Chronic Lung Disease (Bronchopulmonary Dysplasia)

was first described in 1967 as severe chronic lung disease (CLD) in preterm infants with severe Respiratory Distress Syndrome (RDS) who received treatment with 100% O_2, high inspiratory ventilator pressures and no PEEP. With antenatal glucocorticoids, surfactant treatment and improved ventilatory techniques, CLD has almost disappeared in larger preterm infants and now affects very preterm infants with or without antecedent RDS.

DEFINITION: CLD is defined as a **need for increased oxygen:**

- Infants <32 weeks gestation: **oxygen requirement at 36 weeks gestational age (GA) or at discharge** (whichever comes first)
- Infants ≥32 weeks GA: **oxygen requirement at age >28 d or at discharge** (whichever comes first)

INCIDENCE of CLD is inversely related to birth weight and GA:

Birth weight (g)	Incidence of CLD*
501-750	34%
751-1,000	20%
1,001-1,250	5%
1,251-1,500	3%

*UCSF 1998-2002

PATHOLOGY includes areas of atelectasis and emphysema, hyperplasia of airway epithelium and interstitial edema. Late changes include interstitial fibrosis and hypertrophy of airway smooth muscle and pulmonary arteriolar musculature.

ETIOLOGICAL FACTORS include:

- **Lung immaturity** with (a) ↑ susceptibility to damage from oxygen, barotrauma and volutrauma, (b) surfactant deficiency and (c) immature antioxidant defenses.
- **Oxygen toxicity**
- **Barotrauma** and **volutrauma**
- **Pulmonary edema** (excessive fluid administration, patent ductus arteriosus)
- **Inflammation** (multiple associated biochemical changes)

RISK FACTORS include:

1. Maternal:

- Chorioamnionitis
- Abruptio placenta
- No antenatal steroids
- Prenatal indomethacin
- Intrauterine growth retardation

2. Neonatal:

- Prematurity (<28 weeks GA)
- Male gender
- Severity of RDS
- Patent ductus arteriosus
- Lung disease (CDH, pulmonary hypoplasia)
- Risk: ↑ in Caucasians, ↓ in African-Americans
- Birth weight <1,000 g
- Low Apgar scores
- Air leaks
- Infection
- Genetic factors

CLINICAL FEATURES:

- Hypoxia due to V/Q mismatch
- ↑ work of breathing

- Abnormal chest radiograph
- Pulmonary hypertension
- ↑ airway resistance is late feature
- Cor pulmonale (late)

PREVENTIVE MEASURES:

- **Minimize barotrauma & volutrauma** by using low ventilator inspiratory pressures and tidal volumes. Tolerate mild hypercarbia ($PaCO_2$ ≤55 mm Hg). Higher PEEP (*e.g.*, 6 cm H_2O) may help prevent CLD. Early extubation and nasal CPAP may help, but benefit has not been proven.
- **Minimize oxygen toxicity**: Maintain O_2 saturation between 85 and 92% in preterm babies. Higher O_2 saturation also ↑ risk of Retinopathy of Prematurity (ROP).
- **Careful attention to intake of fluid and Na^+.** Mild hyponatremia in small preterm infants is common, is tolerated well and is not an indication to ↑ Na^+ intake.

TREATMENT of ESTABLISHED CLD:

- **Adequate caloric intake** (140-160 kcal/kg/d) because of ↑ work of breathing
- **After 36 weeks GA, maintain O_2 saturation >95%** to prevent pulmonary hypertension and cor pulmonale. (Low risk of ROP after 36 weeks GA). Some infants with CLD will require O_2 therapy after discharge.
- **Restrict intake of fluid and Na^+.** Hyponatremia with serum sodium ≤125 mEq/L should be treated with fluid restriction, not diuretics and ↑ administration of Na^+.
- **Diuretics**, especially furosemide. Do not use unless there already is restricted intake of fluids and Na^+. Side effects are common and include **hypercalciuria** (leading to osteopenia, & nephrocalcinosis), **metabolic alkalosis** (due to Cl^- loss) and **hypokalemia.** Alternate day diuretics may be effective with fewer side effects.
- **Bronchodilators** may be effective. Pulmonary function testing to document bronchoconstriction prevents unnecessary use of these drugs. "Tightness" or "clamping down" diagnosed by auscultation is often due to atelectasis, not bronchoconstriction.
- **Steroids** are **almost never indicated in CLD**, rarely have any lasting benefit and significantly ↑ **the risk of adverse neurologic outcome.** Steroids should **be used only in very severe CLD** (*e.g.*, infant on high O_2 and high ventilator settings who is worsening). Other side effects include systemic hypertension, adrenal suppression, infection, growth suppression and cardiac hypertrophy.
- **Infection prevention:** Immunization against RSV infection (see section on Immunizations, P. 71).

OUTCOME:

1. **Mortality** with severe CLD is ~25%. Main causes of death are cor pulmonale, lower respiratory tract infection and sudden death.
2. **Long term complications** are common and include:
   - Respiratory: Recurrent infections, central apnea, bronchial hyper-reactivity
   - Cardiovascular: Pulmonary hypertension, cor pulmonale, bronchopulmonary shunts
   - Growth delay
   - GI**:** Feeding difficulties, GE reflux, aspiration
   - Associated conditions (but unlikely due to CLD): hearing loss, developmental delay, cerebral palsy, intraventricular hemorrhage and white matter CNS damage.