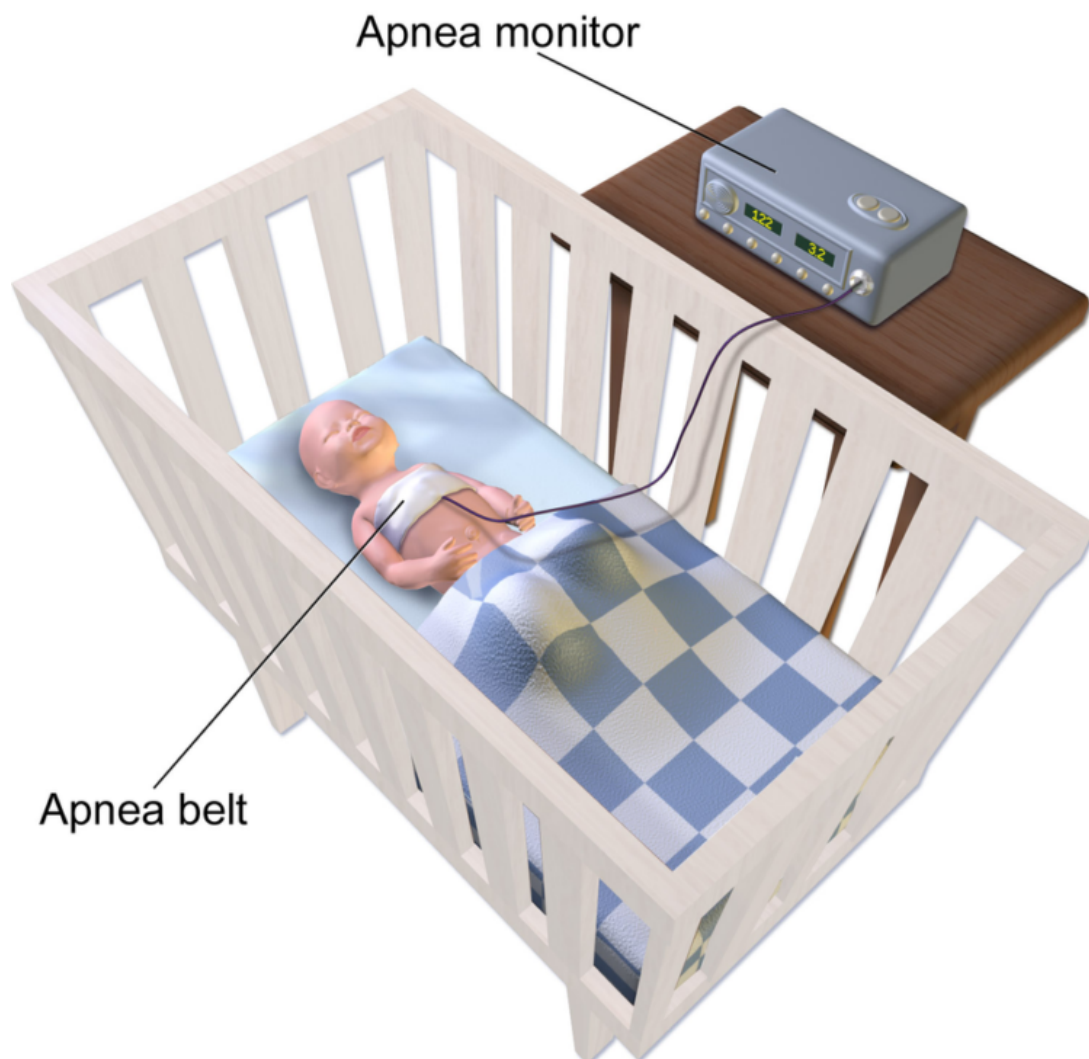


Apnea of Prematurity — Treatment and Guidelines

[See online here](#)

Apnea of prematurity is a condition that is believed to be caused by the immaturity of the respiratory center in the brainstem of premature babies and is characterized by periods of apnea that are longer than 20 seconds. Apnea that is less than 20 seconds but associated with significant bradycardia and/or oxygen desaturation can be also considered as apnea of prematurity. A full diagnostic workup to exclude sepsis, seizures, intracranial hemorrhage and other causes of apnea should be performed. Tactile stimulation is usually sufficient for mild apnea. Oxygen supplementation might be needed in moderate cases of apnea while medical treatment should be provided to severe cases.



