PROBLEMS of the NEONATAL PERIOD

Whirlwind Tour of Common Neonatal Problems

- Respiratory conditions
- Infections
- Hypoglycemia
- Bilirubin metabolism: neonatal jaundice
- Bowel obstruction
- Birth injuries
- Rashes

Respiratory distress in the neonate

- Pulmonary causes:
  - Respiratory Distress Syndrome: surfactant deficiency
  - Transient Tachypnea of the Newborn: retained fetal lung fluid
  - Meconium aspiration syndrome
  - Sepsis
  - Congenital pneumonia
  - Persistent pulmonary hypertension
  - Space-occupying lesions: pneumothorax, chylothorax, pleural effusion, congenital diaphragmatic hernia

Respiratory distress syndrome (RDS)

- Surfactant insufficiency and pulmonary immaturity

- Incidence correlates with degree of immaturity
  - 33% in infants between 28-34 wks
  - <5% in infants > 34 wks

- Incidence increased:
  - male infants
  - infants of diabetic mom (6-fold ↑)
  - multiple births, second-born twin
Respiratory distress syndrome

- Clinically:
  - respiratory distress, rales, hypoxemia, poor air entry
- Radiographically:
  - hypoexpanded lungs
  - reticulogranular opacification
  - air bronchograms
  - white-out lungs

Strategies for prevention of RDS

- Prevent premature delivery
  - Tocolytics, antibiotics
- Decrease antenatal inflammation/infection
  - Chorioamnionitis, maternal infections
    - increased risk for preterm labor
- Antenatal glucocorticoids
  - Effective but do not prevent all RDS or bronchopulmonary dysplasia

Benefits of antenatal corticosteroids

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<thead>
<tr>
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<th>RR</th>
<th>(95% CI)</th>
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<tbody>
<tr>
<td>Reduction in RDS</td>
<td>0.66</td>
<td>(0.59, 0.73)</td>
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<td>Reduction in IVH</td>
<td>0.54</td>
<td>(0.43, 0.69)</td>
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<td>Reduction in NEC</td>
<td>0.46</td>
<td>(0.29, 0.74)</td>
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<tr>
<td>Reduction in mortality</td>
<td>0.69</td>
<td>(0.58, 0.81)</td>
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<tr>
<td>Systemic infection</td>
<td>0.8</td>
<td>(0.65, 0.99)</td>
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- No increased risk to mother of death, chorioamnionitis, puerperal sepsis
- Surfactant administration effective in reducing incidence and severity of RDS

TTN (Transient Tachypnea of Newborn)

- Delayed clearance of fetal lung fluid
- Term or near-term infants
- Delivered via c-section, no labor, short labor, precipitous delivery
- Chest Xrays: lung hyperaeration, prominent pulmonary vascular markings, interstitial fluid, pleural effusion
- Transient respiratory symptoms (tachypnea >> hypoxia >> dyspnea)
- Resolves within 2 (-5) days

Cochrane Review, 2006
Transient Tachypnea of Newborn

- slightly hyperexpanded lungs
- "sunburst" hiliar streaks
- fluid in minor fissure
- Prominent pulmonary vascular markings
- → CXR normalizes in 1st 24 hrs

Meconium Aspiration Syndrome

- Incidence of meconium staining:
  - associated with fetal distress and increasing gestational age
  - 20% of all deliveries
  - 30% in infants ≥ 42 weeks
- Hypoxia, acidosis lead to fetal gasping (→ aspiration)
- Meconium Aspiration Syndrome (MAS) found in 2-20% of infants with meconium-stained fluid
- Most common cause of respiratory distress in term newborns, typically presenting in 1st few hours of life
- Disease range: mild to severe disease –
  - air leaks, pulmonary hypertension, respiratory failure, death
  - iNO, HFOV, and ECMO improve survival
  - Surfactant may be beneficial

Complications of MAS

- pneumothorax
- pneumomediastinum
Extra-pulmonary causes of respiratory distress in the neonate

- Hyperthermia, hypothermia
- Polycythemia
- Hypovolemia, shock, metabolic acidosis
- Sepsis
- Cardiac disease: cyanotic congenital heart disease, left-sided obstructive lesions (coarctation), congestive heart failure, myocardopathy, myocarditis

