Objectives

Upon completion of this course, the learner will be able to:

- Describe the nursing interventions to reduce the incidence of intraventricular hemorrhage in the preterm infant
- Use evidence based practice to influence care of the infant at risk for intraventricular hemorrhage
- Identify developmental and physiological differences between the term and premature infant

Neurodevelopment

- Brain development is activity-dependent
  - experiences and stimuli "shape" the way the connections are made.
  - different beginnings foster different end points
  - Interventions can increase cell maturation, such as environmental enrichment
Anatomy!!

- Ventricles
- Intraventricular Foramen
- Cerebral aqueduct
- Choroid plexus
- Germinal matrix

Introductory sentence Arial – 21pt font

Germinal Matrix

- Highly vascularized and poorly supported
- Involutates over time
  - 23-24 weeks 2.5 mm width
  - 32 weeks 1.4 mm width
  - 36 weeks involute
Periventricular-Intraventricular Hemorrhage (IVH)

- Occurs once germinal matrix hemorrhage extends into the lateral ventricle
- Risk factors: prematurity (less than 34 weeks), respiratory failure, increasing arterial blood pressure, perinatal asphyxia
- Incidence:
  - 10 to 15% of infants with hemorrhages
  - 30 to 40% of preterm infants <30 weeks or <1500 grams
  - Higher risk if <28 weeks
  - 2 to 3% of term infants

---

So why are preemies at high risk?

This is what we are working with...
Pathogenesis

Thought to be caused by capillary bleeding.
• Major factors:
  • Intra-vascular factors
    – Loss of cerebral autoregulation
    – Abrupt alterations in cerebral blood flow and pressure
  • Vascular factors
    – Germinal matrix-vulnerable to hypoxia
    – Reperfusion injury
  • Extravascular factors
    – Poor vascular support in cerebral tissue

IVH Risk Factors

Abrupt changes in cerebral circulation
• Rapid changes in PaCO2
• Rapid changes in aortic pressure
• Rapid infusion of volume expander
• Excessive increase in vasopressor infusion
• Noxious procedures
  – suctioning, PIV insertion, CT insertion, loud noises, aggressive handling
• Large PDA with left-to-right shunt
• Elevated venous pressure from tension pneumothorax or excessive ventilator pressures

IVH Timing and Progression

• May begin in utero, but usually begins after birth
• Hemorrhages may be small at first, then progress to larger hemorrhages later
• Most large or progressive IVH’s begin in the first week of life
  • Why is this important to the bedside nurse?
Symptoms of IVH
• Majority are asymptomatic
  • Dx is cranial ultrasound
    – 4th day 90% detected
    – Serial ultrasounds
• Symptomatic (common)
  • Changes in LOC, movement, tone, respirations, and eye movement
• Symptomatic (uncommon) catastrophic deterioration
  • Stupor, coma, decerebrate posturing, generalized tonic seizures, quadraparesis

IVH
• Diagnostic:
  • Cranial ultrasound (serial) – Papile Classification (1988):
    – Grade I: Subependymal hemorrhage in the periventricular germinal matrix.
    – Grade II: Partial filling of the lateral ventricles without ventricular dilation.
    – Grade III: Intraventricular hemorrhage with dilation
    – Grade IV: Intraventricular hemorrhage with parenchymal involvement or extension of blood into the cerebral tissue
  • LP to rule out septic shock or meningitis

Grade I IVH

http://www.slideshare.net/PediatricHomeService/brain-injury-in-preterm-infants
Grade II IVH

Grade II IVH

Grade III IVH
IVH Outcomes

• Small (Grade I)
  • Neurodevelopmental disability similar to premature infants without IVH
• Moderate (Grade II-III)
  • Neurodevelopmental disability in 40%
  • Mortality 10%
  • Progressive hydrocephalus in 20%
• Severe (Grade PVHI)
  • Major neurodevelopmental disability in 80%
  • Mortality rate 50-60%
  • Hydrocephalus common in survivors

Periventricular Leukomalacia (PVL)

• Ischemic, necrotic periventricular white matter lesions of arterial origin
• Risk factors: systemic hypotension, recurrent apnea with bradycardia
• Pathophysiology
• Incidence
PVL

• Clinical presentation:
  • Acute phase: hypotension and lethargy
  • 6 to 10 weeks later:
    – Irritable
    – Hypertonic
    – Increased arm flexion and leg extension
    – Frequent tremors
    – Abnormal Moro reflex

PVL

• Diagnostic:
  • Cranial ultrasound
  • CT
  • MRI
  • Initial presentation: PV echodensities
  • Later: PV cystic changes