Overview

Apnea can be defined as the **cessation of breathing for more than 20 seconds** or the cessation of breathing for less than 20 seconds that is accompanied by a **slow heart rate** or a **decrease in oxygen saturation**.

Bradycardia in a premature neonate is defined as a heart rate that is less than the resting heart rate by 30 bpm or more. Any oxygen saturation level that is below 85% is considered as pathologic in premature newborns.

Apnea of prematurity can be further classified into central, obstructive or mixed apnea.

- **Central apnea** is characterized by complete cessation of respiration, cessation of airflow and cessation of respiratory effort.
- When airflow is ceased but the neonate still shows a continued respiratory effort, the term **obstructive apnea** is used.
- Most premature neonates who develop apnea of prematurity have a **mixed form of central and obstructive elements**.

When this same presentation happens in a full-term infant, the term **apnea of infancy** is used. The pathophysiology of apnea of infancy is believed to be like apnea of prematurity but the condition is not fully studied or explored.

- Cessation of breathing > 20 seconds
- 90 % of infants under 1 kg in birthweight
- Due to CNS immaturity
- Differentiate from sepsis, hypoglycemia, electrolyte imbalance, IVH, seizure
- Monitoring, supportive care, CPAP
- Caffeine therapy

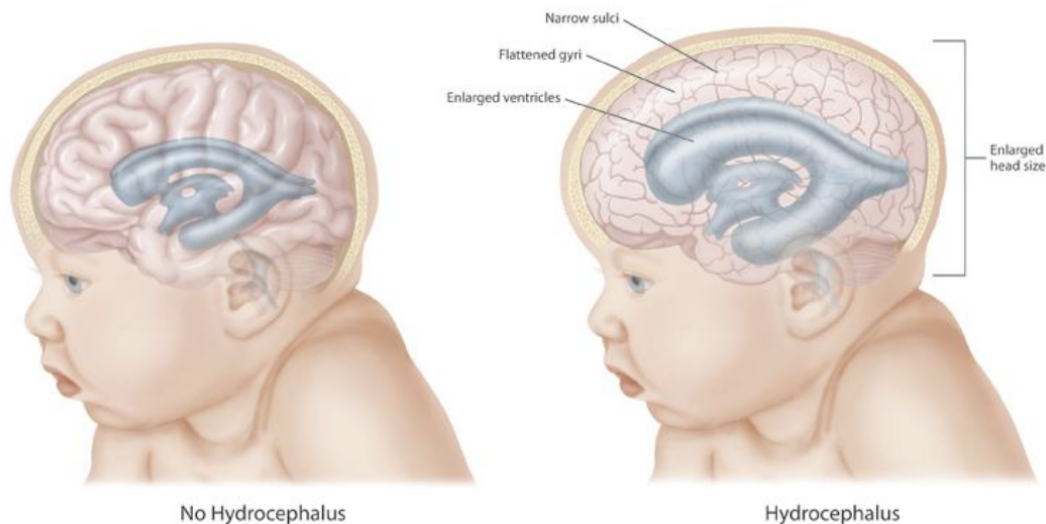
Epidemiology of Apnea of Prematurity

Apnea of prematurity is the most common problem that a premature newborn might face. Up to **70 % of premature babies** have some degree of apnea. The most important risk factor for apnea of prematurity is the **birth weight**. Approximately 25 % of neonates weighing between 1,000 and 2,500 grams at birth develop apnea while up to 84 % of neonates who weigh less than 1,000 grams develop apnea of prematurity.

Half of the cases of apnea of prematurity are mixed apnea, 40 % are central apnea and 10 % are attributed to obstructive apnea. Apnea of prematurity is a **diagnosis of exclusion** because many conditions during the neonatal period can lead to cessation of respiration.

Apnea is more common during the first days of life. Episodes of apnea usually do not happen anymore once the infant reaches 43 weeks of age since conception (gestational age plus age since birth).

Ethnic and gender differences in the incidence of apnea of prematurity were not studied or approached by any large epidemiological studies. Apnea of prematurity increases the **risk of intraventricular hemorrhage, hydrocephalus, prolonged mechanical ventilation and abnormal neurological development** in the surviving infant.



[Image:](#) "Hydrocephalus in comparison to a healthy infant's brain." by CDC. License: Public Domain

Pathophysiology and Etiology of Apnea of Prematurity

The exact etiology of apnea of prematurity is **unknown**. Several experimental studies have shed light on several mechanisms that can explain the increased incidence of apnea in premature infants compared to full-term infants.

