impairment, oral aversion, medical complications, prolonged intubation problems
    - Suck-swallow coordination usually does not appear until ~ 34 weeks gestation
  - Feeding intolerance
  - Risk for NEC

**Management strategies and Nursing Assessment Key Points:**
- Nutritional goal: adequate calories for energy expenditure and growth
- Perform daily calorie counts
  - Include all sources of both enteral and parental infusions, current and discontinued continuous IV infusions with dextrose administered within the past 24 hour period.
- Daily weights with weekly length and head circumference are necessary to measure adequate growth.
  - Utilize isotope or bed scale for intubated patients as appropriate
- Laboratory monitoring required for PN:
  - Adjustment of PN contents & avoidance of excesses or deficiencies of any given nutrient
  - Monitor for PN-associated complications, such as cholestasis and metabolic bone disease
- PN components
  - Glucose
    - Usually initiated at 3.5 mg/kg per minute (5 g/kg day)
    - Slowly increased to 12 mg/kg/min over several days
      - Monitor blood glucose levels with titration of glucose infusion rate
      - Consider insulin drip with persistent hyperglycemia
  - Lipids
    - Usually 1 g/kg per day with increasing increments as tolerated to 3 g/kg per day
    - Monitor triglyceride level
  - Protein
    - Adequate protein intake, including essential amino acids, to achieve positive nitrogen balance required for growth
    - Amino acids at 3.5 g/kg per day with increasing increments as tolerated to 4 g/kg per day
    - Fatty acids prevents essential fatty acid deficiency and maximize overall non-protein energy intake
  - Essential nutrients including minerals
    - Electolytes, vitamins, and trace elements, and other nutrients—Calcium (650 mg/kg per day) and multivitamins, needed for
growth
  o Consider trophic feedings of 10cc/kg/day or 1cc/hr
    ▪ Initiate pre or postoperatively in preterm hemodynamically stable patient to “prime” gut
      • Utilized to accelerate maturation of GI function (structure and functional integrity); accelerate tolerance to enteral nutrition; maintain intestinal barriers to infection; decrease risk associated with PN therapy
  o If adequate oral enteral feeds can’t be achieved, consider alternate methods such as:
    ▪ Nasogastric or orogastric tube feedings while awaiting developmental improvement in the coordination required for oral feeding
    ▪ Gastrostomy may be preferred in order to decrease caloric expenditure in chronically ill infants, such as those with CHD or BPD
    ▪ Consider early feeding team consult as indicated
      • Provide appropriate sized pacifier to encourage non-nutritive sucking in NPO preterm patient
  o Nutritional goals for enteral feeds are usually energy intake of at least 120 kcal/kg/day (see Nutrition Guideline); this can be achieved by providing:
    ▪ 150-160 ml/kg/day of premature formula (24 kcal/oz or 80 kcal/100ml)
    ▪ 160-180ml/kg/day of fortified human milk

**Developmental Delay:** (See Pediatric Neonatal Guidelines on Developmental Care)

**Overview:** Very premature children are more likely to exhibit poor growth compared with those born full term. A follow-up study of growth and BP in ELBW children determined that poor growth persists into school age. Compared with normative growth data of children who were born full term, children who were ELBW infants were lighter, shorter, and had a lower body mass index and smaller head circumference.

**Developmental Care Practices**
- Coordination of medical care (nursing assessments, procedures, therapies) done with consideration to sleep / wake cycles of the infant, and behavioral cues
- Implementation of supportive positioning in order to avoid acquired deformities
  - Allow infant to move in order to develop neuromuscular and skeletal systems
  - Repositioning required as often as every 3-4 hrs
- Handle infants using developmental principles that minimize the stress of the movement; combine flexion and containment with slow transfer movements
- Promote adequate environment when transitioning to oral feeds
- Teach parents proper techniques for positive tactile stimulation and encourage interventions like kangaroo care and massage as indicated

