

Wheezing infants and toddlers

A practical approach

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Although a very common problem, wheezing in infants and toddlers remains a difficult and confusing problem for clinicians. The wheeze is not usually due to asthma but asthma medications have a role if there is significant breathlessness and ongoing morbidity.

When assessing an infant or toddler (0 to 3 years old) with wheeze, many questions will arise: Could the wheeze be due to a serious congenital malformation (lungs, upper airways, heart)? Is this 'acute viral bronchiolitis'? Is the wheeze due to asthma? Is this child going to develop asthma in later childhood? How should the wheeze be managed short-term and long-term? The purpose of this article is to offer a practical approach to this common but confusing problem. Readers with a particular interest in asthma should consult the most recent version of the National Asthma Council Australia's *Australian Asthma Handbook*, which is available as a comprehensive, user-friendly searchable website (www.asthma-handbook.org.au) with an accompanying printed quick reference guide.¹

There is no question that wheezing in very young children is very common. By the age of 3 years, one-third will have

wheezed at least once, and by age 5 years, approximately half – but many of these will wheeze only once. Clearly, wheezing in the preschool years does not mean the child has asthma, nor that most will develop asthma in later childhood.

In this age group, clinicians are forced to base their decision-making predominantly on the parental history, as physical examination is often limited or incomplete, pulmonary function testing is impossible and a chest-x ray is unlikely to be helpful. Further, there is always uncertainty about terminology: what a parent calls 'wheeze' may not be the same as the GP's understanding of 'wheeze'. Thus a systematic approach to managing wheeze in children up to the age of 3 years is needed. Although epidemiology studies have identified various patterns (phenotypes) of wheeze (i.e. transient early wheeze, viral-induced wheeze and atopic asthma), this information is of limited use in individual patients (Figure). It can, however, be of use when communicating with patients, especially when discussing the likely natural history of symptoms.

The major determinants of the clinician's actions are severity and persistence of symptoms. Answering the initial key questions below should enable confirmation that the wheeze is real and that it has significant effects, and also identify its triggers. The further questions posed provide guidance on the management of these young children with wheeze.

KEY POINTS

- Although wheeze in infants and toddlers is very common, it is not usually due to asthma.
- A systematic approach to wheeze in children in this age group should enable GPs to determine an appropriate management strategy, including parent education.
- Determining the pattern of wheeze has limited utility in individual patients.
- Recognition of the infant with acute viral bronchiolitis is important, to avoid unnecessary interventions.
- If the wheezing is associated with significant breathlessness, a trial of an inhaled bronchodilator (reliever) is appropriate – provided the infant is over six months of age.
- If the wheeze and breathlessness is causing significant ongoing morbidity, a one-month trial of an inhaled corticosteroid may be indicated.

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Initial key questions: severity and persistence of wheezing

Question 1. Is the noise a genuine wheeze?

Hopefully when the child is seen by the GP, the wheeze will be present, allowing confirmation that the origin of the noise is indeed intrathoracic. If no noise is present, it may be that the parents are using the term 'wheeze' inaccurately. In this situation, the possibility that the noisy breathing is arising from the upper airways (e.g. laryngeal, nasal or oropharyngeal origin) should be considered, or that the noise may simply be a 'rattle' in the chest, due to excessive bronchial secretions.

Question 2. Is there significant breathlessness with the wheeze?

If YES and the child is under 12 months old

If a child under 12 months of age has significant breathlessness with wheeze, it is almost certain they have acute viral bronchiolitis. This is by far the most common cause of acute wheezing and severe shortness of breath in the first year of life. The infection is usually due to respiratory syncytial virus (RSV), a highly contagious winter virus that infects most children by their second birthday. Currently, there is no effective vaccine for preventing RSV and, apart from supplementary oxygen and respiratory support, no effective treatment. Although most infants with viral bronchiolitis have only a

mild wheezing illness, approximately one in 50 (2%) will have breathlessness severe enough to warrant hospitalisation. Risk factors for admission include young age (i.e. under 6 months) and prematurity (admission rates of 5% at 33 to 35 weeks gestation, and progressively higher the more premature).²

Features of acute viral bronchiolitis on history are several days of coryzal symptoms and fever, followed by the abrupt onset of difficulty breathing, cough and wheeze, in a previously well infant. Clinically, there will be hyperinflation of the thoracic cage and increased work of breathing – with tachypnoea, excessive thoracoabdominal movement, intercostal, subcostal and suprasternal retractions, plus nasal flaring. On auscultation, the classic findings are widespread inspiratory crackles, together with generalised loud expiratory wheezing.