Periventricular Leukomalacia
Periventricular Leukomalacia (PVL)

Outcome:
- Based on location and extent of the injury
- Major motor deficits
- Significant upper arm involvement is associated with intellectual deficits
- Visual impairment
- Lower limb weakness
PVL Outcome

Post Hemorrhagic Hydrocephalus
- Frequent complication of GM-IVH
- Clot obstructing CSF flow at the level of the aqueduct of Sylvius

Hydrocephalus
Hydrocephalus

- Clinical presentation:
  - Rapid increase in head size
  - Episodic apnea and bradycardia
  - Lethargy
  - Increased ICP
  - Tense, bulging anterior fontanel
  - Separated cranial sutures
  - Ocular movement abnormalities

Post Hemorrhage Ventricle Device
External Ventricle Drain/Reservoir/Shunt/

- EVD
- Ommaya reservoir
- Ventriculoperitoneal (VP) shunt

Patient Care and Management

- Prevent preterm birth
- Promote in utero transport
- Promote a no stressful intrapartum course
- Provide efficient resuscitation with expedient intubation
- Cluster care activities and promote appropriate handling
- Minimize noxious stimuli
- Avoid events associated with wide swings in arterial and venous pressures (i.e.: seizures, apnea, etc.):
- Prevent blood pressure swings – slow volume replacement
Patient Care and Management

- Avoid over ventilation leading to pneumothorax
- Use inline suctioning devices
- Use noninvasive monitoring devices
- Monitor and maintain normal pH
- Correct abnormal clotting
- Be alert to signs of hemorrhage (changes in LOC, etc.)

Educate and support the parents

Neuroprotection in the NICU

- IVH Bundles
- Antenatal steroids and Magnesium Sulfate
- Delayed Cord Clamping
- The “Golden” Hour / CPQCC Delivery Room Toolkit
- Neutral head positioning
- NIDCAP
- Developmental care
Potentially Better Practices to Prevent Brain Injury

1. Antenatal steroids & magnesium
2. Optimize management and delivery at center with a NICU
3. Early management by a Neonatologist/NNP
4. Minimize pain and stress
   1. Avoid pain and stress
   2. Developmental Care
5. Optimal positioning (midline)
6. Treat hypotension
7. Judicious indomethacin use
8. Optimize respiratory management
9. Limit sodium bicarbonate use
10. Use post-natal dexamethasone judiciously

The “Golden” Hour (Delivery Room Toolkit)

• Based on principles from cardiovascular and emergency medicine
• First hour of life is a time of critical transition and adaptation
• Management has been show to impact long term outcomes
• Structured focus on thermoregulation, minimizing energy consumption, and respiratory support
• Measurable data points include: time to admission, admission temperature, admission glucose, initiation of IV fluids with glucose and amino acids
• What does your “Golden” hour look like?
The Patent Ductus Arteriosus (PDA) and the Preterm Baby

Tanya Kamba, RNC-NIC, MSN
Neonatal Outreach Educator

Normal Cardiovascular Function: Review

Fetal Circulation

- Gas exchange is liquid to liquid
- Organ of respiration is placenta
- High flow, low resistance
- Fetal lungs
  - Low flow, high resistance
- PA’s constricted
- High right heart and lung pressures
- Low left heart pressures
- Open fetal shunts
The ductus arteriosus serves to divert blood away from the fluid-filled lungs toward the descending aorta and placenta.

In the Preterm Neonate...

A PDA is normal on DOL 3 and may remain open through the first week of life in 50% of preterm infants.
In the Preterm Neonate…

• The presence of a hemodynamically significant PDA with a large left-to-right shunt is a common cause of morbidity in the extremely premature neonate

Incidence of PDA by Postnatal Age

<table>
<thead>
<tr>
<th>Gest (wk)</th>
<th>0-24 hr</th>
<th>24-48 hr</th>
<th>48-72 hr</th>
<th>72-96 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;40</td>
<td>55</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>38-40</td>
<td>85</td>
<td>50</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>34-37</td>
<td>96</td>
<td>42</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>30-33</td>
<td>87</td>
<td>87</td>
<td>31</td>
<td>56</td>
</tr>
<tr>
<td>&lt;29</td>
<td>80</td>
<td>88</td>
<td>40</td>
<td>84</td>
</tr>
</tbody>
</table>

A Hemodynamically Significant PDA May Increase the Risk of…

• Intraventricular hemorrhage
• Pulmonary edema/hemorrhage
• Necrotizing enterocolitis
• BPD/ventilator dependence
• Retinopathy of prematurity
• Surgical intervention
• Death
Pathophysiology of a PDA…

