9

Croup

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CONTENTS

CASE PRESENTATION

Case 1

A 20-month-old boy is brought to his family practitioner by his mother. The boy has a 12-hour history of a loud cough, slight fever to 101°F, and a hoarse voice. The mother reports that the child had a difficult time sleeping the previous night because of the harsh cough. On examination, the boy is playful and smiling with a temperature of 99°F. It is noticed that he has a seal-like barking cough and subtle evidence of audible stridor. His chest is clear on auscultation with a normal respiratory rate. No chest wall recession is noted. The rest of the exam is unremarkable. The patient is sent home with a suspected upper respiratory infection. Later that evening, the family practitioner receives a phone call from the emergency department informing him that the patient has had worsening respiratory difficulty with visible signs of inspiratory stridor and is being admitted to the hospital for further observation.

Case 2

A 25-year-old woman presents to her primary care physician with a 3-day history of sore throat now with dysphagia, hoarseness, and shortness of breath. The patient was noted to have a low-grade fever of 101°F and an oxygen saturation of 95% on room air. Suspected of having an upper respiratory infection, the patient was sent home with a prescription for antibiotics. Later that evening, the primary care doctor receives a phone call from the emergency department informing the physician that the patient has been admitted to the hospital for further observation. In the emergency department, the patient was found to have an oxygen saturation of 85% with improvement after receiving 35% oxygen via facemask. A white blood cell count of 8.7×10^9/L was obtained with a predominance of lymphocytes. The patient's symptoms improved over the next 8 hours. There was no bacterial growth from throat cultures and the patient was discharged on the seventh day after admission.

KEY CLINICAL QUESTIONS

1. What signs and symptoms in these patients help establish the diagnosis?
2. What might have warned the physicians that these patients would become worse?
3. Could any intervention have been done in the outpatient setting to prevent the emergency room visits?

LEARNING OBJECTIVES

1. What is the typical presentation of a patient with croup and why would you suspect this diagnosis?
2. What are the etiological agents of croup?
3. What is the clinical course and complications of croup?
4. What is the pathophysiology of croup and how is it treated?

DEFINITION

Croup is a term used to describe a syndrome that is caused by a variety of respiratory illnesses that involve the larynx, trachea, and bronchi. These illnesses include laryngotaheitis, laryngotracheobronchitis, laryngotracheobronchopneumonitis, and spasmodic croup. The various forms of croup all involve upper airway obstruction causing a seal-like barking cough, inspiratory stridor, hoarseness, and varying degrees of respiratory distress. Croup is most often a self-limiting illness but can result in severe airway obstruction with respiratory failure and death.

EPIDEMIOLOGY

Croup affects children from 6 months to 12 years old. Most cases occur at 2 years old and there is a significant decrease in its incidence after 6 years of age.

It affects boys more often than girls in a ratio of 2:1 *(1)*. Annually, it has an incidence of 50 new cases per 1000 children aged 2 *(1)*. Croup can occur any time during the year but is seen most often in the fall and winter with a recurrence rate of 5% *(1)*.

More rarely, acute laryngotracheitis can occur in adults causing a community-acquired adult croup. This entity was first identified in 1990 by Deeb and Einhorn *(2)* and only 10 cases have been reported since 1996 *(3)*, although the incidence is probably much higher owing to the lack of accurate diagnoses. Because of the relative rarity of adult croup, it has not been extensively studied and cases of the entity have only been examined retrospectively.

ETIOLOGY

Croup is usually a viral illness most frequently caused by the parainfluenza virus type I. Other pathogens known to cause croup include parainfluenza virus types II and III. Combined with type I, these viruses account for 75% of the cases of croup annually *(4)*. Less common causes of croup include parainfluenza type IV, influenza types A and B, adenovirus, respiratory syncytial virus, herpes simplex virus, measles, rhinovirus, coxsackievirus A and B, and echovirus. *Mycoplasma pneumoniae* is an extremely rare cause of croup. Other bacterial causes of tracheitis causing a croup-like syndrome include *Staphylococcus aureus, Haemophilus influenzae, Corynebacterium diphtheriae, Streptococcus pneumoniae,* and *Moraxella catarrhalis.* Non-infectious causes of croup include spasmodic croup but this form is often difficult to distinguish from infectious croup.

