PROBLEMS of the NEONATAL PERIOD

Respiratory conditions
Asphyxia and birth injuries

Murmurs and other cardiac problems

Gastro-intestinal problems:
Bacterial and viral infections
Metabolic problems:
hypoglycemia, hyperbilirubinemia

Surfactant deficiency: multifactorial
Meconium aspiration hemorrhage
Hypoxia
Sepsis

Hyaline membrane disease

Surfactant insufficiency and pulmonary immaturity

Incidence correlates with degree of immaturity
>75% <26 weeks
33% in infants between 28-34 wks
<5% in infants > 34 wks
May happen even at term

Incidence increased:
C-section in absence of labor
male infants
infants of diabetic mom (6-fold ↑)
multiple births, second-born twin
**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**

<table>
<thead>
<tr>
<th>Benefit</th>
<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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<tr>
<td>Reduction in IVH</td>
<td>0.54</td>
<td>(0.43, 0.69)</td>
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<tr>
<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 (first 48hrs)</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**

*Cochrane Review, 2006*

**Chronic lung disease in neonates:**

**Definition:**
Need of additional O₂ at 4 weeks of age

**Staging:**
- When 36 weeks corrected age if <32 week premature
- When 8 weeks of life if >32 weeks premature

- **Mild:** FiO₂ 21%
- **Moderate:** FiO₂ 22-29%
- **Severe:** FiO₂ ≥30%
Radiologic signs of BPD

**“OLD” BPD:**
- Bronchiolar mucosal metaplasia
- Atelectasia
- Interstitial fibrosis
- Disrupted alveolar architecture
- Emphysema
- Vascular remodeling

**“NEW” BPD:**
- Alveolar simplification
- Reduced gas exchange surface
- Reduced bronchial diameter
- Moderate interstitial fibrosis
- Reduced/dysplastic capillary bed

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Long-term consequences of BPD

Respiratory distress: differential diagnosis

- **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: differential diagnosis

- 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, congestive heart failure, myocardopathy, myocarditis

## 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

## Transient Tachypnea of Newborn

- Slightly hyperexpanded lungs
- "Sunburst" hilar streaks
- Fluid in minor fissure
- Prominent pulmonary vascular markings
- CXR normalizes in 1st 24 hrs

## Pneumonia

- Early onset: n.1 = GBS
- Acquired:
  - Staph. aureus, staph. epidermidis
  - Gram-negative bacteria (klebsiella, pseudomonas,…)
  - Candida
- Xray: can mimic other diseases

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**Meconium Aspiration Syndrome**

- Incidence of *meconium staining*:
  - associated with fetal distress and increasing gestational age
  - 10% 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

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**Air Leak Syndromes**

1. **Pneumothorax**
   - 0.07% of healthy newborns
   - 1/10 is symptomatic
   - with positive pressure ventilation, CPAP, meconium, RDS, surfactant
   - Symptoms:
     - Mild or abrupt change in vitals (tension PTX)
     - Unilateral decreased breath sounds

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**Diagnosis:**
- Transillumination
- Chest XR: AP + cross-table lateral
- Thoracocentesis

**Treatment:**
- Oxygen washout
- Chest tube
Air leak Syndromes:

2. Pulmonary Interstitial Emphysema

- Dissection of small airway walls
- Complication of mechanical ventilation (HFO), extreme prematurity
- Treatment: low-PEEP ventilation, permissive hypercapnia, selective intubation

Air Leak Syndromes:

3. Pneumomediastinum

- Usually caused by lesion or large airways (trachea, carina, main bronchus)
- Central air leak
- Leads to subcutaneous emphysema

Air leak Syndromes

4. subcutaneous emphysema

- Full-term neonate, large for gestational age
- Failure to progress
- Vacuum extraction (4 attempts!)
- Poor respiratory effort, vigorous resuscitation, cries at 5 minutes APGAR 4/5/9
- At 2 hours: grunting, some facial swelling
  - Transfer the baby…

Birth Injuries

- Cephalohematoma
- Caput succedaneum
- Subgaleal hematoma
- Erb’s palsy
- Klumpke’s palsy
- Clavicular fracture
- Phrenic nerve injury with diaphragmatic paralysis
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

Hypoxic-ischemic encephalopathy

- 1/100 live birth in the U.S.
- Accounts for 20% neonatal death (50% fetal+ neonatal deaths)
- Main causes: (a combination of…)
  - Maternal condition (hypertension, diabetes, infection, hypoxemia, shock…)
  - Placental and cord factors (abruption, compression, infarction…)
  - Fetal factors (infection, anemia, congenital heart disease…)
  - Obstetrical factors (dystocia, failure to progress…)

