The preschool wheezer

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Abstract

Wheeze is one of the most common reasons for seeking medical attention for young children. The management of preschool wheeze presents physicians with challenging problems. This article addresses the different patterns of preschool wheeze and explains how one might differentiate between them. It looks at the risk factors and important preventative measures that can be taken. Current therapies are reviewed and the paucity of evidence supporting common use is highlighted. Fortunately, the majority of preschool wheezers will grow out of their symptoms.

Keywords atopic; bronchodilator; montelukast; phenotype; preschool; prevention; steroid; transient; wheeze

All children cough and around 50% of children will wheeze before reaching school age, but the majority of these children will be normal. Up to 40% of infants experience wheeze in the first year of life.[1] A UK population-based study showed the prevalence of reported wheeze in 1998 was 29%, a significant increase from the same survey in 1990 when it was 16%.[2] The cost of treating preschool wheezing children is a considerable one, estimated to be 0.15% of the UK National Health Service budget.[3] An asthma diagnosis is more common in this age group then in older children (Figure 1).[4]

There is good evidence-based treatment for asthma in older children, but only a proportion of preschool wheezers fit an asthma diagnosis. Different patterns (or phenotypes) of preschool wheeze have been determined, and are described below. These evolve with time and it can be difficult to distinguish one from another at presentation.

Phenotypes of wheezing in young children

A series of studies from Tucson, Arizona, on a cohort of over 1000 newborn babies followed throughout childhood, have clarified the natural history.[5–7] In the first 6 years of life 50% of children never wheezed, small numbers (approximately 1%) had

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The average weekly incidence of first and new episodes of asthma in patients presenting to GPs in England and Wales between 1976 and 2000

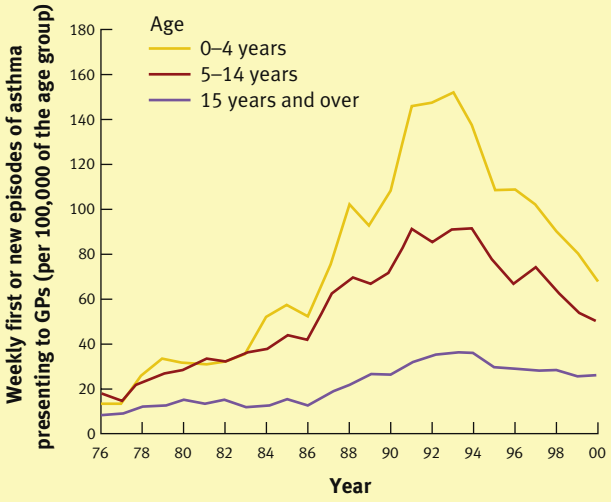

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Figure 1

atypical wheezing related to other abnormalities or disease states (see Table 1), and the remainder with typical wheeze could be divided into 3 groups: transient early wheeze, persistent atopic wheeze and late-onset non-atopic wheeze.

Transient early wheeze

In the Tucson study these the largest group had transient early wheeze, making up 20% of the cohort. These children generally start wheezing in their first year of life and stopped by 3 years of age. The primary risk factor is reduced pulmonary function in infancy with lung function tests shortly after birth showing reduced forced expiratory flow indicating small airways. This is not associated with a family history of asthma or atopy, and airway function in this cohort remained low up to the age of 16 years.

Causes of wheeze in young children

Typical wheeze	Atypical wheeze
Transient early wheeze	Upper airway abnormalities
Persistent atopic wheeze	Gastro-oesophageal reflux
Late onset non-atopic wheeze	Bronchopulmonary dysplasia
	Pulmonary oedema secondary to cardiac disease
	Foreign body aspiration
	Tuberculosis
	Causes of pulmonary suppuration

Table 1

Other risk factors for transient early wheezing include prematurity, male gender, exposure to siblings and other children at day care centres, prenatal maternal smoking, and postnatal exposure to tobacco smoke.