Perinatal Infections

- Major risk factors for early onset sepsis
  - Prematurity < 37 weeks gestation
  - Chorioamnionitis
  - Prolonged ruptured membranes > 24 hours
  - GBS positive mother
  - Male infant

Perinatal Infections

- Bacterial infections:
  - Group B Streptococcus
  - E. coli
  - Listeria monocytogenes
- Viral infections
  - Herpes simplex
  - Hepatitis B and C
- TORCH infections: Incidence is 0.5-2.5%; many infants are asymptomatic at delivery
  - Toxoplasma gondii, treponema pallidum
  - “Other”: syphilis
  - Rubella
  - Cytomegalovirus (most common)
  - Herpes

Neonatal Group B Streptococcus

Prevention of GBS neonatal sepsis

- Routine antenatal cultures at 35-36 weeks
- Treat women:
  - with positive cultures with onset of labor
  - with previously infected infants
  - with GBS UTI

Strategy misses women who deliver prematurely and women with no prenatal care
**Management of neonatal infections**

- Septic work-up for infection
  - CBC with differential, bands and platelet count
  - Blood culture(s)
  - +/- C-reactive Protein (good negative predictive value)
  - +/- Lumbar Puncture
  - Specific workup for viral infection

- Treatment
  - Symptomatic: ampicillin and gentamycin (or ampicillin and 2nd/3rd generation cephalosporin for bacterial meningitis). Acyclovir if concerned for herpes.
  - Length of treatment depends on clinical findings, CBC, LP, and culture results.
  - Asymptomatic infant at risk (e.g., a non-reassuring CBC): treat for 48 (-72 hrs) until bacterial cultures negative

**Perinatal Hepatitis B**

Prevention of transmission:
- Hepatitis B vaccine prior to hospital discharge for all infants (<12 hr if Mom HBsAg positive)
- HBIG (hepatitis B immunoglobulin) plus vaccine for infants born to HBsAg + mother @ <12 hrs of life decreases transmission from 20-90% to 5-10%
- All infants receive routine Hepatitis B vaccine during infancy (1 mo and 6 mos); check if susceptible
- Breastfeeding safe with HBsAg positive mother with vaccine plus HBIG treatment for the infant

**Perinatal Hepatitis C**

High-risk mothers screened during pregnancy
- Vertical transmission rate is 5-10%
- Hepatitis C antibody titers obtained on infant at 6 and 12 months, or Hepatitis C PCR at 4 mos

What about breastfeeding with Hepatitis C+ mother?
- Variable amounts of virus in milk
- Studies have not shown increase risk of transmission of Hepatitis C with breastfeeding

**Perinatal TORCH Infections**

- Non-specific findings in infants
  - SGA, IUGR, postnatal growth failure
  - Microcephaly, hydrocephalus, intracranial calcifications
  - Hepatosplenomegaly, hepatitis, jaundice (elevated direct component)
  - Anemia (hemolytic), thrombocytopenia
  - Skin rashes, petechiae
  - Abnormalities of long bones
  - Chorioretinitis, cataracts, glaucoma
  - Nonimmune hydrops
  - Developmental and learning disabilities
Perinatal (TORCH) Infections

Specific findings:
- **Syphilis**: osteochondritis, periosteal new bone formation, rash, snuffles
- **Cytomegalovirus**: microcephaly, periventricular calcifications, hydrocephalus, chorioretinitis, petichiae, thrombocytopenia, hearing loss (progressive)
- **Toxoplasmosis**: hydrocephalus, chorioretinitis, generalized intracranial calcifications (random distribution)
- **Rubella**: cataracts, “blueberry muffin rash”, patent ductus arteriosus, pulmonary stenosis, deafness

“Blueberry” muffin rash: cutaneous hematopoeisis

Ocular findings

Neonatal Herpes Simplex

- Neonatal Herpes simplex infections:
  - HSV-1 (15 to 20%) and HSV-2 (80 to 85%)
  - Neonatal infection
    - with *primary* HSV is 35-50%; with *recurrent* HSV is 0-5%
  - Increased risks of transmission
    - prolonged rupture of membranes
    - forceps or vacuum delivery, fetal scalp monitoring
    - preterm infants
  - 75% of cases have neither history of maternal infection nor skin lesions
  - consider treatment based on clinical presentation and suspicion of infection.
Herpes simplex: clinical presentations