- Term infants-
  - Left ventricular distension may produce a higher ventricular end-diastolic pressure at smaller ventricular volumes
- Preterm infants
  - Ventricles are less distensible than term and generate less force per gram of myocardium
  - The relative lack of ventricular distensibility is more a function of the tissue rather than poor muscle function

Redistribution of Systemic Blood Flow

Even with a small PDA blood is shunted away from the:
- Skin
- Bone
- Muscle
- GI tract
- Kidneys

Shunting May Cause…

- Decreased perfusion
  - Due to a drop in diastolic pressures
  - Decreased blood flow to organs
  - Localized vasoconstriction… why?
  - Organs may experience significant hypoperfusion before there are any signs of left ventricular compromise
PDA Presentation

- Usually asymptomatic when ductus is small
-Bounding pulses
- Palmar pulses
- Active precordium
- Wide swings in oxygen saturation
- Murmur
- Widening pulse pressure (>20mm Hg)
- Low diastolic pressure

PDA Presentation

- ↑ Vascular markings on CXR
- ↑ Heart size is a late sign
- Apnea or worsening respiratory status
- Prolonged capillary fill time from ↓ systemic output
Diagnostics for Diagnosis of PDA

- Chest x-ray
- Echocardiogram
- BNP

Laboratory Findings with PDA

- B-Type Natriuretic Peptide (BNP) is released from the heart in response to increased wall tension.
- Can be useful to help evaluate the left to right shunting through the ductus.
- Normal Value
  - Normal <25
  - >100 indicates significant left to right shunt

PDA: Treatment Modalities

- Conservative measures are employed initially:
  - Fluid Restriction
  - Diuretics (lasix)
  - Positive end-expiratory pressure: useful in reducing left-to-right shunt via PDA
Fluid restriction

- Restricted fluid administration reduces the risk of PDA and NEC and demonstrates trends towards reducing the risk of BPD, IVH, and death (Cochrane Database, 2010)
- Total fluids on admission will be 80mL/kg/day
  - Slow increases
  - Be cautious of flushes
  - Document, document, document

PDA Treatment Modalities

- Pharmacologic
  - Indomethacin (Indocin)
  - Neoprofin (Ibuprofen)
  - Acetaminophen (Paracetamol)

Indomethacin IV Administration

**Special Considerations:**
Rapid infusions of intravenous indomethacin have been associated with significant reductions in cerebral blood flow.
UCSF Indomethacin Therapy:
Intravenous Administration

- Administer by syringe infusion pump over 30 minutes
- Flush what is left in the tubing with 1 ml NS over 30 minutes
- Administer into dedicated peripheral IV

Indomethacin Therapy

- **Notify provider for...**
  - Creatinine > 2 mg/dL
  - UO < 1 mL/kg/hr
  - Abdominal distension
  - Platelets < 100k
  - Bilious gastric residual
  - Hemoccult positive stool

Contraindications to Indomethacin

- Suspected CHD
- Known GI or renal anomaly
- Poor renal function
- Bleeding disorders or thrombocytopenia
- Necrotizing enterocolitis
- Sepsis
Ibuprofen Side Effects

- Inhibits platelet aggregation, so signs of bleeding should be monitored.
- Ibuprofen solution may be irritating to the tissue; therefore, it should be administered carefully to avoid IV extravasation.
- Ibuprofen is known to displace bilirubin from albumin binding sites and should be used with caution in patients with an elevated total bilirubin.

Ibuprofen Contraindications

- Proven or suspected infection that is untreated.
- Congenital heart disease.
- Active bleeding, especially ICH or GI.
- Thrombocytopenia, coagulation defects.
- Suspected NEC.
- Significant impairment of renal function.

Ibuprofen – Adverse events

- Bleeding.
- Skin lesion/irritation.
- Hypoglycemia.
- Hypocalcemia.
- Adrenal insufficiency.
- Respiratory failure.
- IVH and renal insufficiency have also been reported.
Acetaminophen Therapy

- NSAIDs come with many risks
- Acetaminophen is an alternative for hemodynamically significant PDA
- IV or Oral
- No need to stop feeds

Early Treatment Versus Delayed Conservative Treatment of the Patent Ductus Arteriosus (PDA:TOLERATE)

- Goal of the trial is to compare 2 treatment approaches
  - Early treatment
  - Conservative approach
- Hypothesis is the treatment of a moderate PDA will decrease need for respiratory support, diuretics, gavage feeding, ligation, and further intervention

https://clinicaltrials.gov/ct2/show/NCT01958320
Alphabet Soup of Preemie Problems: RDS & BPD

NICU Respiratory History

• **1940's and 50's** Oxygen and more oxygen
• **1963** Patrick Bouvier Kennedy died of RDS at 34 weeks/2100 gms
• **1971** George Gregory uses CPAP for RDS
• **1980's** Jet ventilators used for neonates
• **1990** FDA approval for surfactant use
• **1990's -2000's** the more pressure the better
• **Today** back to CPAP and gentle ventilation

Old School...