**Pain and sedation:**

**Overview:** Varying degrees of discomfort or pain may occur during a preterm infants’ hospitalization. In 2006, the American Academy of Pediatrics and the Canadian Pediatric Society (AAP/CPS) published new guidelines recommending that each healthcare facility that treats neonates establish a neonatal pain control program.
• Management strategies and Nursing Assessment Key Points:
  o Appropriate utilization of pain scales for pain assessment
  o PIPP Scale for Pre-term pain assessment
    ▪ Performed every 4 hours, before and hourly after interventions
    ▪ The PIPP is a seven-item, four-point scale (0, 1, 2, 3) for assessment of pain in premature and term infants
      • It includes behavioral, physiologic, and contextual indicators (gestational age and state of alertness)
      • A total score of 21 for infants of lesser gestational age and a total score of 18 for infants of greater gestational age at birth is possible
      • For all age groups
        o Score of 6 or less generally indicates minimal or no pain
        o Score >12 indicate moderate to severe pain
  o Reduction of painful events
    ▪ Consider the use of noninvasive therapeutic approaches for achieving analgesia in newborns
    ▪ "Clustered Care" approach should be utilized
      • Consider peripheral or umbilical arterial catheter, and/or Reduction in the number of procedures performed and episodes of patient handling without compromising care is most effective in reducing discomfort
      • Decrease the number of bedside disruptions by timing routine medical interventions with other care procedures
      • Anticipate blood study requirements to minimize the frequency of phlebotomy
        o Central venous line in patients requiring frequent blood draws or long-term intravenous (IV) access
        o Noninvasive monitoring such as transcutaneous monitoring (eg, oxygen saturation or bilirubin levels), or near infra-red spectroscopy (NIRS) as appropriate to avoid frequent phlebotomy

Analgesia for painful procedures
• Preemptive analgesia before and during elective painful procedures should be provided to all neonates; often includes a combination of non-pharmacologic and pharmacologic techniques
• A stepwise protocol for pain management interventions may be used to provide adequate care to neonates based on the intervention being performed; (World Health Organization Analgesic Ladder for Pain Management in Adults; The Italian Society of Neonatology guidelines)
  o Step 1 – non-pharmacologic measures
    ▪ Includes pacifier, oral sucrose, swaddling, kangaroo care, and sensorial saturation
    • Benefits include reduced crying, dampened physiological response, reduced facial expressions, and improved composite pain scores
- Indications: minor procedures
- Dosing: (Sucrose)
  - 24 to 26 weeks PMA – 0.1 ml
  - 27 to 31 weeks PMA – 0.25 ml
  - 32 to 36 weeks PMA – 0.5 ml
- Step 2 - topical anesthetics
  - Topical anesthetic cream (EMLA, LMX, etc.)
    - Indications include circumcision, venipuncture, peripheral IV (PIV) placements, lumbar puncture
    - Dosage
      - 0.5 g to max dose of 1 g applied to site and covered with occlusive dressing for 45-60min prior to procedure
      - 1 to 2 g in male infants for circumcision
    - Side Effects: mild skin irritation, methemoglobinemia (rare)
    - Other considerations:
      - Limited data available in the pre-term population < 37 weeks
      - Do not use on non-intact skin
      - Indicated in neonates ≥ 37 weeks gestational age for circumcision
      - Apply to the smallest area possible; do not leave on longer than recommended to limit potential of systemic absorption
- Lidocaine
  - Indications include venous or arterial punctures, PIV or central/arterial line placements, lumbar punctures, circumcision and local surgical analgesia
  - Dosage:
    - 0.5% (5mg/ml) or 1% (10mg/ml) solutions
    - Maximum dose of 3 to 5mg/kg
  - Side effects: tissue necrosis, arrhythmias (if in combination with epinephrine)
- Step 3 – systemic analgesia
  - Stepwise use based on procedure and response
    - Potency; non-opioids followed by opioid analgesics and sedatives
    - Routes of administration: oral/rectal followed by intravenous bolus, intravenous infusion, subcutaneous infiltrations, nerve blocks and deep sedation/general anesthesia
  - Acetaminophen for mild to moderate procedural and post-operative pain
    - Oral: 10 to 15mg/kg every 6-8 hrs
    - Rectal: 20 to 25mg/kg every 6-8 hrs
    - Intravenous: loading dose of 20 mg/kg followed by doses of 10mg/kg every 6 hrs
      - Recommended total daily doses are based on gestational and postnatal age:
        - 24 to 30 weeks gestation – 20 to 30 mg/kg/day
        - 31 to 36 weeks gestation – 35 to 50 mg/kg/day
- 37 to 42 weeks gestation – 50 to 60 mg/kg/day
- 1 to 3 months postnatal – 60 to 75 mg/kg/day