- **Disseminated** (systemic) disease:
  - Early onset (1st week of life), 25% of cases
  - Sepsis syndrome, liver dysfunction, pneumonia
- **CNS disease**: meningoencephalitis
  - 2nd-3rd week of life, 35% of cases
  - Fever, irritability, abnormal CSF, seizures
  - Early treatment improves outcome, but 40-50% infants have residual neurodevelopmental disability
- **Localized disease**: skin, eyes, mouth, 40% of cases

Cutaneous HSV: clustered vesicular eruption → ulceration

Diagnosis of TORCH Infections

- CMV
  - urine culture
- Toxoplasmosis
  - maternal antibody titers and neonatal IGM antibody
- Syphilis
  - RPR or VDRL positive, obtain titers, order treponemal-specific test (FTA or MHA-TP)
- Herpes simplex
  - Surveillance: conjunctival, nasopharyngeal, and rectal swabs for Direct Fluorescent Antibody (DFA) 24-48 hours after birth if suspect exposure
  - Culture of vesicle scrapings when lesions are present
  - DFA of vesicle scrapings
  - PCR: detect HSV-DNA in CSF

Hypoglycemia

- Inadequate glycogenolysis:
  - cold stress, asphyxia
- Inadequate glycogen stores:
  - prematurity, postdates, intrauterine growth restriction, small for gestational age (SGA)
- Increased glucose consumption:
  - asphyxia, sepsis, polycythemia
- Hyperinsulinism:
  - Infant of Diabetic Mother (IDM)
Hypoglycemia

- Treatment
  - Early feeding when possible (breastfeeding, formula, oral glucose)
  - If glucose < 35 or infant symptomatic, give intravenous glucose bolus (D10 @ 2-3 ml/kg)
  - Following bolus infusion, a continuous IV infusion of D10 is often required to maintain normal glucose levels

Hyperbilirubinemia

- Increased red cell mass and breakdown
- Increased enterohepatic circulation
- Delayed/abnormal conjugation
- Abnormal excretion

Increased bilirubin load

- Elevated hemoglobin level, RBC mass
  - Polycythemia
- RBC degradation due to shorter RBC half-life
  - 70 days (preterm infants), 70-90 days (term infants) vs 120 days in adults
- Extravasated blood: cephalohematoma, caput/bruises, swallowed blood, intracranial or intra-abdominal hemorrhage
- Effects of plasma albumin-bilirubin binding
  - Newborns have lower albumin levels → lower bilirubin-binding capacity → increased risk of acute bilirubin encephalopathy

Unconjugated hyperbilirubinemia: increased breakdown

- Hemolysis
  - Incompatibility: ABO, Rh, minor blood groups (Kell, Duffy) [Antibody screen, DAT]
  - Enzyme defects: G-6-PD, pyruvate kinase
  - Sepsis
  - RBC membrane defects: Hereditary spherocytosis
  - Extravascular blood
Clinical findings suggesting hemolysis
- Onset of jaundice in 1st 24 hours
- Rapid rate of rise of bili (>0.5mg/dL per hour)
- Hepatosplenomegaly, pallor
- Family history (G6PD, spherocytosis)
- “set-up” with incompatibility, Coombs (+DAT), elevated reticulocytes, abnormal hemolytic smear

Findings suggesting sepsis or inborn error
- Emesis, lethargy, poor feeding
- Hepatosplenomegaly, tachypnea, temperature instability

Unconjugated hyperbilirubinemia: impaired conjugation
- Delayed/abnormal conjugation
  - Neonatal hepatitis
  - Sepsis
  - Prematurity
  - Breast milk jaundice
  - Hypothyroidism
  - Sepsis
  - Congenital enzyme deficiency eg Crigler-Najjar
  - Metabolic diseases, e.g., galactosemia

Management of indirect hyperbilirubinemia
- Increased susceptibility to neurotoxicity seen with asphyxia, sepsis, acidosis, prematurity, and hemolysis.
  - Treat these infants at lower levels of unconjugated bilirubin.
- When to worry:
  - Jaundice in the 1st 24 hours
  - Rapid rise in TsB >5 mg/dl/24 hrs
  - Porolonged hyperbilirubinemia
    - > 1 week (term) infant
    - > 2 weeks (preterm)
  - Direct bilirubin > 2mg/dl
  - Symptomatic bilirubin encephalopathy

