Croup

Julian Vyas

Correspondence to: julianv@adhb.govt.nz

Julian Vyas *trained as a respiratory paediatrician in the UK, and Melbourne. He is a consultant respiratory paediatrician at Starship Children's Health in Auckland. His clinical interests include cystic fibrosis, interstitial lung disease and lung growth and development.*

Acute viral laryngo-tracheo-bronchitis (croup) is a common illness with which all physicians who see acutely ill children will be familiar. With ubiquitous diseases it is sometimes difficult to differentiate between an uncommon presentation of said disease, and a similar clinical phenotype of a less common condition. The aphorism 'commonest things are commonest' has value when disease is considered within a population. However, on an individual patient basis, this will inevitably result in occasions when uncommon conditions are mistakenly diagnosed as their more common symptomatic similars.

Croup is a condition which usually causes troublesome, but transient morbidity. Despite this, there is an increasing tendency to give treatments that can limit disease severity, and possibly forestall hospital admission. Accurate distinction between croup and its clinical counterparts is important if treatment is mooted, or if the croup fails to wane over an appropriate time.

The purpose of this paper is to review the clinical presentation of croup, and other similar conditions and to review current theories in the management of croup.

Typical presentation

Croup affects children between six months and two years of age. It has a viral prodrome for one to two days, followed by the development of a hoarse voice, barking cough and inspiratory stridor. The expected duration of illness is two to three days of stridor and a persistent (but gradual) decline of the cough over a further five to seven days. The absence of any of these presenting features, presence of additional symptoms or signs, or failure to follow a typical course should alert the practitioner to the possibility that the disease is not croup.

Atypical features of croup

1. Onset at less than six months

A child of less than six months of age presenting with acute onset stridor should not be considered to have croup. Presence of cutaneous haemangiomata may indicate the presence of an upper airway haemangioma. Consider other congenital, or perinatal causes (e.g. vocal cord palsy, congenital laryngeal abnormality).

2. Croup-like symptoms when well

- A hoarse voice when the child is well may indicate an acute viral infection but on top of a pre-existing problem with the vocal cords (e.g. vocal cord palsy, episodes of gastro-oesophageal reflux, laryngeal polyps).
- Stridor may indicate laryngeal disorder (e.g. vocal cord palsy) or large airway narrowing (if this is present but located below the thoracic inlet the stridor may be biphasic).
- A barking cough may indicate tracheomalacia. The nature of a 'TOF (tracheo-oesophageal fistula) cough' is different from a croup cough in that the nature of the bark is more severe and harsh. Parents often report that the cough is of a nature that when heard in public strangers will proffer unsolicited advice to the parents to 'get it seen to'. Quite why this is so is unclear. If a child has had a congenital tracheo-oesophageal fistula, tracheomalacia is always present. However, tracheomalacia can be an isolated occurrence.

3. Acute onset

- *With pyrexia:* A child who appears toxic (pale, clammy, tachycardic) may have bacterial tracheitis, or acute epiglottitis. Routine vaccination for Haemophilus influenzae has virtually eradicated acute epiglottitis as vaccine efficacy is of the order of 98% in preventing all types of invasive disease from HiB, of which acute epiglottitis is but one clinical phenotype. It must also be remembered that not all children will have been vaccinated. Children with epiglottitis are typically older (two to five years) than

those with croup, although cases have been reported in younger children and even in adults.

- *Without pyrexia or coryzal prodrome:* A history of possible foreign body ingestion may need to be specifically asked about. Features include onset over a very short period, child seen to be playing with things in or near his or her mouth beforehand, focal auscultatory signs. Gastro-oesophageal reflux has been reported to cause acute onset stridor, barking cough and hoarse voice. This can occur in the absence of any premonitory symptoms.
- Angio-neurotic oedema can cause acute upper airway obstruction.

These symptoms and signs, which alert the practitioner that a child may not have simple croup, are summarised in Table 1.