Nonsteroidal anti-inflammatory agents
- Contraindicated use in preterm infants; associated with GI bleeding, platelet dysfunction and decreased GFR
- Maternal use during pregnancy may lead to premature closure of the ductus arteriosus causing severe pulmonary hypertension

Morphine
- Indicated for continuous sedation of ventilated infants, following major surgery, and intermittently for pain control during invasive procedures
- Dosage:
  - Intramuscular (IM)/IV: initial dose of 0.05-0.1 mg/kg/dose every 4-6 hrs (some may need q 8hr dosing) to a max dose of 0.1 mg/kg/dose; titrate to effect
  - Continuous infusion: 0.01mg/kg/hr to be titrated to effect to a max recommended dose of 0.1mg/kg/hr (may need higher dosing in patients with drug tolerance)
- Side Effects: abdominal distension, constipation, gastroesophageal reflux disease (GERD), nausea, vomiting, pruritus, rash, hypotension, delayed feeding

Fentanyl
- Indications include prior to intubation, for postoperative pain or for patients with pulmonary hypertension
- As per American Academy of Pediatrics (AAP), not recommended for continuous use in the ventilated preterm neonates
- Dosage: intermittent, slow IV pushes of 0.5-3mcg/kg/dose
- Side effects: bradycardia, chest wall rigidity

Thermoregulation:
Overview: A relatively large body surface area in combination with an inability to produce enough heat, predispose preterm infants to hypothermia. Hypothermia may contribute to metabolic disorders such as hypoglycemia or acidosis. In extremely premature infants (less than 26 weeks per gestational age), hypothermia is associated with increased mortality and, in survivors, pulmonary insufficiency.

Hypothermia
- Defined as temperature <36.5°C (World Health Organization)
- Etiology in preterm infant:
  - Immature thermoregulation system; thermal instability
    - Inability to maintain core temperature by non-shivering thermogenesis
    - Minimal peripheral vasoconstriction ability
    - Higher temperature of extremities compared to central core temperature
    - Large surface area to body mass ratio
    - Very thin permeable skin, allowing greater loss of water and heat than seen in term neonates
- Very low percentage of body fat (specially brown adipose tissue), which leads to poor insulation
  - Symptoms:
    - Apnea, respiratory distress
    - Decreased cardiac output, bradycardia, hypotension
    - Poor oral feeding, feeding intolerance, hypoglycemia
    - Irritability, lethargy, weak cry
  - Complications
    - Metabolic acidosis
    - Coagulopathy
    - Death

### Hyperthermia

- **Etiology**
  - Hyper-metabolic state (sepsis, cardiac problems, and drug withdrawal)
  - Dehydration
  - Central nervous system (CNS) injury or malformation
  - Environmental
- **Symptoms**
  - Apnea, tachycardia, vasodilation
  - Hypernatremia from dehydration, poor oral feeding
  - Seizures, Irritability, lethargy, weak cry
- **Complications**
  - Hemodynamic instability
  - Seizures
  - Death

#### Management strategies and Nursing Assessment Key Points:

- Monitoring axillary temperatures
  - 36.5° to 37.5°C (97.7° to 99.5°F) for the term neonate
  - 36.3° to 36.9°C (97.3° to 98.6°F) for the preterm neonate
- Avoid rectal temperatures in < 34 weeks gestation (& < 2.2 kg) due to the risk of intestinal perforation
- Avoid use of tympanic thermometers; probes may be too large and may provide unreliable temperature
- If both central (abdominal/esophageal) and peripheral temperatures are monitored, the expected difference is ~ 0.5° to 1°; difference of 2° C or greater has been associated with cold stress resulting in peripheral vasoconstriction in infants beyond the first day of life
- Prevention and treatment strategies
  - Follow neutral thermal environment guidelines based on weight and gestational age
  - Environmental room temperature should be kept at 22° to 27° C (72° to 78° F), and humidity maintained at 30% to 60% in the isolette (per institutional guidelines)
  - Avoid heat loss through evaporation, convection, radiation and conduction
    - Dry the infant immediately and remove wet linen to minimize
evaporative heat loss

- Use warm blankets and pre-warm any surfaces that come in contact with the infant’s skin
- Avoid air drafts
- Skin-to-skin holding (kangaroo care)

○ Utilize barriers to heat loss
  - Polyethylene bags or wraps used in infants less than 29 weeks of gestation (in some institutions): should be wrapped from neck to feet as soon as possible, and remain wrapped until temperature is stable for at least 1 hr
  - Polyethylene or insulated caps can be used after drying the head (per institutional guidelines)
  - Cover open skin defects (gastroschisis, myelomingocele) with sterile saline-soaked gauze and a sterile waterproof barrier

