# Respiratory distress syndrome (pediatrics)

This article has been translated from WikiSkripta; ready for the **editor's review**.

**Respiratory Distress Syndrome** (RDS) is caused by anatomical and functional immaturity of the lungs - a lack of surfactant. It almost exclusively affects premature newborns. It manifests clinically immediately after birth as rapidly progressing respiratory insufficiency. The incidence and severity of RDS is inversely proportional to the gestational age of the newborn. Treatment measures include the use of distension ventilatory support CPAP (*Continuous Positive Airway Pressure*), early administration of surfactant, gentle ventilation, diagnosis and treatment of open Botall's duct (PDA), and others. Lung maturation can be accelerated by administrating corticosteroids to a pregnant woman prior to delivery. The uncomplicated course of RDS usually lasts 3-5 days.[1][2]

**Transient tachypnea of the newborn** (TTN) or *wet lung syndrome* is caused by prolonged purging the lungs of lung fluid. It occurs in premature babies, but also in some mature newborns after Caesarean section, after asphyxia, and in newborns of diabetic mothers. Symptoms of respiratory distress are evident from birth, sometimes requiring ventilatory support, usually resolving quickly.[2]

## Pathophysiology

In children with RDS who are not treated with surfactant administration, **necrosis of the epithelial cells of the alveoli** occurs as early as half an hour after birth. Epithelial cells peel away from the basement membrane and form **clusters of hyaline membranes**. At the same time, diffuse **interstitial edema** occurs. Lymphatic vessels are dilated due to delayed absorption of fluid in the lungs. Within 24 hours, there is an extensive generalized formation of membranes, which accumulate mainly in the terminal and respiratory bronchioles, especially at the branching point of the airways. **Alveoli are collapsed** and are not lined with these membranes. Hyaline membranes are made up of debris from dead pneumocytes, coagulated plasma proteins released from damaged capillaries, and exudated fibrin. In unconjugated hyperbilirubinemia they may be yellow in colour.[3]

**After 24 hours**, the first **macrophages** begin to appear in the lumen of the airways, and within the next 2-3 days, they **absorb the membranes**. After 48 hours, the **epithelium begins to renew**, and surfactant begins to appear on the alveoli's surface. In the uncomplicated course of RDS, **the hyaline membranes disappear by the 7th day of life**. In ventilated children, however, healing occurs more slowly and causes scarring and fibrosis of the alveoli and airways under the guise of bronchopulmonary dysplasia.[3]

**A very immature neonate** has lungs still in the saccular stage of development with a relatively small internal surface area and a large proportion of interstitial tissue. Functional immaturity is manifested by an insufficient ability to maintain functional residual volume (FRC) based on **insufficient surfactant production**. The result is **focal atelectasis surrounded by foci of tissue hyperinflation** which produce a typical granular pattern on the X-ray image.[2]

**Surfactant,** which is found inside the alveoli of the lungs, prevents the alveoli from collapsing at the end of expiration by reducing their surface tension. Its production begins in the second half of pregnancy (from the 24th to the 28th week of pregnancy)[4] in the endoplasmic reticulum of the type II pneumocytes which secrete it to the inner alveolar surface and reabsorb it for recycling. Surfactant consists of approximately 90% phospholipids (mainly lecithin and phosphatidylglycerol) and 10% proteins.[2][1]

Type II pneumocytes are susceptible to asphyxia. Their maturation is delayed in fetal hyperinsulinemia and on the contrary accelerated by antenatal administration of corticosteroids and chronic intrauterine stress (gestational hypertension, IUGR, twin pregnancy ).[4]

Shortly after birth, a right-left shunt through the foramen ovale predominates, which can worsen hypoxemia. After 18–24 hours, the left-right shunt through the PDA becomes dominant due to the decreasing pulmonary vascular resistance, which causes pulmonary edema and impairs alveolar gas exchange. Administration of surfactant during this period may worsen the condition.[4]

The **risk factors for RDS** include: immaturity, male sex, family predisposition, caesarean section before spontaneous onset of labor, perinatal asphyxia, chorioamniitis, multiple pregnancy, maternal diabetes mellitus.[4]

## Clinical picture

Immediately after birth, the development of symptoms of respiratory distress:

- **tachypnea** = accelerated breathing, respiratory rate > 60/min.;
- **dyspnoea** = difficult breathing, which is manifested by the contraction of the intercostal spaces and attachment of the diaphragm during inspiration and the lifting of the nasal wings ("alar flexion");
- **grunting** = a sound phenomenon produced by exhalation against a closed glottis, helps to maintain positive pressure in the airways, i.e. to maintain functional residual capacity (FRC).
- Tachycardia – heart rate > 160/min
- Central cyanosis - decreased saturation value during pulse oximetry.[2]