Treatment guidelines (AAP nomogram)
- Treatment based on clinical risk status (well vs ill infant), serum bilirubin level, GA, chronologic age (hrs of life)
- More conservative treatment of preterm infants (< 37 wks with more immature blood-brain barrier), or infants with sepsis or acidosis.
- Phototherapy vs exchange transfusion
**Enterohepatic circulation**
- Conjugated bilirubin is unconjugated and reabsorbed in gut in fetus
- Enhanced by:
  - Gut sterility (urobilinogen and stercobilinogen)
  - Bowel dysmotility (preterm infants, effects of magnesium or morphine)
  - Ileus
  - Obstruction: atresia, pyloric stenosis, meconium plugs, cystic fibrosis
  - Delayed feeding

**Conjugated (direct) hyperbilirubinemia: impaired excretion**
- Obstruction to biliary flow: biliary atresia, choledocal cyst, cystic fibrosis, stones
- dark urine (urine + for bilirubin), light colored stools, persistent jaundice (> 3 weeks)
- Hepatic cell injury: syphilis, TORCH infections
- Hepatic dysfunction: E. coli (UTI)
- Toxic effects: hyperalimentation cholestasis
- Metabolic errors: galactosemia
- Chronic “overload”: erythroblastosis fetalis, G-6PD, spherocytosis

**Polycythemia**
- Hematocrit > 65% on a spun, central venous blood sample
  - Complications associated with hyperviscosity:
    - Plethora, slow capillary fill time
    - Respiratory distress
    - Hypoglycemia
    - Hyperbilirubinemia
    - Irritability, lethargy, poor feeding
    - Cyanosis, heart murmur, and cardiomegaly
    - Seizures and strokes
    - Necrotizing enterocolitis
    - Renal vein thrombosis

**Polycythemia: Treatment**
- *Symptomatic* neonates with polycythemia, or infants with very high hematocrit (≥ 70%) → dilutional exchange, correcting Hct to approx 55%.
  
  \[
  \text{Volume of blood} = Wt \text{ (kg)} \times 80 \text{ cc/kg} \times (\text{Hct}_{\text{obs}} - \text{Hct}_{\text{desired}}) \div \text{Hct}_{\text{obs}}
  \]

- Blood is removed through umbilical artery or umbilical venous catheter and normal saline is infused for blood volume replacement (IV, UVC, or UAC).
Bowel Obstruction in the Neonate

- Clinical presentations of bowel obstruction
  - Emesis: Bilious emesis suggests a lesion distal to ampulla of Vater; sporadic emesis suggests partial obstruction, malrotation, duplications, or annular pancreas
  - Failure to pass meconium (although some infants with “high” lesions will pass meconium)
  - Symptoms start soon after birth with high lesions or with complete obstruction, symptoms delayed in lower lesions or partial obstruction
  - Fetal diagnosis: polyhydramnios and fetal u/s

Causes of bowel obstruction in the newborn

Intrinsic:
- Atresia
- Stenosis
- Meconium ileus
- Anorectal malformations
- Volvulus
- Annular pancreas
- Peritoneal bands

Functional:
- Hirschsprung
- Meconium plug ileus

Duodenal atresia

- 70% of neonates have other anomalies: Down syndrome, annular pancreas, cardiac malformation, multiple atresias
- Clinical findings: dehydration with metabolic alkalosis
- Xray findings: “double-bubble” (dilated stomach and dilated proximal duodenum)
- Management: NG tube, correct electrolytes and surgical consultation

Malrotation with volvulus

- Malrotation (8th-10th week) can lead to volvulus
  - Complete obstruction
  - Vascular compromise:
    - gangrene of the gut, peritonitis, sepsis, and shock.
- Infants present with emesis, bowel distention. Intermittent emesis with incomplete obstruction
- Xrays: dilated stomach and duodenum, little air in distal bowel, diagnosis by UGI (barium enema)

Surgical emergency
Hirschsprung’s Disease

- Lower bowel obstruction: agenesis of ganglion cells (Auerbach and Meissner plexuses)
  - Rectal lesion extending in varying degree; in 80-90% patients no extension beyond sigmoid colon
  - Associated w/ Downs (15%), Waardenburg syndrome
  - Delayed meconium passage (>24-48 hrs) in 90% of patients
  - Clinical findings: Abdominal distention, emesis, obstipation
  - Barium enema: narrowing segment, “corkscrew” appearance of colon, delayed clearing of barium
  - Diagnosis: rectal suction biopsy

