



## **Updates in Diagnosis and Management of Croup**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

Croup is a common respiratory disease that affects 3% of children aged six months to three years. It represents 7% of annual hospital admissions for fever and/or acute respiratory disease in children under the age of five. Boys are more susceptible than girls to the condition, with an overall male/female predominance of 1.4/1. Viruses are detected in up to 80% of patients with croup with identifiable pathogens. The onset of symptoms is usually sudden and usually occurs at night: stridor, hoarse voice and respiratory distress are often seen due to upper airway obstruction. Croup is a clinical diagnosis, children with an uncertain diagnosis, anterior and lateral soft-tissue neck radiographs may be useful to support an alternative diagnosis. Management includes: general care, humidified air, heliox, corticosteroids, and epinephrine, Objective: This study aimed to discuss croup in terms of its etiology, pathogenesis, clinical features, diagnosis, assessment, and finally management.

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## 1. INTRODUCTION

Croup is a common respiratory disease that affects 3% of children aged six months to three years. It represents 7% of annual hospital admissions for fever and/or acute respiratory disease in children under the age of five. Croup is a manifestation of upper airway obstruction due to swelling of the larynx, trachea, and bronchi, resulting in inspiratory stridor and barking cough [1].

### How to diagnose croup and find the best treatment for croup?

Many patients have a mild fever, but fever is not necessary for diagnosis. Less commonly, stridor may be associated with acute epiglottitis, bacterial tracheitis, foreign body airway obstruction, or acute viral infection, most commonly parainfluenza types 1 and 3. Other viruses implicated in the disease include influenza A, influenza B, adenovirus, respiratory syncytial virus, and metapneumovirus [2]. Laboratory testing is rarely necessary for the diagnosis of croup. Viral cultures and rapid antigenic testing have minimal impact on treatment and are not routinely recommended. Radiography and laryngoscopy should be reserved for patients in whom alternative diagnoses are suspected. Randomized controlled trials have shown that a single dose of oral, intramuscular, or intravenous dexamethasone improves symptoms and reduces return visits and hospital stays in children with croup of all severity. In patients with moderate to severe croup, the addition of nebulized epinephrine improves symptoms and reduces length of hospitalization [3].

**Epidemiology:** Croup is one of the most common causes of acute respiratory distress in young children. The disease mainly affects people between the ages of 6 months and 3 years, with an annual peak incidence in the second year of life of almost 5% [4]. Croup, however, occurs in infants from 3 months of age and in adolescents. Although rare, adults can also develop symptoms of croup. Boys are more susceptible than girls to the condition, with an overall male/female predominance of 1.4/1. In North America, croup season peaks in late fall (September to December), but cases are recognized year-round, even in summer. In odd years, the number of children admitted with

croup in peak season is about 50% higher than in even years, strongly correlated with the prevalence of parainfluenza virus infection in the community (North America) [5].

**Etiology:** Viruses are found in up to 80% of croup cases with identifiable pathogens. Parainfluenza virus (types 1 to 3) accounts for 75% of all cases and human parainfluenza virus 1 is the most common type [6]. Other viral etiologies include influenza A and B, adenovirus, respiratory syncytial virus, rhinovirus and enterovirus. Viral infection of the subglottic area and laryngeal mucosa causes inflammation and edema, which drastically reduces air movement and leads to respiratory distress and stridor. Bacterial croup is less common and can be caused by *Mycoplasma pneumoniae* and *Corynebacterium diphtheria*, a known historical cause of croup, whose occurrence is now very rare in immune populations. The type of infectious agent does not affect outcomes or initial management [7].

**Clinical manifestation:** The symptoms usually begin abruptly and most of the time appear at night, which is announced by the appearance of a very characteristic and characteristic barking cough [8]. Stridor, hoarse voice, and shortness of breath are commonly seen as a result of upper airway obstruction. These symptoms are usually preceded by nonspecific upper respiratory symptoms for 12 to 48 hours before barking cough and breathing difficulties develop. Symptoms of croup are generally short-lived, and about 60% of children show that the barking cough resolves within 48 hours. However, some children still have symptoms for up to 1 week [9].