# Examination

- ABB: hypoxemia, hypercapnia, mixed acidosis;
- X-ray of the lungs: a typical image of RDS - reticulogranular pattern and reduced transparency up to complete obscuration of the lungs ("white lung").[2]
- Examination of the blood count and inflammatory parameters to rule out sepsis.
- Glycemia - hypoglycemia may be accompanied by tachypnea and symptoms of respiratory distress.[4]

# Complications

- septicemia, pulmonary interstitial emphysema, pneumothorax, pneumomediastinum, pneumoperitoneum, pneumopericardium, pulmonary apoplexy, apnea/bradycardia, bronchopulmonary dysplasia (BPD), patent Botall's duct (PDA), persistent pulmonary hypertension of the newborn, necrotizing enterocolitis (NEC), retinopathy of prematurity (ROP), hypertension, failure to thrive, intracranial hemorrhage, periventricular leukomalacia (PVL).[5][1]

# Treatment

- symptomatic: oxygen therapy (humidified heated oxygen), possibly ventilatory support (nasal CPAP, artificial pulmonary ventilation), infusion therapy;
- causal: intratracheal administration of surfactant;
  - prophylactic administration of surfactant immediately after birth is recommended for extremely immature newborns, especially if lung maturity has not been induced and if they require intubation in the delivery room;
- if an infection is suspected, antibiotic therapy, if there are signs of circulatory failure, circulatory support (volume expansion, catecholamines);
- prevention: induction of lung maturity *in utero* - by administering corticosteroids (e.g. *Diprophos, Dexona*) to pregnant women before delivery.[2][4]

# European Consensus Guideline (2019)[6]

### Prenatal care

1. Mothers at risk of preterm delivery < 28 to 30 weeks' gestation should be transferred to perinatal centers experienced in RDS care (C1).
2. All women at risk of preterm delivery of a potentially viable fetus before 34 weeks' gestation should be offered antenatal administration of a single course of corticosteroids, ideally at least 24 hours before delivery (A1).
3. Administration of the corticosteroid bark can be repeated 1x in case of threatened premature birth before the 32nd week of pregnancy, if the first bark was administered at least 1-2 weeks ago (A2).
4. MgSO4 should be given to women in impending labor before the 32nd week of pregnancy (A2).
5. In women with symptoms of preterm labor, cervical length and fetal fibronectin should be measured, to prevent stillbirths, short-term administration of tocolytics should be considered, which would allow for a full course of corticosteroids and/or "in utero" transfer to a perinatal center ( B1).

### Stabilization in the delivery room

1. Delay umbilical cord cutting for at least 60 s to promote placental-fetal transfusion (A1).
2. Stabilize spontaneously breathing newborns using CPAP with at least 6 cm of H2O through a face mask or nostrils (B1). Do not use *sustained inflation* because it has no long-term benefit (B1). Newborns with persistent apnea or bradycardia should be given positive-pressure lung inflations with peaks of 20-25 cm H2O (peak inspiratory pressure, PIP).
3. A blender should be used when administering oxygen for resuscitation. Use FiO2 0.3 initially for neonates < 28 weeks gestation, FiO2 0.21-0.3 for neonates between 28 and 31 weeks gestation, and FiO2 0.21 after 32 weeks gestation. FiO2 should be adjusted according to pulse oximetry values (B2).
4. In newborns < 32 weeks of gestation, SpO2 of 80% or more (and heart rate > 100/min) should be achieved within 5 minutes (C2).
5. Intubation should only be performed in newborns who do not respond to positive pressure ventilation via a face mask or nostrils (A1). Children who require intubation when stabilized in the ward should be given surfactant (B1).
6. When stabilizing children < 28 weeks of gestation in the delivery room, plastic bags or foils and a radiator (radiant warmer) should be used to reduce the risk of hypothermia (A1).

### Treatment with surfactant

1. Children with RDS should be given surfactant of animal origin (A1).
2. Standard practice should be to give surfactant early if needed (*early rescue surfactant*) (A1), but there are situations where surfactant should be given in the delivery room, such as when intubation is needed during postpartum stabilization (A1) .
3. Children with RDS should be given surfactant early in the course of the illness. The proposed procedure is to treat children who deteriorate at FiO2 > 0.3 on CPAP with a pressure of at least 6 cm H2O (B2).
4. For rescue treatment, poractant alfa with an initial dose of 200 mg/kg is better than 100 mg/kg poractant alfa or 100 mg/kg beractant (A1).

5. LISA is the preferred method of administering surfactant to spontaneously breathing children on CPAP if physicians are experienced with this technique (B2).
6. A second and rarely a third dose of surfactant should be given if signs of RDS such as persistent high oxygen demands persist and other problems have been ruled out (A1).