The adult form of croup is also caused by various viral and bacterial pathogens as well as a fungal cause. The viral causes of adult croup include herpes simplex, cytomegalovirus, and influenza type B. The bacterial causes include *S. aureus* and *H. influenzae*. The fungal cause of adult croup is Aspergillus. Table 1 highlights the more common causes of croup in children and adults. The reason for the difference between adults and children is a result of viral-specific memory T-helper cells and B-lymphocytes in adults.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of croup is extensive and includes any etiology causing stridor in young children. In addition to the viral causes of croup, the differential diagnosis includes the bacterial pathogens causing tracheitis. One of the most important, and often overlooked, causes of a croup-like presentation in children is foreign body aspiration. In contrast to croup, foreign body aspiration would not present with a seal-like barking cough and a history of aspiration or choking can be obtained in 90% of cases *(5)*. Table 2 lists some other disease entities causing stridor in children.

Table 1
Causes of Croup in Children and Adults

Organism	Adults	Children
Viral	Herpes simplex	Parainfluenza virus
	Cytomegalovirus	Influenza type A, B
	Influenza type B	Respiratory syncytial virus
		Adenoviruses
		Rhinovirus
		Varicella-Zoster
		Measles
		Echovirus
		Coxsackievirus
		Corona virus
		Enterovirus
Bacterial	*Staphylococcus aureus*	*Mycoplasma pneumoniae*
	Haemophilus influenzae	*Corynebacterium diptheriae*
		Streptococcus pneumoniae
Fungal	Aspergillus	

Table 2
Differential Diagnosis of Stridor in Children

Acute laryngeal fracture	Angioneurotic edema	Arnold-Chiari deformity
Burns or thermal injury	Dandy-Walker syndrome	Diphtheria
Epiglottitis	Inhalation injury	Laryngeal papillomatosis
Laryngomalacia	Measles	Neoplasm
Peritonsillar abscess	Retropharyngeal abscess	Subglottic stenosis
Vascular ring	Vocal cord paralysis	

Epiglottitis used to be a major cause of stridor in children. However, with the use of the *H. influenzae* vaccine, this entity is much less common. It can be distinguished from croup by a sudden onset, high fever, inflammation of the supraglottic region, dysphagia, lack of cough, and a thumb sign on radiography. Another common cause of stridor in children is a peritonsillar abscess. In contrast to croup, the child with a peritonsillar abscess will often have difficulty opening the mouth and visualization of the tonsils will reveal erythema, swelling, and tonsillar exudates.

Although many entities may present with stridor, history and clinical course remain the most important means of making an accurate diagnosis.

PATHOPHYSIOLOGY

Various viruses that are transmitted via the respiratory route cause croup. The virus enters through the nose and begins replication in the nasopharyngeal respiratory epithelium causing coryza as the first symptom. The infection spreads distally causing laryngeal and tracheal erythema and edema with diffuse inflammation of the airway walls. Because of this inflammation, the airways secrete a fibrinous exudate causing partial obstruction of the tracheal lumen. The infection also involves the vocal cords and subglottic larynx. Inflammation of the vocal cords causes vocal cord immobility and hoarseness. In the subglottic region where the airway lumen is the narrowest because of a ring of cartilage surrounding the area, a small amount of edema restricts airflow leading to audible inspiratory stridor and the seal-like barking cough. In younger children, the infection and inflammation can cause significant airway obstruction as a result of the smaller circumference of the lumen. This can result in mild to severe hypoxemia.

Spasmodic croup is a variant of the syndrome that may occur without an infectious agent. This entity is often indistinguishable from viral croup in that up to 40% of children will have features of both spasmodic (multiple recurrences, atopy) and viral croup (fever, upper respiratory infection symptoms) *(6)*. This variant is often triggered by allergy and occurs at night with noninflammatory edema of the airway structures and possible spasm of the glottis resulting in stridor and the seal-like barking cough owing to the same mechanisms described previously. This variant of croup is short-lived and responds well to humidify air with recurrence of symptoms limited to the first few days after the initial episode. Spasmodic croup should be suspected in a child who has had multiple bouts of croup with sudden onset at night and has a history of allergy or gastroesophageal reflux.

In croup caused by bacterial tracheitis, the inflammation can result in necrosis of the mucosa of the airway wall with ulceration and microabscess formation. A loosely attached pseudomembrane may form over areas of necrosis and ulceration and can result in worsening airway obstruction if it becomes detached.