The respiratory center in the **brainstem** of premature newborns is not yet fully developed and the interconnected respiratory neurons are still immature. This finding explains why a central component of apnea is usually observed in premature infants.

Additionally, premature infants have: **poorly developed protective respiratory reflexes decreased the sensitivity of the peripheral dopaminergic receptors to hypoxemia and decreased the ability of the medullary chemoreceptors to sense hypercapnia**. These abnormalities can predispose the premature infant to apnea.

Moreover, premature infants have **poorly developed chest wall muscles and laryngeal or pharyngeal muscles**. These muscles can contribute to the obstructive element of apnea of prematurity. In most cases, the abnormal paradoxical chest movements during sleep and the decreased activity of the genioglossus muscles are the first steps in the pathogenesis of apnea.

These abnormalities result in **hypoxemia** but the central nervous system center of respiration fails to promptly respond to hypoxemia and hypercapnia. Accordingly, a **vicious cycle** ensues with worsening hypoxemia and at a certain point, the brainstem respiratory center becomes too depressed to maintain the respiratory effort.

Once this happens, the central component of the apnea of prematurity ensues and the infant develops complete cessation of airflow and respiratory effort.

Clinical Presentation of Apnea of Prematurity

Apnea of prematurity is a condition that is usually reported by the nurse at the neonatal intensive care unit and not the parents. Periods of apnea are usually noted by the nurse

which prompts the nurse to use a **cardiorespiratory monitor** to distinguish apnea from periodic breathing. In addition to the complete cessation of breathing that is observed in apnea, the nurse should also observe the **heart rate** and **signs of central cyanosis**.

When **bradycardia** happens, it should be reported as a ratio to baseline and as an absolute number. Additionally, the **duration of bradycardia** should be noted as it correlates with the prognosis. Any neonate who is admitted at the intensive care unit should get **pulse oximetry** to determine oxygen saturation. If apnea was associated with significant oxygen desaturation, it should be reported by the nurse to the physician.

To differentiate between central and obstructive apnea, a **pneumography** should be used. Neonates with central apnea have complete cessation of airflow and respiratory effort. Those with obstructive apnea, however, have complete cessation of airflow but with continued respiratory effort. Most neonates have a mix of the two types.

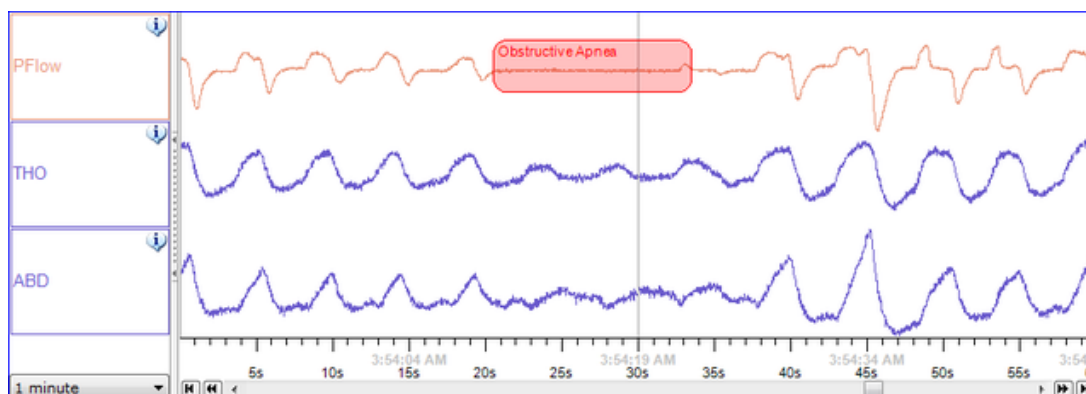
Once the physician is notified about a case of apnea of prematurity, he or she should determine the **severity of apnea** in the neonate. Apnea of prematurity can be classified into the spontaneous event, mild to moderate, or severe apnea.

- A **spontaneous event** is defined as a period of apnea that is less than 20 seconds and not associated with bradycardia or oxygen desaturation. A neonate with a spontaneous event of apnea should recover spontaneously and the episodes should have a frequency of two or less per 24 hours.
- **Mild to moderate apnea** is associated with bradycardia and/or oxygen desaturation that requires therapeutic intervention that is not vigorous.
- **Prolonged apnea** that is associated with bradycardia, oxygen desaturation and central cyanosis which is not resolved without assisted ventilation is classified as severe.