• Intubation based on size, gestational age
• High pressures, high O2
• Chest physiotherapy ATC
• Suction whether you need it or not
• “Babies do not feel pain.”
Changes in Respiratory Management of the Preterm Neonate

- Antenatal steroids
- Surfactant replacement therapy
- Permissive hypercapnia
- Gentler ventilatory modes (HFOV, PC, PS)
- Inhaled nitric oxide
- Non-invasive ventilation: NCPAP/SiPAP, HFNC, RAM
- Judicious use of oxygen
- Improved survival of preterm babies

Lung Development

Respiratory Vulnerabilities

- Newborn susceptible to respiratory distress due to limits on respiratory system:
  - Ribcage not well ossified
  - Respiratory muscles have low endurance and strength
  - Floppy chest wall offers little resistance to collapse
  - Obligate nose breathers
  - Tongue large, trachea and glottis small
Respiratory Vulnerabilities

• Close proximity of trachea to bronchi -> rapid transmission of infection
• Immature mucosal lining -> less protection against infection
• Large dead space -> need to breathe twice as fast as adult to oxygenate

Respiratory Vulnerabilities

• Higher metabolic rate at rest: increased $O_2$ consumption compared to adult
• Operate close to maximum capacity normally
• Little compensatory reserve for increased demands

Respiratory Distress Syndrome

• Most common cause of respiratory distress in premature infants
  • Incidence: inversely proportional to GA
  • Most babies <29 wks have RDS
• Small proportion of term infants develop RDS
• Damage to Type II cells and/or enzyme pathways
• IDM’s, C-sections, asphyxia
### Risk Factors for Developing Respiratory Distress Syndrome

<table>
<thead>
<tr>
<th>Increased risk</th>
<th>Decreased risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Premature Birth</td>
<td>• Chronic intrauterine stress</td>
</tr>
<tr>
<td>• Sex</td>
<td>• PPROM</td>
</tr>
<tr>
<td>• Infant of a Diabetic Mother</td>
<td>• Maternal HTN</td>
</tr>
<tr>
<td>• Asphyxia</td>
<td>• IUGR/SGA</td>
</tr>
<tr>
<td>• C-section without labor</td>
<td>• Antenatal steroids</td>
</tr>
<tr>
<td>• Caucasian race</td>
<td>• Mat. drug use</td>
</tr>
<tr>
<td>• Chorioamnionitis</td>
<td>• Tocolytic agents</td>
</tr>
<tr>
<td>• Hydrops</td>
<td></td>
</tr>
</tbody>
</table>

### RDS Pathophysiology

- **Insufficient volume of surfactant**
  - Unstable alveoli collapse
  - Normal Functional Residual Capacity not established
  - Each breath requires increased energy output

### RDS Prevention

- **Antenatal steroids (Betamethasone 48 hrs PTD)**
  - Accelerate lung maturation
  - Single course for women between 24 and 34 wks gestation at risk for preterm delivery
  - Reduces incidence of RDS by 50% in infants < 31 wks
  - Decreases neonatal mortality by 30%
  - Decreases incidence of IVH and NEC
  - No adverse consequences identified at this dose
  - Ongoing trials evaluating use of repeated doses in undelivered moms at continued high risk
It’s All About Protection

- What we do during those first minutes, to hours can affect outcomes
- All systems immature and vulnerable

The Golden Hour

- Definition
  - Taken from shock trauma medicine indicating the critical first hour as the most important for improving survival
  - For the extremely preterm neonate, initial steps undertaken to optimize coordination and execution of care with the goal of minimizing injury and improving outcomes
  - GOAL: resuscitation without injury!