Hypoxic-ischemic encephalopathy
Diagnosis: MRI

cortical
Basal ganglia
White matter
brainstem

<table>
<thead>
<tr>
<th>Term infant &gt;36 weeks and &lt;6 h of life</th>
<th>One or more of the following criteria:</th>
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<tbody>
<tr>
<td></td>
<td>1. Low APGAR scores:</td>
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<td></td>
<td>2. Prolonged resuscitation at birth:</td>
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<td></td>
<td>3. Severe acidosis:</td>
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<td>4. Abnormal base excess:</td>
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<tr>
<td></td>
<td>&lt;5 at 5 minutes chest compressions or ventilation &gt;10 min pH &lt;7.0 in cord gas or any BG within 60 min &lt;12 mmol/L in cord gas or any BG</td>
</tr>
</tbody>
</table>

III Moderate or severe encephalopathy
Lethargy, stupor, coma, hypotonia, abnormal reflexes, absent/weak suck, seizures, hyperalert, abnormal aEEG

I + II + III = COOLING
Total body hypothermia
- Fast cooling within 6 hours from birth
- 72 hours with body temp 33.5°C
- Slow rewarming
- Continuous aEEG / EEG monitoring, morphine infusion, respiratory support if needed
- Side effects and complications: shivering, altered coagulation, seizures (rewarming)
- The first intervention that significantly reduces risk of death or long-term disability (from 60 to 40%)

Congenital heart disease from symptoms to referral
- Murmur
  - Day 1: Valves (outflow stenoses and A-V regurgitations)
  - 1 week: L-R shunts (PDA, VSD, …)
  - Anytime after day 1: Coarctation
- Cyanosis = right-to-left shunt
  - Intracardiac vs. Ductal vs. Pulmonary
  - Criteria: post-ductal (foot) O2Sat <95%
  - OR pre-ductal (R hand) vs post-ductal gradient >3%
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

- Congestive heart failure
  - Sweating, poor feeding, failure to grow
  - Tachycardia, tachypnea
  - Lactic acidosis, acute cardiorespiratory collapse

- Causes:
  - Structural: hypoplastic left heart syndrome, ...
  - Obstructive: pulmonary stenosis, interrupted arch, ...
  - Left-to-right shunt: Fallot, A-V canal, truncus, ...
  - Myocardial
  - Arrhythmia

- Work up and first move in suspected CHD
  - ☐ Chest XR
  - ☐ EKG
  - ☐ pre-postdualctal O2Sat
  - ☐ Pre-postdualctal AP
  - ☐ Prostaglandins?
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
- Other: intrauterine growth retardation
- Clinical findings:
  - Delayed meconium passage: (24-48 hrs)
  - Abdominal distention, emesis
  - Barium enema is diagnostic and therapeutic

**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

**GBS sepsis: ~50% early-onset**

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

- Late-onset GBS: 1 week – 2 months
  - Less well identified risk factors
  - Less preventable
  - 50% meningitis

**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);
- 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
- **Cytomegalovirus**: microcephaly, periventricular calcifications, hydrocephalus, chorioretinitis, thrombocytopenia, GERD, hearing loss (progressive)
- **Toxoplasmosis**: hydrocephalus, chorioretinitis, generalized intracranial calcifications (random distribution)
- **Rubella**: cataract, “blueberry muffin rash”, patent ductus arteriosus, pulmonary stenosis, deafness

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“Blueberry” muffin rash: cutaneous hematopoiesis

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Ocular findings

- chorioretinitis
- cataracts

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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 (FEVER) 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

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) \([\text{Antibody screen, DAT}]\)
  - Enzyme defects: G-6-PD, pyruvate kinase
  - Sepsis
  - RBC membrane defects: Hereditary spherocytosis
  - Extravascular blood

### Unconjugated hyperbilirubinemia: impaired conjugation
- Delayed/abnormal conjugation
  - Neonatal hepatitis
  - Sepsis
  - Prematurity
  - Breast milk jaundice
  - Hypothyroidism
  - 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
  - Prolonged 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)
  - 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 (> 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
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%.
  \[
  \text{Volume of blood} = \frac{Wt \times 80 \text{ cc/kg} \times (Hct_{obs} - Hct_{desired})}{Hct_{obs}}
  \]
  - Blood is removed through umbilical artery or umbilical venous catheter and normal saline is infused for blood volume replacement (IV, UVC, or UAC).

Neonatal skin conditions

- Common newborn dermatologic problems
  - Erythema toxicum
  - Benign pustular melanosis
  - Milia
  - Neonatal acne
  - Hemangiomata

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.

Milia

Neonatal acne

Pustules w/ scaling “collar”  Post-inflammatory hyperpigmentation

Hemangioma

Nevus flammeus

Hemangioma

Port-wine stain (Sturge-Weber)