PROBLEMS of THE NEONATAL PERIOD

John Colin Partridge, MD, MPH
Professor of Clinical Pediatrics
University of California, San Francisco
San Francisco General Hospital

Family Medicine Board Review course
San Francisco
June 28, 2010

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
- Severity of illness improved by antenatal steroids & surfactant
- Incidence of RDS correlates with degree of immaturity
  - 33% in infants between 28-34 wks
  - <5% in infants > 34 wks
- Incidence increased:
  - male infants
  - 6-fold ↑ in infants of diabetic mom (IDM)
  - multiple births, second-born twin
Respiratory distress syndrome

- hypoepradnized lungs
- reticulogranular opacification
- air bronchograms
- white-out lungs

Strategies for prevention of RDS

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

Benefits of antenatal corticosteroids

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RR</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in RDS</td>
<td>0.66</td>
<td>(0.59, 0.73)</td>
</tr>
<tr>
<td>Reduction in IVH</td>
<td>0.54</td>
<td>(0.43, 0.69)</td>
</tr>
<tr>
<td>Reduction in NEC</td>
<td>0.46</td>
<td>(0.29, 0.74)</td>
</tr>
<tr>
<td>Reduction in mortality</td>
<td>0.69</td>
<td>(0.58, 0.81)</td>
</tr>
<tr>
<td>Systemic infection</td>
<td>0.8</td>
<td>(0.65, 0.99)</td>
</tr>
</tbody>
</table>

- No increased risk to mother of death, chorioamnionitis, puerperal sepsis

TTN (Transient Tachypnea of Newborn)

- Delayed clearance of fetal lung fluid
- Term or near-term infants
- Delivered via c-section, no labor, little labor
- Chest Xrays: lung hyperaeration, prominent pulmonary vascular markings, interstitial fluid, pleural effusion
- Transient respiratory symptoms (tachypnea, occasional hypoxia, rare dyspnea) resolve within 2-5 days
Transient Tachypnea of Newborn

- Slightly hyperexpanded lungs
- "Sunburst" hilar 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 first few hours of life
- Disease range: mild to severe disease with air leaks, pulmonary hypertension, respiratory failure, and death (iNO, HFOV, and ECMO improve survival)

Meconium Aspiration Syndrome

- Patchy, streaky infiltrates
- Hypopexpansion
- Air leaks:
  - Pneumothorax
  - Pneumomediastinum
  - Pneumopericardium

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 including bands and platelets
  - Blood culture
  - +/- C-reactive Protein
  - +/- Lumbar Puncture
  - Specific work-up for viral infection

- Treatment
  - **Symptomatic:** treat with 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 positive mother <12 hours of life
- All infants should receive routine Hepatitis B vaccine during infancy (1 month and 6 months)
- 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 hematopoiesis

Ocular findings

- Chorioretinitis
- Cataracts

Neonatal Herpes Simplex

- Neonatal Herpes simplex infections:
  - HSV-1 (15 to 20%) and HSV-2 (80 to 85%)
  - Neonatal infections with primary HSV is 35-50%
  - Neonatal infections with recurrent HSV is 0-5%
  - Increased risk of transmission with prolonged rupture of membranes, forceps or vacuum delivery, fetal scalp monitoring, preterm infants
  - Since 75% of cases have no history of maternal infection, nor evidence of skin lesions. You may need to start 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

Diagnosis of TORCH Infections

- CMV
  - urine culture
- Toxoplasmosis
  - maternal antibody titer 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

Cutaneous HSV: clustered vesicular eruption → ulceration

Hypoglycemia

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

- **Treatment**
  - Early feeding when possible (breastfeeding, formula, oral glucose)
  - Depending on severity of hypoglycemia and clinical findings, may need to give intravenous glucose bolus (D10 @ 2-3 ml/kg)
  - Following bolus infusion, a continuous intravenous 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
- Increased rate of RBC degradation with shorter half-life of RBC
  - 70 days in preterm infants, 70-90 days in term infants, 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

**Unconjugated hyperbilirubinemia: increased breakdown**

- Hemolysis
  - Incompatibility: Rh, ABO, minor blood groups (Kell, Duffy)
  - Enzyme defects: G-6-PD, pyruvate kinase
  - Sepsis
  - RBC membrane defects: Hereditary spherocytosis
  - Extravascular blood
Enterohepatic circulation

- Conjugated bilirubin is unconjugated and reabsorbed
- Enterohepatic circulation and reabsorption is 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

Unconjugated hyperbilirubinemia: impaired conjugation

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

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 (> 3weeks)
- 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