RDS Treatment Strategies

- Initial DR stabilization - California Perinatal Quality Care Collaborative (CPQCC) guidelines
- Surfactant replacement
- Support ventilation (lung protection is goal)
  - Non-invasive ventilation
  - Gentler mechanical ventilation
- Fluids, electrolytes, glucose, calories, normothermia
- Prevent complications
  - Infection
  - BPD/CLD
- Inhaled nitric oxide
Oxygen therapy

• Most commonly used drug in neonatal care
• No concentration is “safe”
• Use blender, analyzers
• Continuous monitoring (HR, sats)
• Humidify, warm
• Maintain stable delivery, concentration
• Wean slowly with continuous monitoring
• \(O_2\) saturation: target ranges
  • Under 1000gms: 85%-92% (\(PaO_2\) 45-60 torr)**
  • Beyond 36wks: 90-95%

Desaturation Episodes: Critical Points

• Fewer desaturations with proper positioning
  • Abdomen
  • Developmental positioning, nesting
• Minimal handling during desaturation episode
  • Assess need for sedation
• Be patient, most will recover with no intervention
• \(O_2\) titrations used as last resort for desaturation episodes
  • Set tight sat alarms on monitor
  • Document episodes, interventions, infant’s response

Bronchopulmonary Dysplasia (BPD)
BPD

BPD Incidence

- Inversely proportional to gestational age
- Of survivors corrected to 36 weeks
  - 85% of babies born at 22 weeks had an O2 requirement
  - 22% of babies born at 28 weeks had an O2 requirement

(Stoll et al., 2010)

BPD

- Chronic lung disease
- Inversely proportional to gestational age
- Develops after acute pulmonary disease
- Chronic, constant recurrent lung injury
  Lung injury and repair occur simultaneously with organ growth and development
- Prolongs need for O2, mechanical ventilation
Factors that Contribute to BPD

- Nutritional Problems
- Genetics
- Hyperoxic Injury
- Inflammation
- Nutritional Problems
- Genetics
- Fetal Programming
- Other
- Increased Pulmonary Arterial Muscularization
- Sex-specific Differences
- Inflammation
- Barotrauma
- Alterations in Microbiome

BPD: Multifactoral

- Lung immaturity: prematurity
- Lung injury/inflammation
  - Barotrauma/volutrauma
  - $O_2$ toxicity: high or low levels, short or long term
  - Occurs in ventilated infants without $O_2$
- Infection
  - Chorioamnionitis
  - Inflammatory cytokines present in high levels in amniotic fluid of babies who develop BPD

BPD Treatment

- Lung protection
  - Extubate to nasal CPAP or SiPAP with low $FiO_2$ to minimize toxicity to lung
  - No air leak (PIE or pneumo)
  - Best ventilation strategy yet to be determined
  - Sats of 88% to 92% will provide adequate tissue oxygenation, help avoid complications of BPD
  - Better weight gain
  - Prevent development of pulmonary hypertension, right-sided heart failure
  - Avoid hyperoxia: ROP
Retinopathy Of Prematurity

•When babies are born premature, the blood vessels on the retina are not fully developed

•After birth, the vessels may begin to grow very quickly

•This rapid growth can damage the retina

Road to ROP

Definition to ROP

•Improper growth of the blood vessels on the retina and the damage caused by the growth

•One of leading causes of childhood blindness
Incidence

• ROP is rare in infants > 32 weeks GA and heavier than 1500 grams
• Approximately 50% of infants with a birth weight between 1000 and 1250 grams will have some degree of ROP
• 90% of infants < 750 grams and/or born < 28 weeks GA develop ROP

The Road to ROP

• The preterm infant is in a hypoxic environment in utero (Pa02 25 to 35 mmHg)
• The physiologic hypoxia stimulates the expression of vascular endothelial growth factor (VEGF)

The Road to ROP

• In infants born prematurely, the relative increase in oxygen extra utero (hyperoxia) inhibits VEGF, causing vasoconstriction of fragile, immature retinal vessels which progress to vaso-obliteration
• The retina responds by creating LOTS of vessels (vaso-proliferation).
The Road to ROP

• If the new vessels proceed to develop abnormally the capillaries may extend into the vitreous body and/or over the surface of the retina.

• Leakage of fluid or hemorrhage from the abnormal vessels may occur.

The Road to ROP

• Traction may pull the macula out of normal position affecting visual acuity.

• Retinal detachment may occur, resulting in blindness
The Road to ROP

- Zone refers to the location (I, II, III) - how far developing retinal vessels have progressed

ZONES

Stages of ROP

- **Stage 1**: Mildly abnormal growth of retinal vessels. Usually gets better without any treatment and has no long-term effects
Stages of ROP

**Stage 2:** Growth of retinal vessels is moderately abnormal. Usually gets better without any treatment and has no long-term effects.

**Stage 3:** Ridge with fibrovascular proliferation. Growth of retinal vessels is severely abnormal. Infants with Stage 3 may require treatment and have a higher risk for long-term problems.

**Stage 4:** Partial retinal detachment. Usually requires treatment and may lead to long-term vision problems or blindness.