○ Use of external heat sources
  - Chemical mattresses, or transwarmers to improve thermal control in VLBW infants; use with blankets to prevent skin burns
  - Pre-warmed transport incubator to transfer neonates to the nursery
  - Radiant warmer or pre-warmed incubator (isolette)
    - Radiant warmers
      - Allows for easier access to infant while still providing heat for temperature control
      - Servo control should be used
      - Increases insensible water and convective losses; close monitoring of intake/output, and weight required
    - Isolettes
      - Provide convective heat to warm infant
      - Consider to decrease radiant heat loss or gain from the walls (radiation)
      - Minimize heat loss through drafts (convection)
      - Some isolettes allow for the delivery of humidified air to aide with temperature regulation and fluid balance
    - Hybrid incubators function as both radiant warmers and incubators; eliminates need to move infant in case of emergency or procedures

○ Temperature stabilizing methods
  - Servo-control regulation allows the temperature inside incubator to be adjusted based on skin temperature (feedback loop)
    - Skin probe must be securely attached to patient, not over adipose tissue (brown fat areas)
    - Review alarms on a frequent basis and adjust based on patient’s needs to prevent overheating
    - Document the neonate’s temperature, the incubator set point, the skin temperature, and the air temperature as per unit’s guidelines
  - Manual/air control regulation:
    - Air temperature inside incubator used to control heater output
    - Reduces air temperature variability
• Document the neonate’s axillary temperature, the incubator set point, and the air temperature as per unit’s guidelines
• Goal of this mode is to provide the optimal neutral thermal environment

  o Humidity:
    ▪ Indicated for very low birth weight infants (23-30 weeks gestational age)
    ▪ Reduces evaporative heat loss that occurs with large body surface area, increased skin permeability and increased extracellular fluid
    ▪ Initiated at 70% or greater for the first 7 days of life, then gradually decrease to 50% until 28 days old or 30-32 weeks
  o Weaning from isolette to open crib
    ▪ Once medically stable and weight of 1600 g or more
      • Wean incubator temperature to 28°-29° C as a thermal challenge before transfer
      • Swaddling, caps and avoiding drafts to help maintain temperature
      • Return infant to incubator if unable to maintain temperature greater than or equal to 36.5° C, or unable to gain weight

**Hematology and Anticoagulation:**

**Overview:** Blood cell production and maintaining adequate levels of blood components are processes that undergo drastic changes in the first weeks of life. The normal process of adaption to extra uterine life is altered with prematurity. Other comorbidities are associated with prematurity, and have adverse effects on the hematologic system, further complicating the conditions of the neonate. Preterm neonates are at risk for inadequate production of blood cells, and/or blood loss.

**Blood Components**

• Hemoglobin
  o Major iron-containing component of the RBCs
  o Transition from production of fetal hemoglobin to adult hemoglobin begins at the end of fetal life, and is adversely affected by fetal grown restriction and prematurity
  o Values depend on gestational age, volume of placental transfusion and blood sample site
    ▪ Level at 28 weeks is ~14.5 and increases to ~ 15 at term
    ▪ Levels are higher in newborns and decrease by the end of the first week of life

• Hematocrit
  o Percentage of PRBCs in a unit volume of blood
  o Values depend on gestational age, volume of placental transfusion and blood sample site
  o Level at 28 weeks is ~45 and increases to ~ 47 at term
    ▪ May be altered by delayed cord clamping or hemorrhagic insult at birth

• RBCs
  o Responsible for oxygen transport via oxyhemoglobin, and carbon dioxide
transport via carboxyhemoglobin
- Life span is proportional to their gestational age; In term infants, ~ 60-70 days, and in preterm infants, ~ 35-50 days
- If they enter the circulation while they are still immature (or nucleated), it may be indicative of hemolysis, acute blood loss, hypoxemia, CHD or infection
- Level at 28 weeks is around ~ 4, and increases to ~4.4 at term

- **White blood cells (WBCs)**
  - Responsible for mounting an immunologic reaction to foreign proteins in the body
    - Subdivided into granulocytes (which include basophils, eosinophils and neutrophils), lymphocytes and monocytes
  - Benign eosinophilia of prematurity (which is inversely proportional to gestational age) may reflect immaturity of barrier mechanisms in the GI and/or respiratory tract
  - Physiologic stress can increase production of neutrophils and bone marrow release of immature forms
  - WBC count is proportional to gestational age, with total ~30-50% lower in premature infants than term infants