Neonates with central apnea should be evaluated for possible **brain hemorrhages**, **seizures** or **congenital heart disease** before the diagnosis of apnea of prematurity is made.

Diagnostic Workup for Apnea of Prematurity

Before the diagnosis of apnea of prematurity is made, possible causes of apnea in neonates should be excluded. **Severe anemia and sepsis** are two common causes that can be associated with bradycardia and central cyanosis. **Blood, urine and spinal fluid cultures** should be obtained and should be negative for the diagnosis of apnea of prematurity to be made.



[Image](#): "Screenshot of a PSG system showing an obstructive apnea. Flow signal goes flat while effort signals continue"

for a period of time, indicating an obstructive apnea.” by NascarEd - Own work. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Additionally, **inborn errors of metabolism** can also be associated with a decreased respiratory drive or even apnea. **Blood levels of ammonia and amino acids** should be checked in neonates who develop apnea especially if **lactic acidosis** is confirmed. **Serum levels of calcium, magnesium, and glucose** should be checked in apneic neonates.

Neonates who have **hypotonia, difficulty swallowing,** and **absent eye movements** in addition to apnea might have **botulism**.

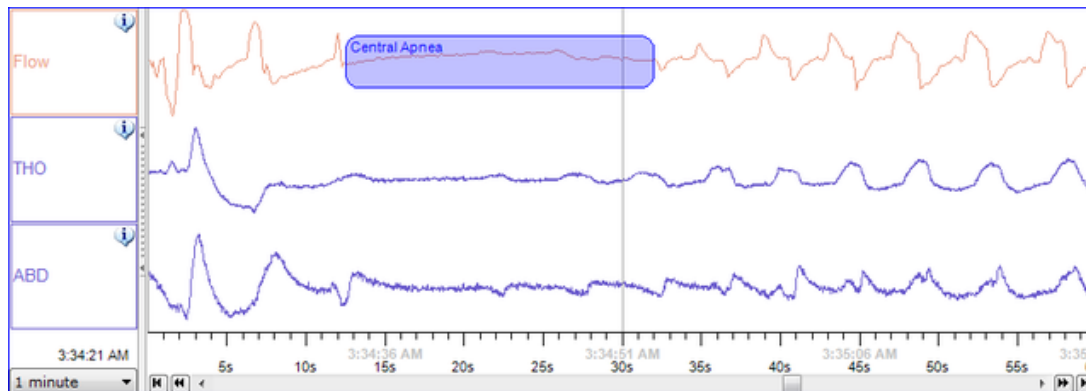


Image: “Screenshot of a PSG system showing a central apnea. Flow and effort signals go flat for a period of time, indicating a central apnea.” by NascarEd - Own work. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Chest radiographs and **lateral neck x-rays** are helpful in excluding causes of obstructive apnea. **Cranial ultrasonography** is helpful in the exclusion of **intracranial hemorrhage**, a condition that can be associated with apnea, cause apnea, or is caused by apnea.

Chest-wall movements should be noted by a continuous multi-channel recording of the chest-wall movement to differentiate between central and obstructive apnea. **Apneic seizures** can be excluded by performing an electroencephalogram.

Treatment of Apnea of Prematurity

If a cause of apnea is identified, it should be treated vigorously for the neonate to survive. For example, **bacterial sepsis-associated apnea** should be treated with intravenous antibiotics and **apneic seizures** might respond to antiepileptic medication.

Neonates with severe apnea should be put on **assisted ventilation** until the cause of apnea is identified to prevent central nervous system damage.

Neonates with isolated spontaneous events usually recover spontaneously or might need simple **tactile stimulation**. A gentle tap to the sole of the foot or back rubbing is all that is needed in this group of neonates and can be lifesaving. **Delivery of high-flow oxygenation through a nasal cannula** can help with mixed cases of apnea.

Neonates who have oxygen desaturation or bradycardia and are diagnosed with mild to moderate apnea should receive **oxygen by bag-mask ventilation**. When the number of apneic episodes exceeds 6 per day, **medical intervention** is indicated.

Theophylline can be used to terminate an episode of apnea in the neonate.

Continuous positive airway pressure (CPAP) therapy should be used in neonates

with obstructive apnea that is not responsive to the previous treatments. CPAP is not effective in central apnea.

References

Nimavat, Dharmendra. [Apnea Of Prematurity: Background, Definitions, Pathophysiology](#) via medscape.com

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