Croup symptoms are almost always worse during the night hours and their severity varies depending on whether the child is agitated or calm. It is not known why croup symptoms are worse at night, but a physiologically plausible explanation could lie in known circadian fluctuations in endogenous serum cortisol, whose concentrations peak around 8:00 a.m. and the minimum between 11:00 p.m. and 4:00 a.m [10]. In asthma, another common respiratory disease in which nocturnal symptoms are generally predominant, postulated mechanisms include the adverse effects of nocturnal cooling of the airways, gastroesophageal reflux, and increased tissue inflammation, in addition to effects of endogenous plasma cortisol and epinephrine.

cycle. Perhaps similar physiological factors play a role in croup [11].

**Pathophysiology:** Infection with a recognized pathogen results in widespread inflammation of the airways and edema of the mucosa of the upper respiratory tract, including the larynx, trachea and bronchi, followed by epithelial necrosis and secretion. Parainfluenza virus also activates chloride secretion and inhibits sodium absorption by the tracheal epithelium, contributing to airway edema. The subglottic area narrows and results in a barking cough, turbulent airflow and stridor, as well as chest retraction. Further narrowing can lead to asynchronous movements of the chest wall and abdomen, fatigue and possibly hypoxia, hypercapnia and respiratory failure [12].

**Diagnosis:** Croup is a clinical diagnosis. The main features are the acute onset of a barking seal-like cough, stridor, hoarseness and respiratory distress. Children can have a fever, sometimes as high as 40°C; however, they should not drool or appear poisonous. Laboratory tests are not necessary to confirm the diagnosis in a child with the typical clinical features of croup, but if the tests are considered necessary, they should be postponed if the child has respiratory distress. In particular, rapid antigen testing and viral cultures do not facilitate the routine acute treatment of a child with croup [13].

Similarly, radiological examinations are not recommended in a child with a typical history of croup and who is responding adequately to treatment. X-rays are not indicated in a clinical picture of epiglottitis or bacterial tracheitis. However, in children with an uncertain diagnosis, anterior posterior and lateral soft tissue neck X-ray may be helpful to support an alternative diagnosis [14]. However, if X-rays are obtained, epiglottitis is suggested by a thickened epiglottis and aryepiglottic folds. A retropharyngeal abscess is indicated by swelling of the soft tissues of the posterior pharynx. Bacterial tracheitis can manifest as an irregular tracheal outline or a membrane covering the trachea. However, X-rays can also be very common in children with these diagnoses [15]. If the radiographs are justified by an atypical clinical picture, the child should be closely monitored during imaging by trained personnel with appropriate airway management equipment, as airway obstruction may occur.

Cardiorespiratory monitoring, including continuous pulse oximetry, is indicated in

children with severe croup, but is not necessary in mild cases. In addition, children without severe croup can sometimes have low oxygen saturation, presumably due to intrapulmonary involvement of their viral infection; therefore, a continuous assessment of the overall clinical condition is important [16].

**Differential diagnosis:** In a child with classic signs and symptoms of croup, alternative diagnoses are rare. However, doctors should remain vigilant as other serious illnesses can present with stridor and respiratory distress [17].

Bacterial tracheitis is due to a secondary bacterial infection of the trachea, resulting in the formation of mucopurulent exudates that may acutely obstruct the upper airway, resulting in a life-threatening condition. Bacterial tracheitis should be considered in the differential diagnosis of any child with acute upper airway obstruction [18] as intubation and respiratory support may be required during the early stages of treatment when thick tracheal secretions may obstruct the airways. The most isolated pathogen is *Staphylococcus aureus*, but others include group A streptococcus, *Moraxella catarrhalis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*. Anaerobic bacteria have also been cultured from tracheal secretions from children with tracheitis [19].