- **Platelets**
  - Responsible for hemostasis, coagulation and thrombus formation
  - Lifespan is ~ 7-10 days
  - Normal range is ~ 150,000 to 400,000/mm³ in the term infant
    - Premature infants have a lower platelet count with a broader range of normal (100,000 to 450,000)
    - Counts are 20% to 25% lower in infants who are small for gestational age
  - Neonatal platelets are hypoactive in the first few days of life which protects the infant against thrombosis, but makes him more susceptible to bleeding and coagulopathies

- **Blood volume**
  - Measured in ml/kg of body weight
  - Affected by gestational age, placental transfusion, twin-to-twin transfusion, placenta previa, nuchal cord or iatrogenic losses
  - Term infants have ~ 80-100 ml/kg, while premature infants have ~ 90-105 ml/kg

**Coagulation**
- Hemostasis is achieved by a combination of biochemical and physiologic events that stop the blood flow when injury occurs to a vessel and may be affected due to one or several factors in the neonatal period, including:
  - Transient diminished platelet function
  - Transient deficiency of clotting factors
  - Immaturity of hepatic enzymes
  - Transient deficiency of vitamin K and factor concentrations, (which are proportional to gestational age)
  - Assessment of platelet count, prothrombin time (PT), vitamin K, partial thromboplastin time (PTT) and/or fibrinogen may be indicated to diagnosis and treat coagulopathies
Anemia

- Low hemoglobin concentration and/or decreased number of RBCs, which in turn diminishes the oxygen-carrying capacity of the blood and the level of oxygen available to the tissues
- Etiology in pre-term and neonatal period, both etiologic and natural
- Hemolysis: Etiology – G6PD deficiency, hemoglobin disorders, infection, blood group compatibilities
  - Blood-group incompatibilities:
    - Rh incompatibility occurs when mother is Rh - and fetus is Rh +. The fetal blood cells enter maternal circulation leading to antibody production, which affect subsequent pregnancies.
    - Signs in the infant include:
      - Anemia, hypoxia
      - CHF; Hydroptic
      - Ascites, Hepatosplenomegaly, hyperbilirubinemia
      - Petechiae, hypoglycemia
      - Positive Coombs test
    - May be prevented by administering anti-D immune globulin to the mother at 28 weeks of gestation, within 72 hours after delivery, and after amniocentesis
    - ABO blood type incompatibility:
      - Fetal-maternal: can be spontaneous, due to traumatic amniocentesis, or external cephalic version
- Anemia of Prematurity
  - Considered physiologic, as it is characteristic of healthy infants (fall of hemoglobin concentration in the first 2-3 months of life)
  - Associated factors include
    - Rate of decline and nadir are inversely related to gestational age
    - Improved extra-uterine oxygen delivery causes a temporarily inactive stage of erythropoiesis
    - Erythropoietin production is diminished in response to anemia
    - Growth causes dilution anemia, as there is a decreased hemoglobin concentration with expanding blood volume
    - Interaction of the intracellular abnormality and extracellular factors such as drugs and infection, leading to hemolysis and shortened erythrocyte life
- Iatrogenic Postnatal Phlebotomy:
  - Excessive blood removed for diagnostic studies
  - Removal of greater than 20% of the blood volume over 24 to 48 hours can produce anemia
- Clinical presentation and symptoms depend on volume of blood loss and the time period over which it is lost
  - Acute blood loss
    - Initial pallor, followed by cyanosis and desaturation
    - Shallow, rapid and irregular breathing
    - Hemodynamic instability, Tachycardia
• Rapid drop in hemoglobin
  o Chronic blood loss
    ▪ Pallor without signs of acute distress
    ▪ Possible signs of congestive heart failure with hepatomegaly
    ▪ Normal arterial blood pressure with normal or elevated venous pressure
    ▪ Low hemoglobin concentration
• Tests to determine etiology of the anemia may include:
  o Hemoglobin concentration
  o Reticulocyte count
  o Peripheral blood smear
  o Coombs’ test: positive results indicate presence of maternal IgG antibodies on the surface of the baby’s RBCs
  o Kleihauer-Betke test: identifies fetal hemoglobin in maternal blood