DIAGNOSIS

Viral croup usually begins with a mild, nonspecific prodrome of 12 to 72 hours. During the prodrome period, the patient may experience a low-grade fever and coryza as the virus replicates in the nasopharyngeal mucosa. Other symptoms during this period include nasal congestion, sore throat, and a mild cough. As the illness progresses, the child will begin to develop a harsh, seal-like barking cough, and a hoarse voice. The cough often wakes the child from sleep and is frightening to the parents. With further airway obstruction, the child may develop inspiratory stridor, which is usually the first clue that the illness is not

a common cold. The symptoms of croup tend to be worse at night, especially in the first and second days of the illness. Crying tends to worsen the symptoms and children with croup prefer to be in an elevated position. The symptoms are usually self-limited and resolve within 1 week.

Findings on the physical exam are usually minimal because the child is usually in less distress during the day than at night. Mild to severe respiratory distress may be apparent. The chest exam is often normal, but sometimes reveals expiratory wheezes. Inspiratory stridor may be evident on observation of the child. In more severe forms of the illness, expiratory stridor may also be present with nasal flaring as well as suprasternal and intercostal retractions. Lethargy and agitation may result from hypoxemia. With severe respiratory distress, tachycardia and tachypnea may be present that appears out of proportion to the rest of the clinical exam ultimately developing into cyanosis. Dehydration may be seen if the child has had difficulty maintaining adequate oral intake. In contrast to epiglottitis, drooling and dysphagia are absent in croup as well as rapid deterioration to toxicity. In bacterial tracheitis, the child will worsen after a few days of illness when the viral illness would be resolving. A child with bacterial tracheitis will often develop high fever, toxicity, and worsening respiratory distress.

A research tool developed by Westley and associates *(3)* is helpful in assessing the severity of croup and monitoring response to treatment. Table 3 outlines this severity scoring.

Adult croup presents with a prodromal upper respiratory tract illness lasting 2 to 4 days and includes cough, sore throat, and malaise. Fever may be low grade or absent and a white blood cell count is usually not elevated with a lymphocyte predominance. Following the prodromal period, there is a rapid deterioration with respiratory compromise and obstruction. Recovery is almost always complete in cases of adult croup with no evidence of complications.

The diagnosis of croup is usually made in the clinical setting. Monitoring the course of the illness is best done by frequent follow-up visits and physical exams, keeping in mind the typical clinical course previously outlined. This technique is the best method for obtaining a good outcome and avoiding preventable complications. Some studies and imaging may be beneficial in aiding the physician in the diagnosis of croup if the presentation is atypical or another cause for the child's condition is suspected.

Radiologic studies include plain films of the soft tissues of the neck that may show the classic "steeple sign." The "steeple sign" is seen on a posteroanterior plain film as a narrow column of air in the subglottic region. On lateral plain film, the "steeple sign" is represented by an overdistended hypopharynx. These findings are found in only 50% of the cases of croup with many children having radiologic plain films with normal findings *(4)*. Because radiography does not correlate well with a diagnosis of croup, radiographic studies should be reserved

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Table 3
Severity Scoring for Croup

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Level of consciousness	
Normal or sleeping	0
Disoriented	5
Cyanosis	
None	0
With agitation	1
At rest	2
Stridor	
None	0
With agitation	1
At rest	2
Air entry	
Normal	0
Decreased	1
Markedly decreased	2
Retractions	
None	0
Mild	1
Moderate	2
Severe	3

Adapted from ref. [3].

if the clinical presentation is atypical for croup or suspicious for another etiology, such as epiglottitis or foreign body aspiration, in which radiography may be diagnostic. A more sensitive, and likely more useful, imaging study in the diagnosis of airway obstruction and stridor is rapid computed tomographic scanning of the neck.

Sometimes pulse oximetry is useful in measuring the degree of hypoxia in a child with croup. However, croup is a disease of the larger upper airways with pulse oximetry being normal except in the most severe cases of obstruction and respiratory distress caused by the illness. Pulse oximetry may be useful in differentiating croup from bronchospasm, in which the oxygen saturation is lower than expected.

