RDS (Hyaline Membrane Disease)

- Occurs primarily in preterm infants, the incidence is inversely related to GA and birth wt, it occurs in 60-80% of infants < 28 Wks, 15-30% of 32-36 Wks, 5% beyond 37 WKs, rarely at term
- Risk factors:
  1. maternal DM
  2. CS delivery
  3. multiple births
  4. asphyxia
  5. cold stress
  6. precipitous delivery
The incidence is highest in preterm male, white infant

The risk is reduced in:

1. chronic or pregnancy induced HTN
2. prolonged rupture of membrane
3. antenatal corticosteroid prophylaxis
4. maternal addiction (heroin)

Surfactant deficiency (decreased production and secretion) is the primary cause of RDS. The failure to attain an adequate FRC and the tendency of affected lungs to become atelectatic correlate with high surface tension and the absence of pulmonary surfactant, Mature levels of pulmonary surfactant are present usually after 35 wk.
- **SURFACTANT**
- A complex mixture of lipids and proteins that lowers alveolar surface tension.
- --the lipid is mainly phosphatidylcholine (lecithin) (70%).
- --the proteins include SP A, B, C and D
  - **SP-B** and **SP-C** are hydrophobic proteins
  - **SP-A** and **SP-D** are hydrophilic proteins
SP-B is important and is needed for:
– Processing surfactant
– Storage of surfactant
– Secretion of surfactant in the type II respiratory epithelial cells.

Deficiency SP B causes severe respiratory distress.

**The Laplace Relationship**

The pressure (P) needed to stabilize the respiratory system from within is directly proportional to twice the surface tension (ST) and inversely proportional to the radius (r) of the structure

\[ P = \frac{2ST}{r} \]
• RDS: Pathology
• The lungs appear purplish red and are liver like in consistency
• A number of the alveolar ducts, alveoli and resp. bronchioles are lined with acidophilic, homogenous or granular membrane
RDS: Clinical Manifestations

- Onset: within minutes to several hours of birth
- Tachypnea, prominent grunting, intercostal and subcostal retractions, nasal flaring and duskiness are noted
- The cyanosis increases, breath sounds may be decreased, fine rales may be heard
- If the condition is not properly treated; hypotension, fatigue occur, the cyanosis and pallor increases, the grunting decreases or disappears as the condition worsen. Apnea and irregular respiration are ominous signs requiring immediate intervention
• Patients may also have a mixed resp and metabolic acidosis, edema, ileus and oliguria

• Death occurs between day 2 and 7 due to:
  1. alveolar air leak: interstitial emphysema, pneumothorax, pneumomediastinum
  2. Pulmonary Hge
  3. IVH
Diagnosis Of RDS

• The clinical course
• CXR: characteristic but not pathognomonic appearance: fine reticular granularity of the parenchyma and air bronchogram, this pattern develop at 6 – 12 hours
• Blood gases and acid base values: hypoxia(progressive), hypercapnea, variable met acidosis
RDS: Differential DX

- Early onset sepsis, pneumonia
- Cyanotic CHD: TAPVR
- Persistent pulmonary HTN
- Aspiration syndrome
- Pneumothorax, pleural effusion
- Diaphragmatic hernia
- Lobar emphysema
- TTN
RDS: Treatment

• Supportive care of LBW infants
• Careful and frequent monitoring of: HR, RR, O2 saturation, PaO2, PCO2, PH, HCO3, electrolytes, glucose, hematocrit, BP, temp
• The TRX is in the NICU
• Calories and fluids
• Warm humidified O2 at concentration sufficient to keep art PaO2 levels between 50 – 70 mm Hg (85-95%) saturation
• If oxygen saturation cannot be kept > 85% at inspired oxygen concentrations of 40-70% or greater, applying CPAP at a pressure of 5-10 cm H₂O via nasal prongs is indicated.
• If an infant with RDS undergoing CPAP cannot keep oxygen saturation > 85% while breathing 40-70% oxygen, assisted ventilation and surfactant are indicated.
• Infants with respiratory failure or persistent apnea require assisted mechanical ventilation, Reasonable measures of respiratory failure are:
  1. Art PH less than 7.2
  2. Art blood PCO2 of ≥ 60mm Hg
  3. oxygen saturation <85% at oxygen concentrations of 40-70% and CPAP of 5-10 cm H₂O.
• High frequency ventilation using smaller tidal vol and high rates (300-1200 bpm)
• Exogenous surfactant:
  improves survival and reduces the incidence of pulmonary air leak
• **Inhaled nitric oxide (iNO)** decreases the need for extracorporeal membrane oxygenation (ECMO) in term and near-term infants with hypoxic respiratory failure or persistent pulmonary hypertension of the neonate.

• Vitamin A supplementation given largely to infants < 1,000 g resulted in a decrease in death and/or BPD at 36 wk (from 66% to 60%) and trends for less nosocomial sepsis and retinopathy of prematurity.