**Hemorrhagic Disease of the Newborn (HDN)**
• Hemorrhagic tendency caused by vitamin K deficiency and decreased activity of factors II, VII, IX, and X
• Types
  o Early: presents within 24 hrs in neonates born to women taking certain anticonvulsants, anti-tubercular medications and vitamin K antagonist such as warfarin
  o Classic: often presents at 2-6 days of life
  o Late onset: usually presents at 2-12 weeks of life in infants not receiving vitamin K at birth or receiving inadequate oral dose and breastfeeding
• Clinical findings
  o Bleeding (may be localized or diffuse, and seldom life threatening)
  o Diffuse ecchymosis and petechiae
  o Abdominal distention
  o Jaundice
• Diagnostic studies
  o If bleeding responsive to vitamin K administration, diagnosis established
  o PT/PTT are prolonged
  o Levels of vitamin K dependent clotting factors are low
• Complications
  o Anemia
  o Intraventricular/intracranial hemorrhage
• Treatment
  o Prophylactic vitamin K at time of delivery (1mg IM for term babies and 0.5mg for premature infants)
  o Vitamin K supplemented formula
  o Blood or blood product transfusion if severe

**Disseminated Intravascular Coagulation (DIC)**
• Acquired hemorrhagic disorder associated with an underlying disease, manifested as uncontrolled activation of coagulation and fibrinolysis
  o Consumption of clotting factors is thought to be initiated by release of
thromboplastic material from damaged or diseased tissue into the circulation
- Neonates are at increased risk of DIC because of inherent imbalances between fibrinolytic, anticoagulant, and pro-coagulant factors, particularly decreased levels of antithrombin and protein C

- **Etiology**
  - Maternal: preeclampsia, eclampsia, placental abruption or placental abnormalities
  - Intrapartum: fetal distress with hypoxia, dead twin fetus and traumatic delivery
  - Neonatal: infection, hypoxia, acidosis, shock, severe Rh incompatibility, thrombocytopenia, tissue injury (birth trauma, NEC)

- **Clinical findings**
  - Hemorrhage is predominant symptom
  - Organ and tissue ischemia, often caused by microvascular thrombosis
  - Anemia, both from blood loss and RBC fragmentation
  - Prolonged oozing from puncture sites, petechiae, purpura and ecchymoses

- **Diagnostic studies**
  - Complete blood count (CBC) – low platelet count
  - PT/PTT may be within normal limits initially, but significantly prolonged as the condition worsens
  - Peripheral blood smear with abnormal blood cells
  - Low fibrinogen levels
  - Positive D-dimer

- **Complications**
  - Microvascular thrombosis
  - Organ failure
  - Intraventricular and parenchymal hemorrhage

- **Treatment**
  - Aggressive treatment of the underlying disease
  - Supportive care
    - Transfusion of blood and volume as needed
    - Replacement of clotting factors (FFP, Cryo, platelets, fibrinogen)

**Thrombocytopenia**
- Acquired disease in which there is a significant decrease in the platelet count (<150,000/mm3) of the term or premature infant
- Thrombocytopenia occurs in 1% to 2% of healthy term neonates and in up to 35% of critically ill neonates

- **Etiology**
  - Platelet destruction from maternal autoantibodies
  - Neonatal alloimmune thrombocytopenia
  - Infection, either neonatal or congenitally acquired
  - Coagulopathies
  - Impaired platelet production, usually associated with congenital malformations

- **Clinical findings**
  - Petechiae, purpura, epistaxis
  - Cephalohematoma
  - Increased bruising
• Bleeding
• Jaundice

• Diagnostic studies
  o Low platelet count
  o Increased immature platelets in the peripheral blood smear
  o PT/PTT will be normal for age
  o Prolonged bleeding time

• Complications
  o Cranial hemorrhage with neurologic sequelae
  o Entrapped hemorrhage
  o Anemia
  o Hyperbilirubinemia

• Treatment
  o Supportive care and treatment of underlying disease
  o Platelet transfusion (recommended goal of platelet level >30000/mm3)
  o Steroids