**Stage 5:** Complete retinal detachment. Requires treatment and may lead to long-term vision problems and blindness.
Stages of ROP

• **Plus Disease** – Sign of ROP advancing quickly.
  Usually requires treatment
• Plus disease frequently leads to vessel contraction and scar formation, which in turn, leads to macular displacement.
• Rush disease: Aggressive form of ROP. Develops between 3-5 weeks after delivery, may progress rapidly.

Prevention

• Treat Oxygen like a drug
• Monitor PaO2 on ABGs – keep 50 to 70 mmHg
• Even if the infant requires only room air, the PaO2 can rise to 60 to 100 mmHg
• Set high alarm limits on pulse oximeter
• If the infant is on supplemental oxygen, keep saturations 85 to 92%
• SpO2 values > 93% are associated with PaO2 values of > 80 mmHg
Prevention

• Protect the eyes
  • Premature infants eyelids are paper thin and do not sufficiently block light.

  Cover eyes whenever possible, especially when under exam lights

The Road to ROP

• Surveillance
• Cryosurgery (rarely done)
• Laser Surgery
• Intravitreal administration of Anti-vascular endothelial growth factor agents (Avastin)
• Retinal Buckling for complete detachment

Follow up Exams for ROP

• Immature Retinal Vasculature
  • Every 2-3 weeks

  • If ROP present:
    • Exam every 1-2 weeks
    • More often depending on severity of disease
The Road to ROP

• Eye exams and mydriatic eyedrops can produce:
  – hypertension
  – reflex bradycardia
  – apnea

Complications of ROP

• Varying degrees of visual impairment may require corrective lenses or surgery.
  • Strabismus (Crossed-eyed)
  • Nystagmus (Rapid involuntary motion of the eyeball)
  • Glaucoma (Abnormal high fluid pressure in the eye)
  • Cataracts (Opacity of the lens)
  • Amblyopia (“Lazy eye” Dimness of sight – Visual transmission not recognized properly)
  • Macular ectopia (displacement of ocular muscles)
  • Myopia (nearsightedness)

Alphabet soup of preemie problems…

MBM & NEC

Tanya Kamka, MSN, RNC-NIC
Neonatal Outreach Educator
Samantha Wynn, RN, BSN, Cynthia Jensen, MS
How long are the small intestines?

Gastrointestinal Development

Neonatal phase

- Exposure to enteral nutrition leads to rapid differentiation and development
- Development of GIT mucosal immunity due to dietary antigens (or lack of)
- Mucosal immune system begins to distinguish between safe nutrients and foreign pathogens
- What are we putting into our babies??

When Good Guts Go Bad...

Necrotizing Enterocolitis
What is NEC?

**Definition**: an acquired disease that affects the GI system, particularly that of premature infants. It is characterized by inflammation of the bowel wall followed by areas of necrosis, most commonly in the terminal ileum and proximal colon, but may affect any or all of the small and large intestines.

Incidence

- BW 501 to 750 g – 12 percent risk, 42 percent mortality with NEC
- BW 751 to 1000 g – 9 percent risk, 29 percent mortality with NEC
- BW 1001 to 1250 g – 6 percent risk, 21 percent mortality with NEC
- BW 1251 to 1500 g – 3 percent risk, 16 percent mortality with NEC

What is or isn’t NEC?
Early vs Late onset

- Early onset
  - Usually term
  - First 7 days
  - Critically ill
  - Never fed
  - Vascular cause of intestinal injury

- Late onset
  - > 7 days
  - Growing preemie
  - Has been fed
  - Luminal cause of intestinal injury

NEC Pathogenesis

- Prematurity
  - Propensity towards gut inflammation
  - Impaired intestinal barrier function
  - Decreased intestinal motility
  - Deficient mucosal enzymes, hormones, pepsin, and gastric acid
  - Immature autoregulation of microcirculation
  - Lack of amniotic fluid
  - Immature mucin layer

- Enteral Feeds
  - Formula feeding
  - Fortification

  - Abnormal intestinal microbiota
    - Decreased commensal flora
    - Increased pathogenic bacteria
    - Prolonged antibiotic therapy
    - Acid suppression medications
NEC Pathogenesis

- Gut Ischemia
  - Abnormal gut vascular regulation
  - More prone to hypoxic events

- Inflammatory response
  - Genetic factors?
  - TLR4?