• Administration of inhaled steroids to ventilated preterm infants during the 1st 2 wk after birth reduced the need for systemic steroids (from 45% to 35%) and tended to decrease rates of death and/or BPD at 36 wk without an increase in adverse effects.
Because of difficulty in distinguishing GBS pneumonia from RDS, ABCs therapy is indicated until the results of blood C/S are available: Penicillin or Ampicillin + an Aminoglycoside

**RDS: Complications**

1. Complications of tracheal intubation:
   a. asphyxia due to obstruction of the tube
   b. cardiac arrest during intubation or suctioning
   c. bleeding
   d. papilloma of the cord
   e. persistent hoarseness or stridor
   f. subglottic stenosis
2. Umbilical a. cath.:
   embolism, thrombosis, spasm, perforation
   ischemia of the abdominal viscera, Renovascular hypertension,
   infection, hge, leg gangrene

3. Umbilical v. cath.:
   a. many of those with umbilical a. cath
   b. cardiac perforation and pericardial tamponade
   c. portal HTN secondary to portal v. thrombosis

4. Extra pulmonary extravasations of air (subcut. Emphysema)

5. PDA: patent ductus arteriosus
6. IVH( Intraventricular hemorrhage )
7. BPD( bronchopulmonary dysplasia)
Prevention of RDS:

1. Avoidance of unnecessary or poorly timed CS
   a. estimation of fetal head circumference by US
   b. determination of lecithin concentration in the amniotic fluid
2. Appropriate MNX of high risk pregnancy and labor:
   antenatal and intrapartum fetal monitoring, early diagnosis of and reduction of the risks of fetal asphyxia
3. Acceleration of pulmonary immaturity:
   administration of betamethasone to women 48 hrs before delivery of fetuses between 24-34 wks of gestation reduces the incidence, mortality and morbidity of RDS and other complications of prematurity: IVH, PDA, NEC, Pneumothorax
4. Administration of a 1st dose of surfactant into the trachea of symptomatic premature infants immediately after birth (prophylactic) or during the 1st few hours of life (early rescue) reduces air leak and mortality from RDS but does not alter the incidence of BPD.
Prognosis:
Although 85-90% of all infants surviving RDS after requiring ventilatory support with respirators are normal, the outlook is much better for those weighing > 1,500 g. Mortality increases with decreasing gestational age. Prolonged ventilation, IVH, pulmonary hypertension, cor pulmonale, severe asphyxia, intracranial hemorrhage, or irremediable congenital malformation and oxygen dependence beyond 1 yr of life are poor prognostic signs.
IVH

- 30% of LBW less than 1500 gm will have IVH, the risk is inversely related to the gestational age, predisposing factors include:
  - prematurity, RDS
  - hypoxic or hypotensive injuries
  - increase or decrease cerebral blood flow
  - increased venous p, HTN, hypervolemia
  - pneumothorax, ↓PLT

IVH occurs in the gelatinous subependymal germinal matrix, this area is the site of origin of embryonal neurons and fetal glial cells which migrate to the cortex
• CL MNS:
  most patients with IVH have no clinical symptoms
  Apnea, pallor or cyanosis, poor sucking, abnormal eye signs, high pitched shrill cry, convulsions, hypotonia, metabolic acidosis, shock, a decreased HCT or failure of the HCT to increase after transfusion may be the 1st indications

Grading of IVH:
  I  bleeding confined to subependymal GM or to less than 10% of the ventricle
  II  IV bleeding with 10-15% filling of the ventricles
  III more than 50% involvement of the ventricles
Diagnosis of IVH:

as the clinical signs are non specific, its recommended that preterm infants less than 34 wks to be evaluated with real-time cranial US,

less than 1000gm: 1st 3-5 days,

1-1.5 kg: 7-14 days, all at risk: follow up 35-40 wk

10-15% of LBW infants with IVH develop hydrocephalus

MRI is a more sensitive tool for evaluation of extensive periventricular injury and may be more predictive of adverse long-term outcome. CT or, more reliably, diffusion-weighted MRI is indicated for term infants in whom brain injury or stroke is suspected
Treatment:
1. TX of seizures, anemia, coagulopathy, shock, acidosis
2. Serial LP, ventricular tap, externalized ventricular drain
3. VP shunt for progressive and symptomatic Post hemorrhagic hydrocephalus

Prevention:
1. Improved perinatal care (brain trauma, preterm birth)
2. Proper care of LBW resp status, fluid and electrolyte MNX (avoidance of acidosis, hypocarbia, hypoxia, hypotension, wide fluctuations in neonatal blood pressure or $P_{CO_2}$, and pneumothorax—are important factors that may affect the risk for development of IVH and PVL).
3. A single course of antenatal corticosteroids
4. Prophylactic administration of low dose indomethacin, 0.1 mg/kg/day for 3 days reduces the incidence of severe IVH (They inhibit free radical formation and accelerate maturation of germinal matrix vasculature)
Apnea

- Is a common problem in preterm infants. It may be due to prematurity or an associated problem.
- Apnea is cessation of breathing for longer than 20 seconds or any duration if accompanied by cyanosis and bradycardia.
- Apnea is a feature of many primary diseases that affect neonates; these disorders produce apnea by:
  1. direct depression of CNS control of respiration
  2. disturbances in O2 delivery
  3. ventilation defects

Apnea must be distinguished from periodic breathing.
Potential causes of Neonatal Apnea and Bradycardia:

1. CNS: IVH, drugs, seizures, hypoxic injury, herniation, neuromuscular disorders, brainstem infarction or anomalies, after GA
2. Respiratory: pneumonia, obstructive airway lesions, upper airway collapse, atelactasis, extreme prematurity (< 1000 GM), laryngeal reflex, phrenic n palsy, severe RDS, pneumothorax, hypoxia
3. Infections: Sepsis, NEC, meningitis, RSV, pertussis
4. Gastrointestinal: oral feeding, bowel motion, intestinal perforation

5. Metabolic: hypoglycemia, hypocalcemia, hypo hyper Na, ↑ammonia, ↑organic acids, ↑ambient temp, hypothermia

6. Cardiovascular: hypotension, HTN, HF, anemia, hypovolemia

7. Other: Immaturity of respiratory centre
• **Treatment:**

1. infants at risk placed on cardioresp. Monitors
2. gentle tactile stimulation
3. suctioning, bag and mask ventilation, CPAP, Mechanical ventilation
4. Oxygen
5. recurrent apnea of prematurity:
   - Caffeine, Theophylline: increase central resp drive, enhance diaphragm contractility
   - Doxapram: potent resp stimulant acts on peripheral chemoreceptors (side effects)
6. transfusion of packed cells for anemic infant
7. treatment of the underlying cause
Transient Tachypnea of Newborn (TTN)

- Occur in both term or preterm, vaginally delivered or by CS
- There is early onset tachypnea, sometimes with retractions or expiratory grunting, occasionally cyanosis
- Patients usually recover rapidly within 3 days
- The lungs are clear
- CXR: prominent pulmonary vascular markings, overaeration, flat diaphragm
- Hypercapnea and acidosis are uncommon
- TRX: is supportive
• The distinctive features of TTN from RDS:
  1. sudden recovery
  2. the absence of X-ray findings

The condition is believed to be secondary to slow absorption of fetal lung fluid
Meconium Aspiration

- During prolonged labor and difficult deliveries, infants often initiate vigorous respiratory movements in utero because of interference with the supply of O2 through the placenta.
- Under such circumstances the infant may aspirate amniotic fluid containing meconium, which may block the smallest airways and interfere with alveolar exchange of O2 and CO2.
- Meconium stained amniotic fluid is found in 10-15% of births (usually term or post-term infants), meconium aspiration pneumonia occur in 5% of such infants.
• Either in utero or more often with the first breath, thick particulate meconium is aspirated into the lungs resulting in small airway obstruction and respiratory distress within the 1st hours with tachypnea, retractions, grunting, and cyanosis in severe cases (it's also a chemical irritant...... pneumonitis± infection)

• Chest roentgenogram: patchy infiltrates, coarse streaking of both lung fields, increased AP diameter, and flattening of the diaphragm

• Routine intubation to aspirate the lungs of normal infants born through meconium stained fluid IS not recommended, depressed infants (hypotonia, bradycardia, fetal acidosis, or apnea) should undergo endotracheal intubation and suction should be applied directly to the tube to remove meconium from the airway
• Treatment of meconium aspiration pneumonia include:
supportive care
standard management of respiratory distress
mechanical ventilation
exogenous surfactant
HFV, iNO3, ECMO

• Prevention: rapid identification of fetal distress and initiating prompt delivery in the presence of fetal acidosis, late deceleration, or poor beat–to-beat variation

• Amnioinfusion
Necrotizing Enterocolitis (NEC)

- Necrotizing enterocolitis (NEC) is the most common gastrointestinal (GI) medical/surgical emergency occurring in neonates.
- The condition is characterized by variable damage to the intestinal tract ranging from mucosal injury to full-thickness necrosis and perforation.
- NEC affects close to 10% of infants who weigh less than 1500 g, with mortality rates of 50% or more depending on severity. Although it is more common in premature infants, it can also be observed in term and near-term babies.
• Although various clinical and radiographic signs and symptoms are used to make the diagnosis, the classic clinical triad consists of abdominal distension, bloody stools, and pneumatosis intestinalis.

• The distal part of the ileum and the proximal segment of the colon are involved most frequently.

• THE TRIAD OF INTESTINAL ISCHEMIA (INJURY), ENTERAL NUTRITION, AND PATHOGENIC ORGANISMS HAD CLASSICLY BEEN LINKED TO NEC
• The major risk factor for NEC is prematurity
• NEC probably result from an interaction between loss of mucosal integrity due to: ischemia, infection, inflammation, and the host's response to that injury (circulatory, immunologic, inflammatory) resulting in necrosis of the affected area
• Coagulation necrosis is the histological finding of intestinal specimens
• Various bacterial and viral agents (E. coli, Klebsiella, cl. Perfringens, staph epidermidis, and rota virus) have been recovered from cultures, nonetheless; no pathogen is identified in most cases
• Aggressive enteral feeding may predispose to the development of NEC

• Signs & Symptoms:

<table>
<thead>
<tr>
<th>GI</th>
<th>Systemic</th>
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<tbody>
<tr>
<td>Abdominal distension</td>
<td>Lethargy</td>
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<tr>
<td>Abdominal tenderness</td>
<td>Apnea/ respiratory distress</td>
</tr>
<tr>
<td>Feeding Intolerance</td>
<td>Temperature instability</td>
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<tr>
<td>Delayed gastric emptying</td>
<td>(Not right)</td>
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<tr>
<td>Vomiting</td>
<td>Acidosis</td>
</tr>
<tr>
<td>Occult/ gross blood in stool</td>
<td>Glucose instability</td>
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<tr>
<td>Change of stool pattern/diarrhea</td>
<td>Poor perfusion/ shock</td>
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<tr>
<td>Abdominal mass</td>
<td>DIC</td>
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<tr>
<td>Erythema of the abdominal wall</td>
<td>Positive results of blood culture</td>
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• **Diagnosis:**
  1. High index of suspicion
  2. Plain abdominal x-ray: pneumatosis intestinalis, portal vein gass, pneumoperitoneum
  3. Hepatic US: portal venous gas despite normal abd x ray

• **DDX:**
Specific infections, GI obstruction, volvulus, isolated intestinal perforation

• **Treatment:**
  1. Supportive care
  2. Cessation of feeding, nasogastric decompression, IV fluids
3. Careful attention to respiratory status, coagulation profile, acid-base and electrolyte balance

4. Blood culture and antibiotics that covers gram negative, positive and anaerobic

5. Removal of umbilical catheter

6. close monitoring: physical assessment, serial abdominal x-rays

6. Indications of surgery:
   a. evidence of perforation
   b. positive abdominal paracentesis

Failure of medical treatment, a single fixed bowel loop on x ray, abdominal wall erythema, palpable mass are relative indications for surgery
Prevention:
1. Breast feeding
2. minimal enteral feeds followed by judicious volume advancement
3. enteral supplementation of probiotics
4. Prophylactic enteral antibiotics can reduce the risk of NEC, although concerns about adverse outcomes persist, particularly related to the development of resistant bacteria.
Hemorrhagic disease of the newborn

- A moderate decrease in factors II, VII, IX, X normally occurs in all newborn infants by 48-72 hours after birth, this is probably due to lack of free Vit K from the mother and absence of bacterial intestinal flora normally responsible for Vit K synthesis.

- Rarely in term and more frequently in preterm accentuation and prolongation of this deficiency between the 2\textsuperscript{nd} and the 7\textsuperscript{th} days of life result in spontaneous and prolonged bleeding.

- Breast milk is a poor source of Vit K and hemorrhagic complications are more frequent in breast fed than artificially fed infants.
The most common sites of hemorrhage or bleeding are: gastrointestinal, nasal, subgaleal, intracranial, or postcircumcision

**Types:**

1. classic
2. early onset: very rare, 0-24 hr, maternal drugs: phenobarbital, phenytoin, warfarin, rifampin, INH; they interfere with Vit K
3. late-onset vitamin K deficiency (1-6 mo) bleeding include:
   - Malabsorption
   - Hepatitis, biliary atresia
   - Cystic fibrosis
   - Alpha1-antitrypin deficiency
   - Short bowel syndrome
   - Intestinal bacterial overgrowth
   - Chronic exposure to broad spectrum antimicrobials
• DDX:
  1. DIC   2. Inherited coagulopathy

Investigations:
PT, PTT are prolonged
blood coagulation time is prolonged
The levels of factors II, VII, XI, X are low

Prevention of vitamin K deficiency bleeding with intramuscular vitamin K is of primary importance in the medical care of neonates. A single dose of intramuscular vitamin K after birth effectively prevents classic vitamin K deficiency bleeding particularly in term infants.
• Vitamin K is the mainstay for prevention of and treatment of vitamin K deficiency bleeding (VKDB). Other coagulation factors are rarely needed. Severe bleeding may warrant the use of fresh frozen plasma.