**Oxygen administration after stabilization**

1. Preterm infants receiving oxygen should have target saturations between 90 and 94% (B2).
2. Alarm limits should be set to 89 and 95% (D2).

**Non-invasive respiratory support**

1. CPAP should be started after birth in all children at risk of developing RDS, i.e. in children < 30 weeks of gestation who do not require intubation for stabilization (A1).
2. The CPAP delivery system is not so important, however, short nostrils (*binasal prongs*) or a mask with an initial pressure of about 6-8 cm H2O should be used (A2). The positive end-expiratory pressure (PEEP) can then be adjusted according to the clinical picture, oxygenation and perfusion (D2).
3. CPAP with early rescue surfactant if necessary (*early rescue surfactant*) is considered the optimal treatment for children with RDS (A1).
4. Synchronized NIPPV (nasal intermittent positive pressure ventilation), which is delivered via a ventilator rather than a BIPAP machine, may reduce extubation failure but may not have a long-term benefit such as a reduction in bronchopulmonary dysplasia (BPD) (B2).
5. During weaning from ventilatory support, HFNC may be used as an alternative to CPAP in some children; the advantage of HFNC is less trauma to the nose (B2).[6]

**Strategy of mechanical ventilation**

1. After stabilization, mechanical ventilation should be used in children with RDS when all other methods of ventilatory support have failed (A1). Mechanical ventilation should last as little time as possible (B2).
2. The choice of ventilation mode is at the discretion of the clinical team, however, when using conventional ventilation, targeted tidal volume should be used (A1).
3. When weaning mechanical ventilation, it is reasonable to tolerate mild hypercapnia if the pH is above 7.22 (B2).
4. Caffeine (A1) should be given to support withdrawal of mechanical ventilation. Early administration of caffeine should be considered in children at risk of needing mechanical ventilation, such as children on noninvasive ventilatory support (C1).
5. A short course of low- or very-low-dose dexamethasone with gradual withdrawal should be considered to promote extubation in children who require mechanical ventilation for more than 1-2 weeks (A2).
6. Inhaled budesonide may be considered in children at high risk for BPD (A2).
7. Opioids can be used individually if indicated based on clinical judgment or pain indicator evaluation (D1). Routine use of morphine and midazolam in ventilated preterm infants is not recommended (A1).

**Monitoring and supportive treatment**

1. Core body temperature (eg rectal) should always be maintained between 36.5 and 37.5°C (C1).
2. Most children should initially receive 70-80 mL/kg/day of intravenous fluids when treated in a humidified incubator, although some very immature children may need more (C2). The amount of fluids must be adjusted individually according to the serum sodium level, diuresis and weight loss D1).
3. Parenteral nutrition should be started from birth. 1-2 g/kg/day of amino acids should be administered on the first day and rapidly increased to 2.5-3.5 g/kg/day (C2). Lipids should be administered from day 1 and increased to a maximum of 4 g/kg/day if tolerated (C2).
4. Enteral feeding with breast milk should be started from the first day if the child is hemodynamically stable (B2).

**Blood pressure and perfusion**

1. Treatment of hypotension is recommended for definite signs of poor tissue perfusion, such as oliguria, acidosis, and poor capillary return rather than based on numerical values alone (C2).
2. If an attempt at therapeutic closure of the patent ductus arteriosus (PDA) is indicated, indomethacin, ibuprofen or paracetamol can be used (A2).
3. Hemoglobin (Hb) concentration should be maintained within acceptable values. The limit for children with severe cardiopulmonary disease is 12 g/dl (HTK 36%), for oxygen-dependent children 11 g/dl (HTK 30%) and for stable children older than 2 weeks 7 g/dl (HTK 25%) (C2 ).

**Other**

1. Surfactant can be used in RDS complicated by congenital pneumonia (C2).
2. Surfactant can be used to improve oxygenation after pulmonary hemorrhage (C1).
3. In premature children, iNO should be used with caution and only in children enrolled in clinical trials or in a therapeutic trial with proven severe pulmonary hypertension (D2).[6]

# Links

## Related Articles

- Neonatal pneumopathy

## External links

- V. Vobruba: Neonatal pneumopathy (http://www.vfn.cz/pracoviste/kliniky-a-oddeleni/klinika-detskeho-a-dorostoveho-lekarstvi/)
- European Consensus Guidelines on the Management of Respiratory Distress Syndrome - 2019 Update (https://www.ncbi.nlm.nih.gov/pubmed/30974433)
- Clinical Image: "Recognizing Respiratory Distress" by Monica Kleinman, MD for OPENPediatrics (https://www.youtube.com/watch?v=Fmt6JB-W_M8)

## References


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