Etiology

Common final pathway – the endogenous production of inflammatory mediators that precipitate intestinal injury

Model of Pathogenesis

- Subclinical event (hypoxia, ischemia)
- Intestines become colonized
- Bacteria bind to injured mucosa
- Inflammatory response
- Increased permeability of mucosa
- Translocation of bacteria
- Inflammatory response accelerates
  - Inflammatory mediators, reactive oxygen species further injure mucosa
- Maladaptive vasoconstrictive response leads to ongoing ischemia/reperfusion injury
- End result – cycle of feedback mechanisms ultimately causing necrosis and perforation
In the adult intestine...
- Fats = Seagulls (complacent, harmless, unhelpful)
- Mucin = The Moat
- Hypoxemia/Hypovolemia = Natural Disaster
- TLR-4, Immune Cells, etc = sentries
- Commensal Biofilm = The Barges
- Bacteria = Sharks
- Hypoxemia/Hypovolemia = Natural Disaster
- In medical terms, it can lead to damage
- inflammation and shock.

In the premature intestine...
- Walls aren't as strong
- Moat isn't as wide
- Lots more sentries
- Not as many barges

Breast Milk
- Has growth factors to increase mucin production
- Has HMOs that distract pathogens and feed commensals

Formula
- Less protection against pathogen invasions
- Over expressed TLR-4 (sentries) sends out alarm causing excessive inflammatory response (town panic & wall damage)

Both are still at risk for "natural disasters" but hopefully the breast fed infant can weather the storm a little better.
Diagnosing NEC

Bell’s Staging for NEC
- Most commonly used in practice
- Staging based on severity of systemic, intestinal, and radiographic findings
- Treatment is directed at the clinical signs rather than the particular stage of NEC
- Each advancing stage includes the characteristics of the previous stage plus additional findings due to increasing severity of the disease

Stage 1-Suspected NEC
- Gastric residuals
- Abdominal distension
- Heme positive stools
- X-ray normal to mild distension
- Temp instability
- A’s and B’s
Stage 2- Proven NEC

- Absent bowel sounds
- Abdominal tenderness
- Pneumatosis intestinalis
- Portal venous gas
- Mild metabolic acidosis
- ↓ Platelets
- Radiograph findings include intestinal dilation, ileus, pneumatosis intestinalis, and ascites
- Stage IIA “mildly ill”, stage IIB “moderately ill”

Stage 3-Advanced NEC

- Severely ill
- Marked distension
- Signs of peritonitis
- Hypotension
- Bradycardia
- Severe apnea
- Metabolic and respiratory acidosis
- Disseminated intravascular coagulation (DIC)
- Stage IIIA intact bowel, stage IIIB perforated bowel visualized as a pneumoperitoneum

Diagnosing NEC

- Based on the presence of the characteristic clinical features of:
  - Abdominal distention
  - Rectal bleeding
  - Abdominal radiographic finding of pneumatosis intestinalis.
- Assessment of infants with suspected NEC includes:
  - Abdominal imaging, blood studies, stool analysis, and sepsis evaluation
- Future Biomarkers? iFABP? PAF?
Presentation – clinical findings

- Abdominal distension
- Feeding residuals, often bilious
- Gross or occult blood in stool
- Abdominal tenderness
- Erythema or bluish discoloration of abdominal wall
- Absent bowel sounds
- Non-specific signs (temp. instability, glucose instability, lethargy, apnea/bradycardia, hypotension)

Visual Exam
Abdominal Distension/ Increased AG

- What is the distension from?
- What has been the baseline abdominal exam
- Last stool
- Is he on CPAP or been recently bag/mask ventilated? Does he have an OGT in place and vented?
- Are there any other concerning signs? – glucose instability, lethargy, temp. instability, apnea, etc.
- Is the infant hungry and eager to nipple feed?
Residuals

- Is the residual bilious?
- Is the baby stooling at least q12h, moderate amounts?
- Has the infant been recently bag/mask ventilated?
- What position has the baby been in?
- Has the last few hours been stressful for the infant?
  (blood draws, lots of handling, procedures)
- Is the physical exam benign?
- Could there be an ileus? – morphine, infection, post-op
- Refeed residual if non-bilious, partially digested milk.

Heme Positive Stools

- Is the stool meconium?
- Is the infant receiving glycerin suppositories?
- Does the infant have a fissure?
- Has the infant had abdominal surgery?