Meconium ileus (inspissated meconium)

- 90% of patients have cystic fibrosis, 10-15% of CF patients have meconium ileus
- Family history may be helpful
- Abdominal distention and emesis within 48 hrs
- Delayed meconium passage
- 1/3 of patients have volvulus, atresia, meconium peritonitis, pseudocyst, and present earlier
- Xrays: dilated bowel loops, intra-abdominal calcification (peritonitis), no air-fluid levels seen

Meconium plug syndrome

- Etiology: colonic dysmotility?
- Hirschsprung’s disease in 50% of these patients
- Clinical findings:
  - Delayed meconium passage: (24-48 hrs)
  - Abdominal distention, emesis
  - Barium enema is diagnostic and therapeutic

Birth Injuries

- Cephalohematoma
- Caput succedaneum
- Subgaleal hematoma
- Erb’s palsy
- Klumpke’s palsy
- Clavicular fracture
- Phrenic nerve injury with diaphragmatic paralysis
**Injuries to the head**

*Caput:* Edema on presenting scalp. Superficial to the periosteum, crossing sutures (vaguely demarcated pitting edema, +/- ecchymosis).

*Cephalohematoma:* Subperiosteal bleeding from rupture of vessels that traverse from the skull to periosteum. Bleeding limited by periosteal attachments, thus swelling does not cross sutures (tight water balloon to palpation).

*Subgaleal hemorrhage:* Blood in loose connective tissue, large potential space → enlarging, mobile hematoma → shock (loose water balloon with fluid wave to palpation).

*Cephalohematoma and subgaleal associated with skull fracture and hyperbilirubinemia*

**Brachial plexus injury: Erb’s Palsy and Klumpke’s Palsy**

- Incidence of brachial plexus injuries: 1.6 - 2.9 per 1,000 live births
- 45% of brachial nerve injuries associated with shoulder dystocia.

*Erb’s palsy:*
- Arm adducted, extended, and internally rotated. Absent biceps and Moro reflexes on affected side. Sensation usually preserved.
- Recovery is often spontaneous and may occur within 48 hrs or up to 6 mos.
- Nerve laceration may be permanent palsy.

*Klumpke’s palsy:*
- Hand grip affected

*Differential diagnosis:*
- Clavicular or humeral fracture

**Neonatal skin conditions**

*Common newborn dermatologic problems*
- Erythema toxicum
- Benign pustular melanosis
- Milia
- Neonatal acne
- Hemangiomata
  - nevus flammeus
  - capillary
  - cavernous
  - mixed
  - port wine stain

**Erythema Toxicum**

- Yellow papules w/ erythematous macular base, evanescent and found over entire body
- Common in term infants
- Most seen 24-48 hours after delivery; can be seen up to 2 wks of age
- Eosinophil-filled papules
- Unknown etiology, benign, resolves spontaneously
Benign pustular melanosis

- Seen in 4.4% of African-American infants, 0.2% in white infants
- Lesion: superficial pustular lesions that easily rupture leaving a scaly “collar” around hyper-pigmented macules, which fade in weeks to months.
- Lesions in clusters under chin, nape of neck, forehead, also on trunk and extremities
- Lesions are sterile and transient. Not associated with systemic disease.

Pustules w/ scaling “collar”  Post-inflammatory hyperpigmentation

Pustules and post-inflammatory hyperpigmentation

Milia  Neonatal acne
Hemangiomata

- Strawberry hemangioma:
  - 2.6% of infants (higher in preterm infants)
  - May be seen at birth or develop during 1st few wks of life; 90% seen by 1 mo of life
  - Start as small, discrete, well demarcated lesions. These grow rapidly during infancy, and eventually involute.
  - Infants with large lesions, lesions on the face, eyelids, airway, mouth, or cavernous lesions should be referred.

- Flame nevus
  - Very common, up to 40% of infants
  - “Salmon patch” on nape of neck, on eyelids, between eyebrows
  - Do not grow during infancy and do not completely disappear. Lesions fade and are less noticeable except during crying or exertion