If YES, but the child is over 12 months old

As acute viral bronchiolitis is an illness of infancy, other possible explanations need to be considered if the child with wheeze is older than 12 months and the breathlessness is severe. These include uncommon conditions such as an inhaled foreign body or pneumonia (viral or bacterial). The most likely cause, however, is either a severe episode of 'viral-induced wheeze' or, in a child with 'multiple-trigger wheeze', a severe episode (i.e. more frequent and/or more persistent wheeze) triggered by a viral upper respiratory tract infection (URTI). These wheeze patterns are discussed later.

Question 3. Is the wheeze persistent and the child under 12 months of age?

A well-recognised pattern of wheezing in the first year of life is the infant who has a soft wheeze more or less continuously from a very early age. This pattern (or phenotype) is termed 'transient early wheeze'.^{3,4} These infants have no obvious breathlessness, there is no associated cough and the wheeze is unresponsive to bronchodilators. The wheeze may become more prominent during viral URIs and when the infant is crying and feeding, and softer when the child is peacefully sleeping. These children are otherwise well and thriving. By the age of 12 to 24 months the wheeze progressively disappears, and the likelihood of subsequent childhood asthma does not appear to be increased.

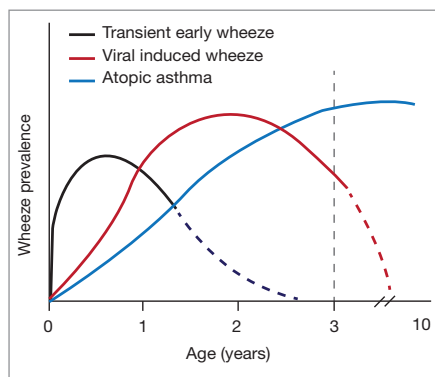
A possible mechanism for the wheeze is that the intrathoracic airways are simply small, or narrow (i.e. at the bottom end of the normal range); presumably, with growth, the airways enlarge and the turbulent airflow subsides. Another possible explanation is that there is excessive 'floppiness' (softness) of the infant's intrathoracic airways, which progressively improves with age.

Question 4. Do the episodes of wheeze occur only with viral URIs?

If YES

If viral URIs ('head colds') are the only trigger for wheeze, then it is most likely the child has the condition known as 'viral-induced

Figure. Prevalence of transient and recurrent patterns of wheezing in infants and young children. Atopic asthma is more likely in those with multiple trigger wheeze.



wheeze.⁴ Clearly, this information is only obtainable once the infant or toddler has had recurrent wheezing. Children with viral-induced wheeze are completely free of cough and wheeze between these discrete episodes. Other terms used to describe this common pattern of wheeze include 'viral-associated wheeze', 'episodic viral wheeze' and 'wheeze-associated respiratory infection' (WARI). These children are typically nonatopic, and are generally not from atopic families. Although there have been some encouraging data with the use of the oral leukotriene receptor antagonist montelukast as maintenance and intermittent treatment in children with this pattern of wheezing, there are little data in the 0 to 3 years age group, and there are practical issues with the currently available oral preparation (also montelukast is not registered in Australia for use in children aged under 2 years, nor for intermittent use).⁵

Episodes of viral-induced wheeze can be severe with significant breathlessness, and some affected children may have an observable response to inhaled bronchodilators. However, the response is not generally a dramatic one, in contrast to the impressive responsiveness of exacerbations of classic childhood asthma.

If NO

As well as viral URTIs, there are other identifiable triggers for wheeze. If the child wheezes with other triggers as well as with viral infections then the term 'multiple-trigger wheeze' is appropriate.^{4,5} A feature in these children is frequent mild wheeze and cough, outside the more discrete, troublesome episodes. Triggers for this frequent minor wheezing may include activity (exercise-induced wheeze), laughter, emotional upset, exposure to environmental tobacco smoke, sudden weather changes and damp or cold air. There may also be additional asthma-like symptoms, such as waking in the mornings with an audible wheeze with no apparent trigger (i.e. no coryzal symptoms) or a frequent nocturnal/early morning cough, or both. These children are likely to have a history of eczema and/or allergic rhinitis, plus a positive family history of atopy. Not surprisingly, young children fitting this pattern of wheezing are more likely to develop classic 'atopic asthma' in later childhood.

Patterns of wheeze, wheeze phenotypes

Description of the clinical pattern of wheeze, specifically the frequency, severity of any associated breathlessness and likely triggers, should be possible after answering these four questions. Although it may sometimes be possible to categorise a child with recurrent wheeze into one of the recognisable patterns (viral-induced wheeze versus multiple-trigger wheeze), these early childhood wheezing phenotypes are often difficult to apply clinically, especially during the first few episodes of wheeze. Instead, they are often only recognised retrospectively, or at least after a substantial period of observation. These clinical groups may, however, be useful when talking to parents of young children with wheeze.