Table 1. Typical vs atypical clinical features of croup

	Croup	Atypical for croup
Age of onset	6 months to 2 years	< 6 months (? congenital abnormality) > 2 years ? other pathology
Cough	Barking	Present when well 'TOF' cough
Pyrexia	Present	Absent
Hoarse voice	Common	Present when well
Inspiratory stridor	Common	Present when well
Biphasic stridor	Uncommon	Problem below thoracic inlet
Pt is toxic	Uncommon	? epiglottitis or bacterial tracheitis
Cutaneous haemangiomata	Not associated	? laryngeal A-V malformation

Spasmodic croup

This is considered separately from acute croup, since although the onset of symptoms can be acute and precipitous, it is probably a different disease entity. It often occurs in older children and can occur without any viral prodrome. Curiously, it can sometimes be reported to be present at night, abate the following day and return the second night. It is often stated that spasmodic croup is associated with the subsequent development of asthma. This review will not assess the strength of this relationship. However, it is suggested that before making a diagnosis of recurrent or spasmodic croup, consideration should be given to the likelihood of other causes of upper airway obstruction being present (e.g. gastro-oesophageal reflux).

Management

The management of croup centres around the use of steam inhalation and humidity, use of steroids and nebulised adrenaline. Factors in the individual child's circumstances, such as severity of symptoms, distance of home to hospital, presence of typical or atypical clinical features will also influence treatment.

Severity

In the past the Westley symptom severity score has been used in an attempt to provide an objective assessment of the severity of croup. Whilst scoring systems provide a degree of reassurance over patient group comparability in studies, their clinical utility is questionable. Despite the fallibility of croup scores, some clinical assessment of severity is required to guide treatment. Croup severity can be clinically delineated into three categories:

- *Mild:* Croup without stridor at rest.
- *Moderate:* Croup with stridor at rest, but no signs of hypoxia, and good volume air entry/chest wall movement.
- *Severe:* A critically obstructed airway. Hypoxia, poor volume air entry, fatigue, altered consciousness.

Treatment

Steam

Inhalation treatment (including mist and steam) has been advocated for many years. In the last decade or so their use has declined. This is in part due to the data published, which demonstrates the absence of benefit from inhalation[1] and also to the increasingly recognised risk of scalding.[2]

Steroids

There is a plethora of evidence to suggest that steroids are of benefit in croup. What is perhaps intriguing is that the time to onset of effectiveness is approximately two hours. This appears short if steroids act as they are thought to (i.e. via an effect on upregulating RNA transcription and the NFκB/IκB system). This would suggest that steroids, when used in croup, might act via different mechanisms than traditionally thought.

Much has been written about the relative merits of different steroids (dexamethasone versus prednisolone/prednisone versus budesonide). There have also been a number of studies examining the differences in

Table 2. Treatment doses for croup

Dexamethasone	0.15–0.6 mg/kg. Single dose
Prednisolone/prednisone	1 mg/kg. Single dose
Budesonide (0.5 mg/ml)	2mg via nebuliser
Adrenaline (1% solution)	0.5 mL diluted to 2–4 mL.
Adrenaline 1:1000	4 mL. Repeat as required

efficacy between differing doses of dexamethasone. Fifoot reported no difference between using 1mg/kg prednisolone against 0.6mg/kg of dexamethasone.[3] Chub-Uppakarn showed 0.15mg/kg of dexamethasone to be equally as effective as a dose of 0.6mg/kg.[4] Sparrow has shown that 0.15mg/kg of dexamethasone is equally as effective as 1mg/kg of prednisolone.[5] Furthermore, whereas steroid treatment used to be given for 48 hours, much data now supports the use of a single dose.[6] Previous meta-analysis has shown that many other studies all support this general view of steroid efficacy.[7]

Some studies have assessed the efficacy of inhaled steroids in croup. These were meta-analysed by Griffin et al.[8] Whilst it appears that they work as effectively as oral steroids on their own, there is no advantage to adding inhaled budesonide to oral dexamethasone.[9]

Given that use in the community requires access to a nebuliser and compressor (or wall oxygen or air) and that it is an expensive drug, it is difficult to advocate the use of budesonide in croup.

Parenteral steroids also have a role in the management of croup. It is not recommended that they be used routinely in the community. This is because the distress that may be caused whilst establishing venous access may provoke an episode of bronchospasm in the child. Unless the practitioner has the technical skills and equipment to protect a child's airway, it is recommended that parenteral treatment not be undertaken in the community.