A second potentially fatal alternative diagnosis is epiglottitis. This disease is now rarely seen due to widespread vaccination against H influenzae B. The sudden onset of high fever, drooling, dysphagia, anxiety and a preference to sit upright and in the so-called sniff position (i.e. sitting forward with head stretched) to open the airways should give rise to epiglottitis, as well as a cough which does not have the characteristic croup cough. In the case of epiglottitis or bacterial tracheitis, the most important aspect of treatment is the maintenance of a safe airway by a physician highly qualified in airway management [20].

Other very rare causes of stridor to be considered in children with atypical symptoms of croup include aspiration of foreign bodies into the upper respiratory tract or esophagus, peritonsillar or retropharyngeal abscess, angioedema and laryngeal diphtheria. A foreign body, the onset is usually abrupt with no prodrome or fever (unless secondary infection occurs). Hoarseness and barking cough are usually absent. Dysphagia may be present and stridor is noted variably.

Children who have stridor secondary to the presence of a foreign body usually have a clear history of ingestion. Peritonsillar or retropharyngeal abscess may present with dysphagia, drooling, stridor, dyspnea, tachypnea, stiff neck, unilateral cervical lymphadenopathy, and radiographs of the lateral neck may show posterior pharyngeal edema and reflexed cervical vertebrae [21-22]. Acute angioneurotic edema or allergic reaction can occur at any age and with rapid onset of dysphagia and stridor and possible allergic skin manifestations such as urticarial rash. Children may have a history of allergy or a previous attack. Laryngeal diphtheria has occurred in people of all ages in the past and inadequate immunization may be observed. Usually a prodrome of pharyngitis symptoms is noted and the onset is gradual over 2-3 days. There is mild fever, hoarseness and barking cough occur with dysphagia and inspiratory stridor, and on physical examination characteristic membranous pharyngitis is seen [23].

## 2. MANAGEMENT

### 2.1 General Care

There is a general consensus that children with croup should do the best they can, and doctors should take special care not to frighten or disturb them during examination and treatment, as restlessness will significantly worsen symptoms. Sitting comfortably on the lap of a parent or caregiver is often the best way to reduce arousal [24].

Although we were unable to find published evidence that oxygen should be given to children with signs of dyspnea, there is broad consensus that oxygen therapy is beneficial in these circumstances. [25] Oxygen can usually be given through a plastic tube without shaking the child, keeping the opening a few inches from the nose and mouth (so-called blown oxygen).

### 2.2 Humidified Air

Treatment of croup with humidified air is not effective, despite its long history of use. Humidification of air is neither completely benign nor does it improve respiratory distress [26].

### 2.3 Heliox

Helium is a low density inert gas with no inherent pharmacological or biological effects. Giving a

mixture of helium and oxygen (heliox) to children with severe dyspnea can reduce the level of discomfort, as the lower density helium gas (compared to nitrogen) reduces the turbulence of the airflow through a pathway narrow respiratory tract [27]. Both heliox and racemic adrenaline were associated with similar improvements in Krupp scores over time.

However, since it is not necessary to show that Heliox offers greater improvements than standard treatments and it can be difficult to use in inexperienced hands, there is insufficient reason to recommend its widespread use in children with severe croup. In addition, there are practical limitations to the use of Heliox, including a limited fractional concentration of inhaled oxygen in a child with significant hypoxia [28].

**Corticosteroids:** Corticosteroids have long been used in children with croup; The evidence for its effectiveness in treating croup is now clear. Children with severe croup and impending respiratory failure who receive corticosteroid treatment have an approximately five-fold decrease in the intubation rate [29] When intubated, they remain ventilated about one-third less and are seven times less likely to be reintubated than patients who are not treated with these drugs.

For patients with moderate to severe croup treated with corticosteroids, an average reduction in the length of stay in the emergency room or hospital by 12 hours, a reduction in the absolute proportion treated with nebulized epinephrine by 10%, and a reduction in 50% for both the number of subsequent visits and admission for treatment [30].