Direct visualization of the laryngeal area and intubation is rarely required in the setting of croup. Laryngoscopy may be necessary if epiglottitis is suspected or the child has a rapidly deteriorating course. Intubation may be required if the illness appears to be deteriorating to complete airway obstruction. Direct visualization may also be useful if foreign body aspiration is suspected. Other uses of direct visualization include a child whose illness does not resolve, continues

to have frequently recurring bouts of croup, or was intubated during the illness and now may have subglottic stenosis.

Laboratory studies are rarely helpful as the white blood cell count is usually normal except for possible lymphocytosis or leukopenia. Arterial blood gases are also usually normal except in severe disease when hypoxia and hypercarbia may be present. If bacterial traheitis is suspected, it can be useful to obtain blood cultures to direct treatment.

TREATMENT

Complications are rare following an episode of croup. The most common complication is airway obstruction with respiratory distress. If a child begins developing hypoxemia, tachycardia, and tachypnea, endotracheal intubation may be required. Pneumothorax, pneumomediastinum, and subglottic stenosis may be complications of endotracheal intubation. Dehydration may result from inability of the child to maintain adequate oral intake. Other complications include lymphadermatitis and ottitis media. The viral type of croup may result in bacterial superinfection resulting in bacterial tracheitis. Pneumonia is a rare complication associated with bacterial traheitis and toxic shock syndrome has been seen in bacterial tracheitis owing to *S. aureus*. Death from croup is exceedingly rare if an appropriate airway is maintained.

Adult croup has not been associated with complications. The initial therapeutic approach to a child with suspected croup is general evaluation of the degree of respiratory distress and maintenance of an adequate airway for effective oxygenation and ventilation. This can be accomplished by monitoring the heart rate, respiratory rate, and pulse oximetry. In the setting of severe respiratiory distress and hypoxia, it may be necessary to provide 100% oxygen via a bag–valve–mask device. If this is unsuccessful and the child's oxygenation does not improve, it may be necessary to maintain an airway with endotracheal intubation. Any patient requiring supplemental oxygen to maintain adequate oxygenation should be admitted and monitored as an inpatient. This determination is made more accurately by observing the clinical picture and degree of distress and stridor rather than by pulse oximetry alone. Most children do not present with severe stridor and respiratory distress and do not require either technique to maintain an adequate airway. These children can typically be managed on an outpatient basis. It is important to avoid stressful situations in the treatment of children with croup because agitation and crying can aggravate the symptoms and worsen the respiratory distress. Another important initial aspect in the treatment of a child with croup is the evaluation of volume status. A child should be provided oral rehydration if tolerated, but it may be necessary to administer intravenous fluids if oral intake is not adequate.

Humidity has been used for hundreds of years to alleviate the symptoms of croup. Also known as mist therapy, it is believed to be beneficial by providing cooler inhaled air with moisture to cause vasoconstriction and alleviation of the mucosal edema. In addition to this effect, it is believed to decrease the viscosity of mucous secretions facilitating removal from the airway. The cool moisture also provides a soothing relief to the inflamed mucosa of the airway walls. Despite its extensive use, humidified air has not been shown in studies to be beneficial in improving the outcome of croup and despite its use being abandoned in many hospitals, no observable differences have occurred in the number of hospitalizations or complications incurred in cases of croup *(6)*. It is still argued, however, that the use of humidified air may be beneficial as a placebo effect, especially in the home, by reducing anxiety in both the child and the parent. Devices used to provide humidity include croup tents, croupettes, masks, and blow-by oxygen.

The use of corticosteroids in the management of croup remains controversial. However, corticosteroids are routinely used by physicians in the management of croup. Use of corticosteroids in the inpatient setting has been shown to be of benefit in the first 6 to 12 hours *(7)*. Its use has been shown to improve croup scores and shorten hospital stays with less requirement of treatment by other pharmacological agents *(7)*. The method of administration of the steroid has also been studied and has shown no difference between nebulized budesonide and oral dexamethasone as evidenced by equal decrease in croup scores *(7)*. In the outpatient setting, studies have also focused on the best method of administration of steroids in the treatment of croup. It has been shown that there is no significant difference between oral administration of dexamethasone versus intramuscular dexamethasone in the improvement of symptoms caused by croup *(7)*. Further studies have shown benefit in the use of 0.15 mg/kg oral dexamethasone over placebo and higher doses of steroid *(7)*. These studies have provided convincing evidence for the use of corticosteroids in the treatment of croup in both the inpatient and outpatient setting. It also appears that the use of oral corticosteroids in a low dose can provide an equal benefit to any other method of administration.