Management of indirect hyperbilirubinemia

- Increased susceptibility to neurotoxicity seen with asphyxia, sepsis, acidosis, prematurity, and hemolysis. Consider treatment at lower levels of unconjugated bilirubin in these cases.
- When to worry
  - Visible jaundice in the first 24 hours of life
  - Serum bilirubin rising rapidly > 5 mg/dl/24 hrs
  - Prolonged hyperbilirubinemia > 1 week term infant and > 2 weeks in the preterm
  - Direct bilirubin > 2mg/dl
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

Treatment guidelines (AAP nomogram)
- Decision to treat depends on clinical risk status (well vs ill infant), unconjugated bilirubin level, chronologic age (hours of life), and gestational age
- More conservative treatment of preterm infants (< 37 wks with more immature blood-brain barrier), or infants with sepsis or acidosis.

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 for a symptomatic neonate with polycythemia, or an infant with excessively high hematocrit (> 70%) is by a dilutional exchange, correcting Hct to approx 55%.
  
  \[
  \text{Volume of blood} = Wt \times 80 \text{cc/kg} \times \frac{(\text{Hct}_{\text{obs}} - \text{Hct}_{\text{desired}})}{\text{Hct}_{\text{obs}}}
  \]

  Blood is removed through umbilical artery or umbilical venous catheter and normal saline is infused for blood volume replacement.
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, delayed in lower lesions of partial obstruction
  - Fetal diagnosis: polyhydramnios and fetal u/s

Causes of obstruction in the newborn

<table>
<thead>
<tr>
<th>Intrinsic:</th>
<th>Functional:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atresia</td>
<td>Hirschsprung</td>
</tr>
<tr>
<td>Stenosis</td>
<td>Meconium plug</td>
</tr>
<tr>
<td>Meconium ileus</td>
<td>Meconium ileus</td>
</tr>
<tr>
<td>Anorectal malformations</td>
<td></td>
</tr>
<tr>
<td>Volvulus</td>
<td></td>
</tr>
<tr>
<td>Annular pancreas</td>
<td></td>
</tr>
<tr>
<td>Peritoneal bands</td>
<td></td>
</tr>
</tbody>
</table>

Obstruction in the newborn

- Atresia: complete obstruction of the lumen
  - 30% occur in duodenum (distal to ampulla)
- Stenosis: narrowing of the lumen
  - intrinsic cause or compression by extrinsic lesions (annular pancreas, peritoneal bands)
  - plain films not diagnostic
  - emesis (amount and onset) depends on degree of obstruction

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
- X-rays: 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
- X-rays: 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 diagnostic and therapeutic
### Birth Injuries
- Cephalhematoma
- Caput succedaneum
- Subgaleal hematoma
- Erb’s palsy
- Klumpke’s palsy
- Clavicular fracture
- Phrenic nerve injury with diaphragmatic paralysis

### Injuries to the head
**Caput:** vaguely demarcated, pitting edema on presenting part of scalp, w/ ecchymosis. Hemorrhagic edema is superficial to the periosteum, often crossing sutures.

**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:** superficial bleed into loose connective tissue. Bleeding not limited/ enlarging, mobile hematoma can lead to shock (loose water balloon with fluid wave to palpation).

*Cephalohematoma and subgaleal can be associated with skull fracture and hyperbilirubinemia*

### Abnormal arm position in a newborn
- Erb’s palsy C-5 and C-6
  - Decreased spontaneous movement and absent biceps reflex on affected side, abnormal Moro, "waiter's tip" appearance
- Klumpke’s paralysis C-7, C-8, T-1
  - Hand paralysis, absent grasp reflex, Horner syndrome usually seen (ipsilateral ptosis, miosis, anhidrosis)
- Fractured clavicle
  - Crepitus felt, decreased spontaneous movements, pseudoparalysis, asymmetric Moro, biceps reflex normal
- Fractured humerus

### Brachial plexus injury: Erb’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.
- The arm is adducted, extended, and internally rotated. Absent biceps and Moro reflexes on affected side. Sensory function usually preserved.
- Recovery is often spontaneous and may occur within 48 hours or up to six months.
- Nerve laceration may result in a permanent palsy.
Neonatal skin conditions

Common newborn dermatologic problems
- Erythema toxicum
- Benign pustular melanosis
- Hemangioma
  - 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 then leave a scaley “collar” around hyperpigmented macules. These fade within weeks to months.
- Lesions most in clusters under chin, nape of neck, forehead, and may be on trunk and extremities
- Lesions are sterile and transient. Not associated with systemic disease.
**Hemangioma**

- **Strawberry hemangioma:**
  - 2.6% of infants (higher incidence in preterm infants)
  - May be seen at birth, but typically develop during first few weeks of life and 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