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Adrenaline

Nebulised adrenaline has been shown to be effective in croup for many years. Its use was confined to just those children with severe croup, as a temporising measure whilst they were transferred to a High Dependency Unit, or Paediatric Intensive Care Unit. However, three studies done in the mid-1990s showed that nebulised adrenaline in those with less severe croup could allow relief of symptoms and the child to return home.[10-12] In all these studies, however, the children also received steroids as well as adrenaline.

For many years it has been stated as necessary that nebulised adrenaline always be of the racemic form (i.e. containing both stereo-isomers). Recently, Duman et al. showed that L-adrenaline is effective in treating croup.[13] There are no studies comparing efficacy between L-adrenaline and racemic adrenaline. Duman's study would suggest that racemic adrenaline is not essential for treating croup.

It was also stated (as fact) for many years that some patients could exhibit a 'rebound' phenomenon after being given nebulised adrenaline. Some authorities consider that this was actually the patient returning to their previous severity of airway obstruction as the effects of the adrenaline wore off. The evidence of the safety to discharge patients home after being stable for three hours post adrenaline nebuliser would suggest that the risk of 'rebound' is exceedingly low.

These treatments are not 'cures' for croup. They will alleviate stridor (but usually do not alter the accompanying barking cough). Children in whom atypical features are recognised, or who persist with stridor at rest despite receiving the above treatments should be referred to their local hospital to be observed. There is a small group of children who require intubation for their croup. Whilst it may seem intuitive that the treatments described may well prevent children progressing to the need for intubation, there are no studies to demonstrate this and so these treatments cannot be relied upon to prevent a need for intubation. Despite the lack of clinical evidence, it is recommended that practice accommodates the need for ensuring a child has a safe airway. For this reason, this author suggests that if stridor at rest persists, repeat doses of steroids should not be given but rather the child should be referred to their local hospital for further assessment.

Summary

Typical croup is a troublesome but self-limiting problem which, for the vast majority of children, does not cause significant morbidity, nor long-term problems. Atypical clinical features should alert the practitioner to the possibility of other causes of stridor or of exacerbating factors.

There is a wealth of evidence to support the use of steroids in croup to lessen upper airway obstruction and prevent admission. The exact steroid chosen and the dose required (of dexamethasone) is less clear cut and is probably not critical.

Nebulised adrenaline may also be of use in the community but the exact position it should occupy within a hierarchy of treatment of croup is not clearly understood. At present it should be given in conjunction with oral steroids and not in place of them.

Competing interest

The author has previously been paid by Astra Zeneca for expert opinion.

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Disclosing errors to patients

'A transformation in how the medical profession communicates with patients about harmful medical errors has begun. Within a decade, full and frank disclosure of these events to patients is likely to be the norm rather than the exception. Making disclosure of harmful errors to patients an expectation in medicine and giving providers the tools to turn this principle into practice may prove to be critical steps in restoring the public's trust in the honesty and integrity of the health care system.'

Gallagher TH, Studdert D, Levinson W. Disclosing harmful medical errors to patients. New Engl J Med 2007; 356:2713–2719.

Unfairness and coronary heart disease

'This study shows that there is a dose-response association between unfairness and coronary events. The risk of incident coronary events among participants who strongly or moderately agreed that they were often treated unfairly was 55% higher than those who reported fair treatment, controlling for age, gender, employment grade, established coronary risk factors and other work-related psychosocial characteristics. Unfairness was also independently associated with poor physical and mental functioning at follow-up, controlling for baseline factors including health functioning.'

De Vogli R, Ferrie JE, Chandola T, Kivimaki M, Marmot MG. Unfairness and health: evidence from the Whitehall II Study. Journal of Epidemiology and Community Health 2007; 61:513-518; doi:10.1136/jech.2006.052563

How normal is normal?

'One of the first data sets that I looked at when I was learning statistics had a number of missing observations. I was told that this was totally normal. I also noticed that the main endpoint followed the bell-shaped curve that is often described as a "normal distribution." This, I was told, was not normal at all; indeed, one of my lecturers became rather excited, commenting, "They say it never happens, but look, here is an example, which just goes to show that you can get a normal curve." I think what they were trying to tell me was that it wasn't normal to get normal data. Nonnormality seemed to be the norm, but I couldn't be sure.'

Vickers AJ. If the normal distribution is so normal, how come my data never are? Medscape Business of Medicine. http://www.medscape.com/viewarticle/556012_print Accessed 17 May 2007.