Racemic epinephrine in nebulized form is also used in the treatment of severe croup. Epinephrine acts to stimulate the α-adrenergic receptors causing capillary constriction and reduction of laryngeal mucous. This allows for a larger airway diameter and reduces respiratory difficulty and inspiratory stridor. The effects of epinephrine are short-lived, lasting for 2 hours. Patients should not be discharged for at least 3 to 4 hours after the administration of epinephrine, given the possibility of return of symptoms after the effects of the therapy have worn off. The use of epinephrine in the treatment of croup should be reserved for those patients who are seriously ill or have had a poor response to other treatment modalities, including mist therapy and analgesics.
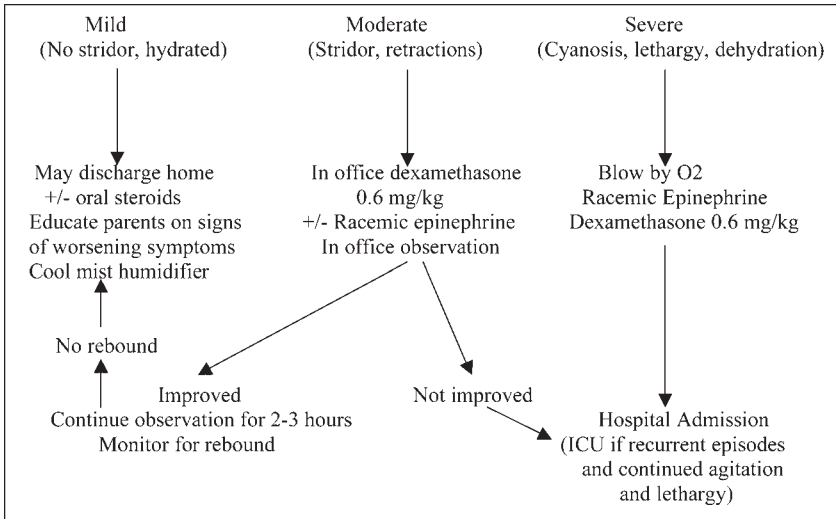
Mild
(No stridor, hydrated)

Moderate
(Stridor, retractions)

Severe
(Cyanosis, lethargy, dehydration)

May discharge home
+/- oral steroids
Educate parents on signs
of worsening symptoms
Cool mist humidifier

In office dexamethasone
0.6 mg/kg
+/- Racemic epinephrine
In office observation

Blow by O2
Racemic Epinephrine
Dexamethasone 0.6 mg/kg

No rebound

Improved
Continue observation for 2-3 hours
Monitor for rebound

Not improved

Hospital Admission
(ICU if recurrent episodes
and continued agitation
and lethargy)

Fig. 1. Algorithm for the management of croup *(9,10)*.

For more than 20 years, the use of a mixture of helium and oxygen called heliox has been used in the treatment of severe croup. This mixture improves laminar gas flow in the airway decreasing the work of breathing. Blood oxygenation is improved over using oxygen alone when this treatment modality is used. Heliox is also beneficial when used with other treatments such as epinephrine and corticosteroids by extending the time in which these drugs have action on the laryngeal airway.

Treatment of adult croup is empiric and aimed at early recognition and airway stabilization. Use of the flexible fiberoptic laryngoscope has been used to assess the degree of airway obstruction *(8)*. Intubation may be necessary with severe respiratory compromise. Adjuvant therapy may also be employed with use of oxygen, humidification, steroids, and nebulized epinephrine, similar to the treatment used for croup in children.

Figure 1 illustrates an algorithm, based on the severity of the illness at presentation, used in the management of croup. The decision to hospitalize is based on the response to initial treatment in all cases.

FUTURE DIRECTIONS

Because the absolute treatment of croup remains controversial, further studies will continue to look at the benefits of modalities such as humidified air and steroids in the management of the illness. Also, children hospitalized for treat-

ment of croup may be at a higher risk of subsequent bronchial hyperresponsiveness and asthma as well as being more prone to cutaneous hypersensitivity reactions. However, these correlations are still under investigation.

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