Moreover, since the pattern of wheeze in the very young can vary over time, the distinction between viral-induced wheeze and multiple-trigger wheeze is unclear in many patients.⁶ Indeed, the difference between these two phenotypes may simply be a marker of disease severity, rather than a different clinical phenotype.⁶

Further questions: managing the wheeze

The obvious next questions to ask are about managing young children with recurrent wheeze.

Should an inhaled bronchodilator be given?

Whether a bronchodilator (reliever) should be given to an infant or toddler depends on whether the wheeze is associated with any breathlessness. If the child is not breathless and is not bothered by the wheeze then 'no treatment' is the best option. As the parents are likely to be distressed about the wheeze, a full explanation about wheeze, and why it occurs so frequently in 0 to 3 year olds, is required. No investigations (such as a chest x-ray, allergen skin testing or a total IgE) are indicated, as the results are highly unlikely to alter the diagnosis or management, nor assist with predicting prognosis.

However, if the child is obviously breathless, with significant increase in the work of breathing, then a trial of an inhaled short-acting beta₂-agonist (SABA) is appropriate, particularly if the child is older than 6 months.^{1,7} The only exception to this is the infant with acute viral bronchiolitis, in whom supplementary oxygen in hospital is the only intervention of proven value. A trial dose of a bronchodilator, such as salbutamol two to four puffs (i.e. 200 to 400 µg), should be administered via a puffer and an age-appropriate small volume spacer device. In the very young (0 to 2 years old), a reasonably tight-fitting facemask should be used; in children over 2 years old, it may be possible to use a mouth-piece instead of a facemask. The alternative, which is expensive and no more effective, is a nebuliser and loose-fitting facemask.

Close monitoring of the bronchodilator response is essential. A positive response should occur within minutes, and include reduced respiratory rate, fewer chest wall and/or suprasternal retractions and better air entry on auscultation. A dramatic response is unlikely, as asthma is unlikely to be the cause of

FEATURES ASSOCIATED WITH INCREASED AND REDUCED LIKELIHOODS OF ASTHMA**Increased likelihood of asthma**

- Wheezing with multiple triggers, in addition to URTIs ('head-colds')
- Wheeze with activity (exercise-induced wheeze)
- Frequently recurring wheeze
- Wheeze causing significant shortness of breath
- Wheeze plus persistent dry night or early morning cough
- Personal history of other atopic disease
- Family history of atopic diseases (parents or siblings)

Abbreviation: URTI = upper respiratory tract infection.

Reduced likelihood of asthma

- Symptoms only when the child has a viral URTI ('head-cold')
- Total absence of symptoms between discrete bouts of wheeze
- No immediate response to a trial of bronchodilators
- No response to a more prolonged (longer than one month) trial of inhaled corticosteroids
- Isolated cough – in the absence of wheeze or difficulty breathing
- Persistent/recurrent productive ('wet') cough
- Clinical features suggesting an alternative diagnosis

testing (spirometry), which is usually the age they start school.³ By definition, a diagnosis of asthma requires objective demonstration of variable airflow limitation and significant improvement immediately after inhalation of a short-acting bronchodilator (i.e. 10 to 15% improvement in forced expiratory flow rate in one second [FEV₁]). Although there is reluctance to using the label 'asthma' in children under 3 years of age, if the child has the classic clinical features of asthma and these respond impressively to bronchodilators, and there is no alternative diagnosis, a working diagnosis of 'probable' asthma is appropriate.

wheezing in children in this age group. However, if the work of breathing resolves rapidly and completely after an inhaled bronchodilator, then a provisional diagnosis of asthma is supported.

If there is a clear positive response, and further doses are planned at home, the child's parents will need to be shown how to give salbutamol via a small spacer device and either a facemask or mouthpiece. As well as education about wheeze and asthma, parents should also be given a written action plan that explains how to manage subsequent episodes and when to call for help. As a general rule, parents should be instructed to give two to four puffs of salbutamol when the child has a wheeze and is significantly breathless, and to repeat this every four hours if wheezing recurs.¹ If the response is poor, or of very short duration, parents should seek help by taking the child to their GP or the local emergency department.

Is there a role for oral corticosteroids?

If the wheeze has resulted in severe respiratory distress with marked tachypnoea, chest wall and/or suprasternal retractions, and difficulty with feeding then more comprehensive treatment with acute asthma medications is appropriate. This will mean frequent doses of a SABA (e.g. salbutamol every one to two hours) by puffer and spacer or nebuliser and, if the response to the initial dose is minimal or transient, a dose of oral prednisolone (i.e. an initial dose of 2 mg/kg, followed by 1 mg/kg each morning for two days is usually recommended,¹ although there is little evidence available regarding optimal dosages).

The risks and benefits of parent-initiated oral corticosteroids remains controversial in this very young age group.

At what age can a certain diagnosis of asthma be made?

The pedantic view is that a certain diagnosis of asthma cannot be made until the child is old enough for objective lung function

Can it be predicted which 0 to 3 year olds with wheeze will go on to develop asthma?

Although epidemiology studies have provided a good understanding of wheeze phenotypes in infants and toddlers, accurately predicting future asthma in individual patients has proven elusive. There is now a large body of evidence derived from birth cohort studies of infants who wheezed in the first three years of life and who have been followed prospectively through childhood to establish the risk factors for asthma in later childhood (ages 6 to 11 years). These features are listed in the Box.¹

Various combinations of these risk factors have been evaluated in an effort to derive the 'asthma predictive index' to determine more accurately which children will develop asthma in later childhood. Unfortunately, the accuracy of these indices in predicting the future has been disappointing.⁸

Are cromones and montelukast used as preventers in 0 to 3 year olds with wheeze?

Although regular preventer treatment is not recommended for viral-induced wheeze in 0 to 3-year-old children, an initial trial of montelukast should be considered in children aged 2 to 5 years with frequent episodic viral wheeze or mild persistent wheeze (multiple-trigger wheeze).¹ As montelukast is not approved for use in children under 2 years of age, an initial trial of a cromone (sodium cromoglycate or nedocromil) may be considered in children aged 1 to 2 years with persistent wheeze.

What is the role of inhaled corticosteroids as preventers in preschoolers with recurrent wheeze?

A trial of an inhaled corticosteroid (ICS) preventer is indicated in children aged 12 months and over who have been diagnosed with probable asthma and need frequent bronchodilators,

especially those who have been hospitalised with severe acute wheeze and breathlessness. Other indicators of significant morbidity that warrant treatment with ICS in children of this age with wheeze include frequent need for oral prednisolone, sleep disturbance with wheeze and cough, limitation of exercise due to wheezing, attendance at emergency departments and urgent unscheduled visits to the GP.

A systematic review of 29 randomised trials concluded that infants and preschool-aged children with recurrent wheeze or asthma have reduced exacerbation rates and less need for bronchodilators if they are treated with ICS, compared with placebo.⁹

What dose of ICS is appropriate in this age group?

The maximum dose of ICS recommended for 0 to 3-year-old children is fluticasone propionate 200 µg per day or budesonide 400 µg per day.¹ Higher doses are unlikely to give any further benefit but are very likely to cause side effects. A reasonable trial period of ICS is four to six weeks, during which time there should be a substantial reduction in symptoms and reduced need for bronchodilators. If uncertain of the response, the ICS should be ceased and the child observed to see if symptoms worsen. Obviously ICS should only be continued long-term in those children with a clear-cut, positive response.

Are combined ICS and LABAs useful in infants and toddlers with wheeze?

The short answer to whether combined ICS and long-acting beta-agonists (LABAs) are useful in infants and toddlers with wheeze is never. Most children who have a poor response to ICS are either nonadherent or have poor inhaler technique, or both – or alternatively they do not have asthma. Both the safety and efficacy of LABAs are in doubt in the very young, and there is a paucity of research data in this age group; also no LABAs are approved for use in children this young. It should be remembered that using a LABA twice daily effectively means taking two puffs of the SABA salbutamol every four hours every 24 hours.

If an infant or toddler fails to respond to ICS, and it is thought that a combined ICS/LABA is required (i.e. fluticasone plus salmeterol or budesonide plus eformoterol; neither TGA approved for use in this age group) to control their wheezing, then referral to a paediatrician is indicated.

Does severe acute viral bronchiolitis in infancy increase the risk of subsequent asthma?

There is evidence that those infants admitted to hospital with severe acute viral bronchiolitis have higher than expected rates of childhood asthma.² However, there remains uncertainty as to whether the severe illness itself causes airway damage and subsequent asthma or, alternatively, whether inherent asthma-related hyper-responsiveness of the infant's airways results in a severe illness with RSV infection.

Conclusion

Wheezing is common in children in the 0 to 3 years age group, and in most cases it is not due to asthma – especially in infants. When assessing these infants and toddlers with only their first or second episode of wheeze, it is impossible to predict their future pattern of wheeze or whether they will develop asthma in later childhood. Unless there is significant breathlessness with the wheeze, inhaled bronchodilators are not indicated. Although unlikely, a dramatic response to bronchodilators supports a diagnosis of asthma. For those infants and toddlers with significant ongoing morbidity as a consequence of their wheeze, a four to six-week trial of low-to-moderate dose ICS is appropriate. **MT**

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