**Epinephrine:** In children with moderate to severe croup, nebulizer therapy with epinephrine has a long history and has been well studied. Based on historical comparisons, the administration of epinephrine to children with severe croup has been reported to significantly reduce the number of intubations or tracheostomies required [31] Atomized racemic epinephrine (2.25%) improved croup scores within 10 to 30 minutes of initiation of treatment in three randomized controlled trials compared with placebo. Objective pathophysiological grades of severity also showed significant improvement after epinephrine treatment in five prospective cohort studies. The clinical effect lasts at least 1 hour, but has essentially disappeared within 2 hours of administration [32].

Reassuringly, as the effects of adrenaline wear off, on average, the patient's symptoms return to their original severity and do not appear to be getting worse. The combined data from five prospective clinical studies in outpatients treated with epinephrine and dexamethasone (or budesonide) and observed for 2-4 hours are also reassuring. Of 253 children, only 12 (5%) were discharged within 48 to 72 hours, and only six of them were admitted to the hospital (2%) [33]. No children had adverse outcomes. These prospectively derived data, together with the results of two retrospective cohort studies, provide beneficial support for the safe discharge of children after epinephrine therapy, provided their symptoms have not reappeared within 2-4 hours after treatment. Treatment [34].

**Analgesics, antipyretics, antibiotics, antitussives, decongestants, and short-acting  $\beta_2$  agonists:** No controlled studies on the effectiveness of any of these drugs in the treatment of croup were found with our literature search. The use of pain relievers or antipyretics is helpful in reducing fever or discomfort in children with croup [35]. Most types of croup have a viral cause. Although so-called superinfections such as bacterial tracheitis and pneumonia are described, the rare frequency (<1 in 1000 cases of croup) makes the use of prophylactic antibiotics unreasonable. There is no physiologically sound basis for the use of cough suppressants or decongestants, and they should not be administered to children with croup. Similarly, given the pathophysiology of croup as an upper respiratory disease, there is no clear reason to use short-acting  $\beta_2$  agonists to treat the disease [36].

#### **2.4 Indications for Admission and Discharge from Medical Care**

While most children with croup can be safely treated on an outpatient basis, there is little published evidence to guide doctors as to which people should be hospitalized [37]. Data from a retrospective cohort of 527 children admitted to Royal Children's Hospital, Melbourne, due to persistent stridor at rest (prior to routine corticosteroid treatment) showed that patients with persistent sternum retraction at the time of presentation in an emergency room underwent endotracheal intubation. at risk, while those without a sternum or chest retraction recovered quickly without specific treatment [38]. In a study comparing dexamethasone with placebo, the group treated with dexamethasone first found

reductions in intake recorded 3 hours later, with differences increasing up to 10 hours after treatment. The absorption rate in the dexamethasone group was half that of those receiving placebo. This finding suggests that observation in an emergency room for at least 3 hours, ideally up to 10 hours after corticosteroid treatment [39] would reduce the rate of absorption, presumably because the positive effects of corticosteroids become apparent over time. A published report on the length of stay in the emergency room and admission showed a significant reduction in admissions after the introduction of a clinical pathway that provides a 6-hour observation in the emergency room after corticosteroid treatment before admitting a child with croup to the hospital [40].

#### **4. CONCLUSION**

Croup is a common respiratory disease that affects 3% of children between the ages of six months and three years. Boys are more prone to the disorder than girls. Viruses are detected in up to 80% of croup patients with identifiable pathogens. Symptoms are typically abrupt and appear primarily at night: stridor, hoarse voice, and shortness of breath are commonly seen as a result of upper airway obstruction. Croup is a clinical diagnosis. Management includes: general care, humidified air, heliox, corticosteroids, and adrenaline.

#### **CONSENT**

It is not applicable.

#### **ETHICAL APPROVAL**

It is not applicable.

#### **COMPETING INTERESTS**

Authors have declared that no competing interests exist.

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