Anticoagulation Therapy
• Anticoagulant therapy in the newborn generally consists of administration of standard heparin or low-molecular-weight heparin (LMWH)
  o Unfractionated heparin
    ▪ Advantages: rapid reversibility and low cost
    ▪ Disadvantages: unpredictable pharmacological response, frequent monitoring needed (frequent lab draws of large blood volumes for preterm babies)
    ▪ Dose:
      • Based on small studies (not done on preterm newborns)
      • IV loading dose usually of 75-100 units(U)/kg followed by initial maintenance dose of 28 U/kg/hr
      • In extremely low birth weight and pre-term neonates, loading dose is often not done because of high risk of bleeding
      • Administered as a continuous infusion via a dedicated line to avoid unintended boluses when flushing the catheter
    ▪ Monitoring:
      • Dosing should be titrated to BOTH activated partial thromboplatin time (aPTT) and anti-factor Xa activity since neonates have an increased clearance rate of heparin and physiologic plasma concentration may be low
      • Anti-factor Xa level should usually be between 0.35-0.7units/ml
      • aPTT should usually be 1.5-2 times the upper limit of normal
    ▪ Adverse Effects:
      • Bleeding
        o STOP heparin infusion
        o Administer Protamine Sulfate (1mg of Protamine per 100 units of Heparin administered within the last 1-2 hrs)
• Heparin induced thrombocytopenia (HIT): rare, but should be considered on any newborn receiving heparin that has a sudden precipitous drop in platelet count
  ▪ Osteoporosis
  o Low molecular weight heparin (LMWH)
    ▪ Advantages: greater bioavailability, longer duration of anticoagulant effect, more predictable response and requires minimal laboratory monitoring and dose adjustment
    ▪ Disadvantages: frequent injections, cost
    ▪ Dose:
      • Has been studied on the neonatal population born after 36 weeks gestational age (limited data on preterm infants)
      • For prophylaxis: initiate at 0.75 mg/kg per dose twice each day
        o Target concentration of anti-factor Xa for prophylaxis is 0.1 to 0.3 U/mL, which is lower than the target range for treatment
      • For treatment: initiate at a dose of 1.7 mg/kg per dose subcutaneously twice each day in term infants and 2.0 mg/kg per dose twice each day in preterm neonates; doses adjusted to maintain an anti-factor Xa of 0.5 to 1 units/ml
    ▪ Monitoring:
      • Dosing should be titrated to BOTH activated partial thromboplastin time (aPTT) and anti-factor Xa activity since neonates have an increased clearance rate of heparin and physiologic plasma concentration may be low
      • Anti-factor Xa level should be between 0.35-0.7 units/ml
      • aPTT should be 1.5-2 times the upper limit of normal
    ▪ Adverse Effects:
      • Bleeding
        o Discontinue medication
        o Administer Protamine Sulfate (1mg of protamine per 100 units of LMWH administered within four hours given via slow IV push)
      • Complications at site of repeated injections
  o Thrombolytic therapy
    ▪ Guidelines suggest NOT using thrombolytic therapy for neonatal thrombosis unless the thrombus occludes a major vessel causing critical compromise of organs or limbs
    ▪ Contraindications:
      • Major surgery or hemorrhage within the previous 10 days
      • Neurosurgery within three weeks
      • Severe asphyxial event within 7 days
      • Invasive procedure within the previous three days
      • Seizures within 48 hours
      • Prematurity < 32 weeks gestation
- Systemic septicemia
- Active bleeding, or the inability to maintain platelets >100,000/μL or fibrinogen > 1 g/dl
  - No clinical trials have evaluated thrombolytic agents in newborns
  - Recombinant tissue-type plasminogen activator (tPA) is thrombolytic agent of choice
    - Dose in neonates extrapolated from doses in older children and adults; for systemic therapy, tPA is given in a continuous infusion at a rate of 0.1 to 0.6 mg/kg per hour for six hours, without a loading dose
    - Adverse Effects:
      - Local non-severe bleeding
      - Re-thrombosis
      - Severe bleeding, including intraventricular hemorrhage, other severe bleeding, and death due to hemorrhage
        - Treatment of bleeding after use of tPA includes STOPPING tPA infusion, use of cryoprecipitate, and administration of platelets if needed

Management strategies and Nursing Assessment Key Points
- Monitor routine CBC with differential, coagulation factors as indicated
- Cluster blood draws if possible, reduce blood waste and send the minimum amount of blood needed to reduce iatrogenic blood loss
- Avoid drawing anticoagulation levels from any heparinized access to ensure accuracy of result
- Monitor for complications related to hematological abnormalities
- Transfuse blood products as slowly as hemodynamically tolerated to avoid blood pressure swings

References:


