

RESPIRATORY DISTRESS SYNDROME (RDS) HYALINE MEMBRANE DISEASE (HMD) PROGRESSIVE NEONATAL ATELECTASIS

I. Etiology

A. Inadequate surfactant production, release

1. Primary surface-active component of surfactant: dipalmitoyl lecithin (dipalmitoyl phosphatidylcholine, disaturated lecithin, disaturated phosphatidylcholine)

a. Composition of pulmonary surface-active material

Lipid	85%	Phosphatidylcholine (lecithin)	75%	Palmitate (disaturated)	71%
Protein	13%	Phosphatidylglycerol	9%	Myristate	6%
CHO	2%	Cholesterol	6%	Monosaturated	14%
		Sphingomyelin	2%		

2. Synthesis

a. Choline incorporation pathway - Pathway I

- 1) Predominant pathway for production of lecithin
- 2) Increased activity at 35-36 weeks gestation (85-90% of gestation)

3. Phosphatidylglycerol (PG) (acidic phospholipid) may be important in stabilizing surfactant

4. Physiologic disturbances which may inhibit surfactant production, cause pulmonary vasoconstriction

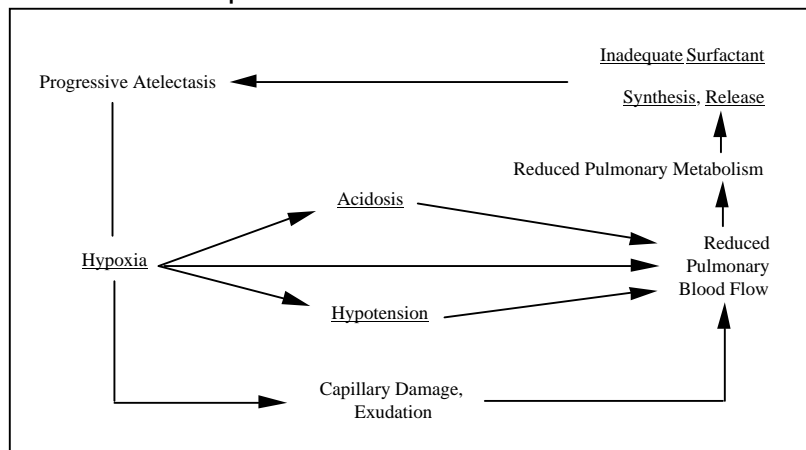
a. Acidosis - pH under 7.25-7.30

b. Hypoxemia - PaO₂ under 50 mmHg

c. Hypotension - hypoperfusion of lungs

← All present
← in perinatal
← distress

5. Cycle of events in patients with RDS



B. Consequences of inadequate surfactant

1. Elevated surface tension - atelectasis
2. Reduced functional residual capacity
3. Increased intrapulmonary absolute or true shunt (R L):
PaO₂, [(A-a) DO₂]

a. (R L) shunt at ductus arteriosus and/or foramen ovale with pulmonary hypertension: PaO₂; a/A ratio [PaO₂/(FIO₂ x 713) - PaCO₂]; [(A-a) DO₂]

4. Increased ventilation/perfusion inequality

5. Decreased compliance
6. Increased work of breathing by 4- to 10-fold
 - a. Increases O₂ consumption
 - b. Increases CO₂ production
 - c. Increases energy expenditure tiring

II. Factors Predisposing to the Development of RDS

- A. Prematurity (under 37-38 weeks gestation) - Most Important
 1. Incidence by gestational age
 - a. 28-30 weeks gestation: 55-65%
 - b. 30-32 weeks gestation: 40-45%
 - c. 33-35 weeks gestation: 20-30%
 - d. 36 or more weeks gestation: 1-5%
 2. Incidence by birth weight
 - a. Under 2500 gm - 15%
 - b. Under 2000 gm - 20-25%
- B. Perinatal distress
- C. Second of twins (vaginal - lack of effect of labor ?)
 1. Intrapartum hemorrhage
 2. Breech presentation (vaginal delivery)
 3. Maternal hypotension
- D. Infants of diabetic mothers (at least those mothers classified as class A, B, C or possibly D)
 1. Five- to sixfold increased risk for RDS
 2. False elevations of L/S, DSL
- E. Cesarean section - procedure, indications for procedure; No Preceding Labor
- F. Familial - surfactant B deficiency, other
- G. Meconium aspiration syndrome
- H. Diaphragmatic hernia
- I. Moderate to severe erythroblastosis fetalis - hydrops fetalis
- J. Male sex

III. Factors, Agents Which May Induce Surfactant Production

- A. Heroin
- B. Prolonged rupture of fetal membranes (PROM) - contradictory data
- C. Antenatal bacterial infection - ?
- D. Severe maternal diseases - placental insufficiency
 1. Diabetes mellitus [classes D(?), E, F, R]
 2. Severe toxemia
 3. Chronic hypertension
 4. Hemoglobinopathies
- E. Antenatal - maternal steroid administration
 1. Amniotic fluid cortisol levels increase after 34-36 weeks gestation
 2. Cord blood cortisol levels higher among infants born to mothers who have been in labor
 3. Elevated cord blood cortisol levels are associated with an absence of RDS; low levels are associated with an increased incidence of RDS
 4. Steroids increase lung lecithin, L/S ratio, number of Type II cells, tracheal flux of surface-active material, and enzymes of choline incorporation pathway
 5. Steroids appear to enhance fetal lung maturation by one or more of the following effects:

- a. Enzyme induction (surfactant, antioxidant)
 - b. Increased cyclic AMP synthesis
 - c. Differentiation of lung cells - maturation of parenchymal structures
 - d. Enhanced water clearance
 - e. Decreased vascular permeability
 - f. Enhanced surfactant response
6. Steroid administration
- a. Indications
 - 1) Premature labor and/or rupture of membranes between 24 and 34 weeks with immature or unavailable L/S ratio
 - or** 2) Gestation over 34 weeks with immature L/S ratio
 - and** 3) Delivery can be safely delayed at least 6 hours (preferably 24-48 hours)
 - 4) Prolonged rupture of membranes ≤ 32 weeks in the absence of clinical chorioamnionitis
 - 5) May repeat dosage weekly for 2-3 courses or until 32-34 weeks
 - b. Contraindications
 - 1) Presence of infection (chorioamnionitis) and/or other indications for immediate delivery (severe antepartum hemorrhage)
 - 2) Presence of maternal conditions for which steroids are contraindicated (chronic intrauterine infection, diabetes mellitus - ?)
 - c. Steroids currently used
 - 1) Betamethasone (Celestone Soluspan): 12 mg IM every 24 hours for 2-4 days; repeat weekly
 - 2) Dexamethasone: 6 mg IM every 6 hours for 2-4 days
 - d. Beneficial effects
 - 1) Enhances surfactant effect
 - 2) Reduces incidence of and mortality from RDS
 - 3) Reduces incidence of IVH - periventricular leukomalacia
 - 4) Reduces incidence of PDA
 - 5) Reduces incidence of necrotizing enterocolitis
 - 6) Higher systemic blood pressure (23-27 weeks)
- F. Theophylline - ?, Prolactin - ?, Thyroxine - ?, TRH - ?, epithelial growth hormone - ? β -adrenergic agents - ?, Interferon

IV. Prevention of RDS

- A. **Term delivery** - most effective means to prevent RDS
- B. Antenatal steroids (see above)
- C. Prevent perinatal distress
- D. Amniotic fluid L/S ratio greater than 2-3:1
 - 1. Perform amniocentesis to determine L/S ratio before elective Cesarean section or induction of labor if unsure of dates
 - a.

<u>L/S Ratio</u>	<u>% RDS</u>
1) $<1.5:1$ - immature	95%
2) $1.5-2.0:1$ - intermediate	47%
3) $>2.0:1$ - mature	2%
4) $2.5-3.5:1$ - infants of diabetic mothers (minimum level) <u>plus</u> PG	
5) Affected by meconium, blood	
 - b. Determine phosphatidylglycerol (PG) (particularly diabetes), disaturated lecithin (cold acetone precipitable fraction)
 - 1) Does not appear to be affected by blood, meconium

- 2) May use vaginal pool samples
- c. Foam stability test ?
- d. Lamellar body counts
- E. Exogenous surfactant production
 - 1. Types
 - a. Genetically engineered human surfactant (genes for protein) - in process
 - b. Human - amniotic fluid (HIV?)
 - c. Cow, bovine (calf) lung (Survanta, Infracurf)
 - d. Porcine (Curosurf)
 - e. Synthetic (e.g., EXOSURF™)
 - 1) Lack of infectious risks
 - 2) No foreign protein
 - 3) Ease of manufacturing
 - 4) Room temperature storage
 - 5) Readily usable (e.g., no vortexing prior to use)
 - 2. Administration of exogenous surfactant
 - a. Time
 - 1) Birth
 - 2) Rescue (first 3-6 hours)
 - b. Route - intratracheal; positive-pressure ventilation not interrupted
 - c. Dosage
 - 1) 67.5 mg/kg dipalmitoylphosphatidylcholine (DPPC) - Exosurf
 - 2) 60-120 mg surfactant
 - 3. Surfactant studies
 - a. Prophylactic (delivery room) vs rescue (within 3-6 hours, established diagnosis)
 - b. Multiple doses required unless $FIO_2 < 0.3$, minimal ventilatory settings
 - 1) 4 doses, each separated by 12 hours (Exosurf)
 - 2) 4-6 doses, each separated by 6 hours (Survanta)
 - c. Cow (Survanta), bovine (Infracurf), porcine (Curosurf) or synthetic (Exosurf)
 - 1) Most effective - surfactant; studies ongoing
 - a) Survanta appears to work more rapidly
 - b) Exosurf may work longer, but is less effective on very immature infants (?)
 - 4. Guidelines for mechanical ventilation during instillation—no interruption
 - a. Maintain PEEP to prevent alveolar closure and facilitate surfactant distribution
 - b. May need to increase P-max (PIP) to maintain chest wall motion
 - c. Reduce P-max after instillation in response to chest wall motion, air entry, $PaCO_2$
 - d. Reduce FIO_2 in response to SaO_2 , PaO_2 levels
 - 5. Beneficial effects of exogenous surfactant administration
 - *a. Reduced mortality from RDS
 - *b. Reduced air leak incidence
 - †c. Improved pulmonary compliance
 - †d. Reduced supplemental oxygen requirements
 - †e. Improved a/A ratio, A-a DO_2 - reduced RDS severity
 - †f. Reduced positive-pressure ventilatory requirements
 - g. Improved x-ray appearance
 - h. Reduced number of NICU days, ancillary charges ?

- i. Reduced incidence of bronchopulmonary dysplasia - ? reduced severity likely
 - j. Reduced incidence of intraventricular hemorrhage - ?
 - k. Reduced cardiopulmonary destruction ?
- *significant effects
† improved pulmonary status

6. Summary of clinical replacement studies (bovine, porcine, synthetic)

	PROPHYLACTIC STUDIES		RESCUE STUDIES	
	Surfactant	Control	Surfactant	Control
Mortality*	12.3%	25.0%	by 50.0%	15-30%
Pneumothorax*	11.4%	29.0%	8.4%	44.0%
PIE*	5.7%	43.5%	6.5%	35.0%
BPD	30.8%	37.3%	19.6%	29.0%
NEC	7.5%	10.3%	7.0%	06.8%
IVH	21.2%	31.3%	30.8%	47.0%
Grade IV IVH	17.1%	21.0%	31.6%	30.5%
PDA	34.9%	32.0%	59.8%	46.0%

*p≤0.05

7. Toxicity of exogenous surfactant administration

- a. Endotracheal tube obstruction
- b. Increased incidence of PDA?
- c. Pulmonary hemorrhage (<1000 gm - PDA)
- f. Apnea? (earlier extubation?)

8. Questions regarding exogenous surfactant administration

- a. Rescue vs prophylactic therapy
- b. Optimal dosage, treatment intervals, number of treatments
- c. Length of response in patients
- d. Lack of response in certain patients
 - 1) Structural immaturity
 - 2) Infection
 - 3) Inhibitors
- e. Effectiveness in lungs with secondary deficiency of surfactant?
- f. Effectiveness in other disorders (e.g., meconium aspiration, diaphragmatic hernia, pneumonia, ARDS) - appears useful
- g. Interaction with endogenous surfactant (mild or no RDS)
- h. Toxicity - ?

V. **Clinical Manifestation of RDS**

- A. Onset: within first six hours after birth
- B. Cyanosis in room air
- C. Downes' or RDS score

RDS Score	0	1	2
Cyanosis	None	In room air	In 40% FIO ₂
Retractions	None	Mild	Severe
Grunting	None	Audible with stethoscope	Audible without stethoscope
Air entry (crying)	Clear	Decreased or delayed	Barely audible
Respiratory rate	Under 60	60-80	Over 80 or apnea

1. Set of five clinical observations to assess severity of respiratory distress

- a. Retractions
- b. Grunting
- c. Air entry
- d. Respiratory rate
- e. Cyanosis

2. Not a substitute for arterial blood gases (pH, PaCO₂, PaO₂)

3. Downes' or RDS scores

- a. ≥4: Respiratory distress

- b. 5-7: CPAP
- c. ≥ 8 : Impending respiratory failure

VI. Radiographic Characteristics of RDS

- A. Diffuse reticulogranular (ground glass) appearance due to atelectasis (Group B β -hemolytic streptococcal pneumonia may have similar appearance)
 - 1. **Hypo-aeration**
 - 2. Thymus often present
- B. Interstitial, intrapulmonary emphysema (PIE)
 - 1. Often precedes pneumothorax
 - 2. Usually signifies severe disease
- C. Cardiac border, diaphragms may be blurred
- D. Complete opacification of lung fields present in severe disease - "white out"

VII. Physiologic Disturbances in Neonates with RDS

- A. Hypoxemia - PaO_2 , $[(A-a) \text{DO}_2]$
 - 1. Intrapulmonary true or absolute shunt (R L shunt)
 - a. 40-80% of cardiac output may be shunted (normally 10-25% shunted)
 - b. No correction of PaO_2 with 100% oxygen
 - 2. Intracardiac true or absolute shunt (R L shunt)
 - a.* Foramen ovale
 - b.* Ductus arteriosus
 - *Pulmonary hypertension
 - 3. Mismatched ventilation to perfusion (V/Q)
 - 4. Diffusion impairment - doubtful except in recovery phase
 - 5. Alveolar hypoventilation due to tiring from increased work of breathing
- B. Acidemia - respiratory plus metabolic
 - 1. $(\text{H}^+) \text{ — pH}$
 - 2. PaCO_2 - respiratory
 - 3. Base deficit (negative base excess) - metabolic
- C. Capillary leakage - pulmonary plus systemic

VIII. Pulmonary Pathology of HMD

- A. Gross: airless, red-purple, liver-like appearance to lungs
- B. Microscopic: diffuse atelectasis with widely scattered, overdistended alveoli
 - 1. Hyaline membranes are pathological hallmark (50 microns thick)
 - a. Appear 8-12 hours after onset of disease
 - b. Line alveolar ducts, terminal bronchioles
 - c. Contain serum proteins, fibrin, RBCs, necrotic and desquamated bronchiolar epithelium
 - 2. Engorged lymphatics
 - 3. Constricted pulmonary arterioles

IX. Differential Diagnosis

- A. Pneumonia (Group B streptococcus, other)
- B. Wet lung syndrome
- C. Aspiration syndrome
- D. Pulmonary edema
- E. Surgical disorder (e.g., pneumothorax, effusion, diaphragmatic hernia)

X. Management

- A. Maintain neutral thermal environment

- B. Monitor vital signs, including central venous and central aortic pressures, Downes' score, input and output, daily weight
 - C. Maintain perfusion by volume expansion (blood pressure, central venous pressure, capillary refill)
 - 1. Maintain mean aortic blood pressure above 25-35 mmHg, depending on gestational age
 - a. Slow infusion of volume expander (5% albumin, fresh frozen plasma, packed RBCs)
 - b. Inotropic agents (dopamine, dobutamine)

$$\text{mg/100 ml} = \frac{\text{ug/kg/min} \times \text{wt in kg} \times 6}{\text{ml/hr}}$$
 - D. Maintain hemoglobin above 13.5 gm% (maximize tissue oxygen delivery)
 - E. Provide fluid, caloric intake
 - 1. Intravascular 10% dextrose in water, often with 400 mg 10% calcium gluconate per 100 ml fluid at 48-72 ml/kg/day during the first day
 - 2. Add electrolytes (Na, K) during the second day after birth
 - 3. Initiate gavage feedings, making appropriate adjustments in total fluid administration if:
 - a. Ileus resolved
 - b. Meconium passage
 - c. $\text{FIO}_2 \leq 0.3-0.4$
 - 4. Initiate parenteral nutrition with fat emulsion to provide calories on second or third day after birth (electrolyte values stabilized)
 - 5. Liberalize fluid restriction after definite improvement has occurred in lung disease
 - a. No PDA
 - b. Sodium and/or BUN/creatinine values are elevated
 - c. Weight loss over 10-15%
 - F. Antibiotics after appropriate cultures
 - 1. Ampicillin: 100-200 mg/kg/day in two divided doses
 - 2. Gentamicin: 2.5 mg/kg/dose every 12-24 hours
 - 3. Cefotaxime: 150 mg/kg/day in two divided doses
 - 3. Discontinue after 48-72 hours if cultures are negative—unless clinical situation dictates otherwise
- plus*
or

G. Monitor arterial blood gases

1. Arterial blood gases

Normal	Respiratory Failure
pH: 7.30-7.40	<7.20
PaCO ₂ : 35-40 mmHg	>55-65 mmHg
PaO ₂ : 60-90 mmHg (room air)	<50-60 mmHg in 40-50% oxygen
O ₂ saturation (SaO ₂) >90-92% (87-93% if below 28 weeks >92% with chronic lung disease >95% pulmonary hypertension)	<85%

2. Maintain pH: 7.30-7.45

a. Metabolic acidosis

1) Volume expansion

2) NaHCO₂ (mEq): Body weight in kg x 0.3 x base deficit
from Sigard-Anderson nomogram or 0.5-2 mEq/kg

a) Dilute to at least 0.5 mEq/ml

b) Infuse at a rate no greater than 1 mEq/kg/min

b. Respiratory acidosis

1) Positive-pressure ventilation to improve alveolar ventilation

2) NaHCO₃ may cause further PaCO₂ elevation if ventilation inadequate

3. Maintain PaCO₂: 30-45 mmHg

4. Maintain PaO₂: 50-90 mmHg (SaO₂ >92%)

a. Monitor PaO₂ with an umbilical or peripheral arterial catheter or by percutaneous artery puncture, or SaO₂ by pulse oximetry

b. Deliver warmed, humidified oxygen (headbox) to relieve cyanosis

c. Lower inspired oxygen concentrations only by small decrements; measure PaO₂ 15-20 minutes after every change, or monitor oximeter

d. Visual guide to oxygenation should be used for only a short time

1) PaO₂ may reach 32-42 mmHg before central cyanosis appears

2) Hyperoxia cannot be detected

e. Toxicity of oxygen

1) Inspired oxygen damage to lungs

2) Retinopathy of prematurity??? (multiple factors)

H. Provide assisted ventilation

1. Continuous positive airway pressure (CPAP): nasal tube or prongs, endotracheal tube (face mask, head hood - intracranial hemorrhage?) - may delay positive-pressure ventilation

a. Indications

1) Spontaneous ventilatory efforts

and 2) Absence of severe apneic episodes

and 3) Normal or nearly normal PaCO₂

with 4) Downes' score of 5-7

and/or 5) PaO₂ under 60 mmHg in 45-50% oxygen

2. Mechanical ventilation with end-expiratory pressure (PEEP): endotracheal tube

a. Indications

1) Severe apneic episodes or gasping, slow respiratory efforts

2) Shock

3) PaCO₂ above 60-65 mmHg or PaCO₂ rapidly rising with pH below 7.25

4) PaO₂ below 60 mmHg in 60% oxygen (CPAP 6 cm H₂O)

5) Persistent metabolic or respiratory acidosis with pH under 7.20

- and/or 6) Downes' score ≥ 8
3. Initial ventilatory settings (pressure-limited, time-cycled)
 - a. Pmax: 20-30 cm H₂O
 - b. PEEP: 4-5 cm H₂O
 - c. Rate: 30-50/minute
 - d. Inspiratory time: 0.3-0.4 seconds
 - e. FIO₂: 0.3-1.0
 4. Newer methods of ventilatory management
 - a. High frequency
 - 1) High-frequency positive-pressure ventilation
 - 2) High-frequency jet ventilation (?)
 - 3) High-frequency oscillatory ventilation
 - 4) Liquid ventilation
 - b. Nitric oxide inhalation
 - 1) 10-20 ppm
 - 2) Pulmonary hypertension
 - c. Extracorporeal membrane oxygenation (ECMO) - "bridge" support
 - 1) Weight above 2000 gm, gestational age above 34 weeks
 - 2) Reversible lung disease
 - 3) Severe hypoxemia [MAP X FIO₂ X 100/postductal PaO₂] $\geq 40-45$ (oxygenation index) despite maximal ventilatory therapy
- I. Be alert to presence of **patent ductus arteriosus**
1. Clinical (may or may not be present)
 - a. Systolic or continuous murmur may or may not be present
 - b. "Brisk" or bounding pulses
 - c. Active precordium
 - d. Gallop and/or hepatomegaly may be present
 - e. Worsening of respiratory status (CO₂ retention and/or hypoxemia) requiring increased ventilatory support or supplemental oxygen
 2. Laboratory
 - a. Chest x-ray: cardiac enlargement with or without pulmonary edema may or may not be present
 - b. **Echocardiogram**
 3. Management
 - a. Fluid restriction to less than 90-100 ml/kg/day
 - b. Maintain hemoglobin above 13.5 gm%
 - c. Maintain PaO₂ 60-90 mmHg
 - d. Maintain normal calcium levels
 - e. Administer furosemide (Lasix), 1-2 mg/kg IV q12-24h, or as necessary
 - f. Consider prostaglandin inhibitor (**Indomethacin**) administration, 0.1 (<1250 gm) to 0.2 mg/kg/dose q12h for three doses, with each dose followed by furosemide
 - 1) Infuse over 4-6 hours
 - 2) May infuse continuously (below 1250 gm)
 - 3) May give 0.1 mg/kg over 4-6 hours daily for 7 days for infants <1250 gm
 - g. Consider ligation of PDA if patient cannot be weaned substantially from ventilatory support after 24-72 hours of medical therapy or if PDA recurs after Indomethacin (approximately 33%)
- J. Postnatal steroids
1. Initiation
 - a. Day 1-3 (ELBW infants - <750 gm)

- 1) Blood pressure support
- b. Evidence of chronic lung disease
- c. Wean from ventilator, oxygen support
- d. Extubation (?)
- 2. Dosage
 - a. 0.1-0.5 mg/kg/day in two divided doses (Dexamethasone)
- 3. Length of treatment
 - a. 3-7 days, then taper
 - b. 2-3 weeks, then taper
 - c. 6 weeks, then taper
 - d. 4-6 doses (extubation)
- 4. Complications - potential side effects
 - a. Brain growth inhibition
 - b. Cardiomyopathy
 - c. Retinopathy of prematurity
 - d. Altered pituitary-adrenal axis responsiveness
 - e. Infection (bacterial, fungal, viral)
 - f. Hyperglycemia
 - g. Hypertension
- K. Sedation - pain control
 - 1. Narcotics
 - a. Fentanyl: 10-15 µg/kg bolus → 3-5 µg/kg/h
 - b. Morphine: 0.1 mg/kg IV q3-6h or 6-15 µg/kg/h (hypotension)
 - 2. Anxiety relief sedative
 - a. Lorazepam (Ativan): .03-.05 mg/kg/dose q6h (most cost effective)
 - b. Midazolam (Versed): 0.05-0.2 mg/kg/dose
 - 3. Sedative
 - a. Chloral hydrate: 30-50 mg/kg/dose q4-6h
 - 4. Neuromuscular blocking agents
 - a. Vecuronium: 0.1 mg/kg/dose
- L. Monitor bilirubin level - phototherapy
- M. Monitor for intraventricular hemorrhage, periventricular hemorrhage
- N. Monitor for necrotizing enterocolitis when enteral feedings are started

XI. Prognosis

A. Survival rate

1. By birth weight

Birth Weight (gm)	Survival Rate (%)
<1000	40-60
1000-1499	60-95
<1500	60-80
1500-2000	85-95
>2000	90-95
Overall	85-95

2. By mode of therapy

Therapy	Percentage Survival
Oxygen alone	90-100%
CDP (CPAP)	90-100%*
PEEP	70-90%*

*70-95%

3. Lowest survival rates

- a. Under 26 weeks gestation
- and b. Under 750 gm

- plus* c. Mechanical ventilation
- B. Major factors associated with later neurosensory impairments, including mental retardation
 - 1. Birth weight below 750 gm
 - 2. Gestational age below 25 weeks
 - 3. Inadequate nutrition
 - 4. Intraventricular hemorrhage - parenchymal; ventricular dilatation
 - 5. Periventricular leukomalacia - intraparenchymal echodensity
 - 6. Severe perinatal distress with seizures, abnormal tone, encephalopathy
 - 7. Severe, recurrent, symptomatic hypoglycemia
 - 8. Chronic lung disease (bronchopulmonary dysplasia) - ventilator support, oxygen
 - 9. Socioeconomic-environmental factors, maternal education
 - C. Neurodevelopmental outcome of infants with birth weights below 750-800 gm
 - 1. 22-35% incidence of significant handicaps among survivors
 - 2. Multiple sensory and neurodevelopmental handicaps (nearly 10% are blind from ROP)
 - 3. Combined results: 5-35% with handicaps
 - 4. 50-60% with school-related learning, behavioral problems
 - D. Follow-up at seven years necessary for learning disabilities, behavioral disorders
 - E. Pulmonary
 - 1. Absence of bronchopulmonary dysplasia
 - a. Hypoxemia, hypercarbia, reduced compliance and/or functional residual capacity disappear by 12 months
 - b. Increased airway resistance may be present if positive-pressure ventilation used in treatment
 - c. Probably no increased incidence of lower respiratory tract infections
 - d. Radiographic abnormalities may persist for over one year
 - e. Asthma may develop, particularly if family history positive
 - F. Presence of bronchopulmonary dysplasia (BPD)
 - 1. Incidence (5-70%) increases as gestational age/birth weight decreases, and as severity of underlying lung disease increases
 - 2. Primarily limited to infants requiring positive-pressure ventilation, oxygen
 - 3. Increased incidence of respiratory infections for 1-3 years, asthma
 - 4. Abnormal x-rays may persist
 - 5. Many patients are asymptomatic by school age, except asthma
 - 6. Therapy: Nutrition, bronchodilators, diuretics, oxygen; steroids for severe disease (inflammation?)
 - G. Growth patterns
 - 1. Most appropriate-for-gestational-age premature infants above 1000 gm birth weight have normal growth patterns after 1-3 years postnatal age
 - 2. Small-for-gestational-age infants and infants below 750 gm birth weight may never reach 50th percentile for growth, or reach this percentile only after 5-6 years
 - H. Visual deficits
 - 1. Retinopathy of prematurity - primarily below 1000 gm birth weight, 29 weeks gestation
 - a. Incidence: 70-75%
 - b. Blindness: 5-10%
 - 2. Suggested ophthalmologic examinations for retinopathy of prematurity (ROP)

- a. Skilled ophthalmologist - pediatric disorders including ROP
- b. Below 1800 gm and/or below 35 weeks gestational age: before discharge
- c. Below 1300 gm or 30 weeks, medically stable: 4-7 weeks postnatal age
- d. Greatest detection of abnormalities: 6-9 weeks postnatal age (below 29-30 weeks gestational age at birth) or 32-34 weeks corrected age
- e. Abnormal clinical features
- I. Hearing deficits: 1-10% in premature infants
 - 1. High-risk factors
 - a. Diuretics
 - b. Antibiotics
 - c. Positive-pressure ventilation (endotracheal tube)
 - d. NICU noise
 - e. Cytomegalovirus
 - f. Hyperbilirubinemia
 - g. Family history
 - h. Persistent pulmonary hypertension
 - i. Hypoxia
 - 2. Screening test: Auditory brainstem response
- J. Speech, dentition disorders
 - 1. Intubation
 - 2. Endotracheal tube
- K. Child abuse/neglect
 - 1. The LBW infant is at least three times more likely to be subjected to physical abuse and neglect, compared with the full-term, AGA infant
 - 2. Risk factors include inadequate support structure, family history of child abuse, serious marital problems, inadequate child spacing, inadequate child care arrangements, unplanned or unwanted pregnancy, and apathetic and dependent personality types
- L. Other complications
 - 1. Short-term
 - a. Malposition of endotracheal tube (right mainstem bronchus, esophagus)
 - b. Obstruction of airway
 - c. Extubation
 - d. Hemorrhage
 - e. Gastric distention
 - f. Air leak
 - g. Respiratory alkalosis, acidosis
 - h. Mechanical failure of ventilator
 - i. Infection - nosocomial
 - 2. Long-term
 - a. Subglottic stenosis
 - b. Vocal cord injury
 - c. Hoarseness, stridor
 - d. Nasal, palatal, facial deformities
 - e. Seventh nerve palsy
 - f. Bronchospasm
 - g. Peptic ulcer

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RDS - BPD

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