Presentation – Laboratory Findings

- Glucose instability
- Abnormally high or low WBC
- Left shift of WBC
- Thrombocytopenia
- Metabolic acidosis
- DIC
- CRP
Radiologic Findings

Normal Abdominal Xray

- Uniform size and shape of loops
- Diameter approximates vertebra
- Gas throughout entire bowel tract
- Gas pattern should vary on subsequent x rays
- No free air in abdomen and liver is opaque

Presentation – Radiographic Findings

- Non-specific bowel dilatation
- Thickening of bowel wall
- Fixed, dilated loop unchanged on >1 radiograph
- Pneumatosis intestinalis
- Portal venous gas
- Pneumoperitoneum
- Falciform ligament may be outlined
- Football sign
Ultrasound

• Used to look for bowel wall thickening
• Free air
• Portal Venous gas

Management- Suspected NEC

• NPO
• Fluid/electrolyte and parenteral nutrition management
• Gastric decompression
• Labs
• Antibiotics (Ampicillin and Gentamicin, Vancomycin, Cefotaxime, Flagyl?)
• Correct metabolic acidosis
• Serial xrays
• Respiratory & Circulatory support
• Rule out other causes of distension
• Transfusions?
• Close monitoring
Management – Definite NEC

- Obtain consult with surgical team
- Serial KUB’s
- NPO 7-10 days
- Careful I/O’s – maintain bowel perfusion, may require fluid resuscitation
- Circulatory support
- Respiratory support
- PT, PTT, fibrinogen, platelets
- Frequent abg’s, electrolytes
- Antibiotics 7-14 days

Surgical Treatment

Medical management is appropriate in most cases
- Operative intervention indications:
  - Perforation, evidence of necrotic bowel (fixed loop, metabolic acidosis, DIC, shock), or progressively worsening clinical condition despite intensive medical management
- Surgical Options:
  - Peritoneal drain
  - Exploratory laparotomy for resection of necrotic bowel

Surgical Considerations

- Peritoneal drain +/- irrigation
- Allows time for baby to stabilize
- Better able to delineate viable gut when do operate
- Borderline bowel segments may recover
- Intestinal perforation may be definitively treated
- Laparotomy indicated if not improving in 24-48 hrs
Surgical Considerations

- Exploratory laparotomy for resection of necrotic bowel
- Primary Anastomoses
- Ostomy & Mucous Fistula
- Clip & Drop
Prevention

- Human milk
  - Pasteurized MBM is not as protective
- Intestinal priming (gut stimulation feedings)
- Promotes structural and functional maturation
- Promotes acquisition of normal flora
- Stimulate release of gastric hormones
- Slow, but not too slow, feed advance
- Minimize prolonged antibiotic use
- Antenatal glucocorticoids for lung maturation also accelerate intestinal maturation
- Prebiotics, probiotics, postbiotics

How can Human Milk Prevent NEC?

1. [Link to infographic](http://www.human-milk.com/infographic/leaflet.html)

Oligosaccharides & the Gut

- Human Milk Oligosaccharides
  - 3rd most abundant biomolecule in human milk
  - Un-digestible by humans
  - “It’s All About the Breast Milk Sugars, Baby”

Colostrum Care

- Oropharyngeal administration
  - Use syringe to place directly onto the oral mucosa in the buccal cavity for absorption via the mucosa
  - Allows for systemic absorption of the cytokines and pancreatic secretory trypsin inhibitor (PSTI)
  - Rich source of Oligosaccharides
  - May reduce time to full feeds

Trophic feeds

- Improved feeding tolerance
- More rapid advancement to full feeds
- Improved weight gain
- Shortened duration of TPN
- Less phototherapy
- Reduction in direct bilirubin
- Decreased length of stay
- Does not increase risk of NEC!
- May be considered for an infant who is hemodynamically stable on a low dose of dopamine and/or with an Umbilical Arterial Line in place

Feeding Protocol for Preterm Infants

- Goal
  - Preterm: 150-160 ml/kg/day of 24cal/oz; fortify when feed volume is 60ml/kg/day
  - Term: 150-165 ml/kg/day of 20cal/oz
- Consider increasing concentration of feeds if poor weight gain, volume intolerance or fluid restriction, or increased energy requirements.
- Preterm infants should receive 24cal/oz for at least one week before increasing to 27cal/oz
- Consider hind milk
**Prevention - Disadvantages of NPO**

- “The wisdom of stopping all enteral intake is counter-intuitive to the ontologic processes that started in utero”
  Edmund Gamma, Lyle Browne, State Univ. NV
- Has not uniformly provided protection, may simply delay the onset of NEC
- Predisposes to injury when finally fed
  - Gut atrophy
  - Decreased mucin production and enzyme activity
  - Decreased secretion of IgA
  - Increased transmural penetration of bacteria, and antigens
  - Increased susceptibility to infection
  - Autodigestion

**Enteral Nutrition**

- Breast milk is best
- Donor breast when MBM not available
- Use of standardized feeding guideline
  - Reduced risk of NEC
  - Less variability
  - Achieve full feeds earlier

**Neonatal nurses go beyond the numbers to take in the entire baby. Their nursing is particular, contextual, and holistic. It is an art. Xrays and lab values pale in comparison with the vigilance and commitment of an expert nurse.**
QUESTIONS??