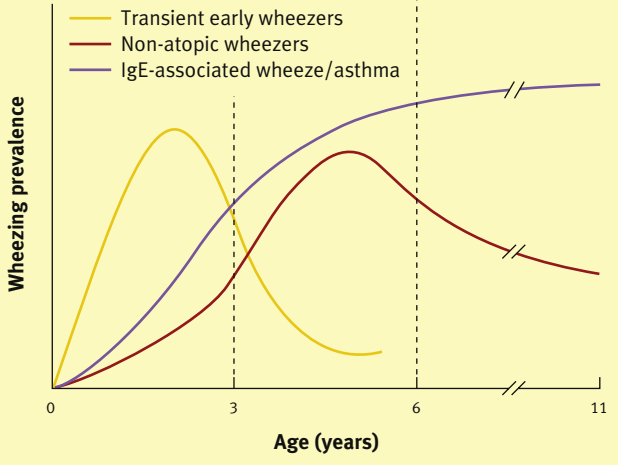
Persistent atopic wheeze

Children with persistent 'atopic' wheezing made up 14% of the Tucson cohort. More than half started wheezing before the age of 3 years and asthma persisted through childhood. They had normal lung function in infancy but developed airways obstruction in the first years of life. These children wheezed without viral infections, and were more likely to have a family history of asthma, elevated serum IgE and peripheral eosinophilia. Early allergic sensitization plays an important role in persistent wheeze/asthma. A European cohort of 1300 children studied from birth to 13 years found that sensitization to perennial (e.g. house dust mite, cat and dog hair) but not seasonal allergens developing in the first 3 years of life was associated with a loss of lung function at school age.[8] Such exposure to high levels of allergens in early life led to the development of airway hyperresponsiveness with wheeze in sensitized children. Exposure in later years had a much weaker effect. Interestingly, there is evidence that factors which decrease the risk of atopic sensitization include exposure to other children and farm animals.[9]

Late-onset non-atopic wheeze

These made up 15% of the Tucson cohort. Their cumulative prevalence increased in the first six years but then started to decline. These children had normal lung function early in life before any respiratory insult. Then, as they were exposed to viral respiratory agents,[7] they developed wheeze independently of allergic sensitization. This phenotype appears to be almost as common as atopic wheezing in the preschool group but is associated with less severe and less persistent wheeze and becomes less common among school-aged children (Figure 2).

Hypothetical yearly peak prevalence of wheezing according to phenotype in childhood



Adapted from Stein RT, et al. *Thorax* 1997; **52:** 946–52.

Figure 2

Clinical features

The child is likely to present with a history of noisy breathing but may not be making any noise when seen. It is important to determine what the family mean by the word 'wheeze' as parents often use this word to describe other noises, such as hearing or feeling a loose rattle on the chest or nasal snuffling. Studies using a video questionnaire[10] or objective recording of lung sounds, have shown poor parental recognition of wheeze. From the history it is important to determine the pattern and duration of wheezy episodes and the severity when they occur. Any precipitants of episodes should be identified, e.g. viral infections. History and examination should elicit whether the child or family are atopic (e.g. evidence of eczema) and whether there is evidence of any other systemic disease (e.g. cystic fibrosis, heart disease). At acute presentation the child will be tachypnoeic and hyperinflated with lower intercostal indrawing and widespread expiratory wheeze. In addition, generalized inspiratory crackles may be heard in children with viral infections. Severe respiratory distress, evidence of hypoxia (SaO_2 < 92%) or poor response to treatment warrants referral to hospital. Between episodes the child may be entirely normal. Persistence or recurrence of focal signs, evidence of inspiratory wheeze or stridor, hypoxia between episodes or failure to thrive are all indications for further investigation in secondary care. It may be difficult at presentation to fit the child into the phenotypes described above but for management purposes there are two main patterns:

- acute episodic wheeze and cough with no interval symptoms. Main/only trigger viral infections and no evidence of atopy
- chronic symptoms or frequent episodes with interval symptoms. Evidence of atopy and a variety of triggers which may include viral infections.

Investigation

Most preschool children with wheeze do not require any investigation. A chest X-ray should be performed if there are persistent signs. Oximetry is useful during acute episodes. A sweat test should be performed if cystic fibrosis is suspected. Where there is suspicion of structural abnormalities or unusual diagnosis then special investigations including bronchoscopy and CT scanning are carried out in secondary/tertiary centres. Further tests should be guided by the history and examination if other causes of 'atypical wheeze' are suspected (Table 1).

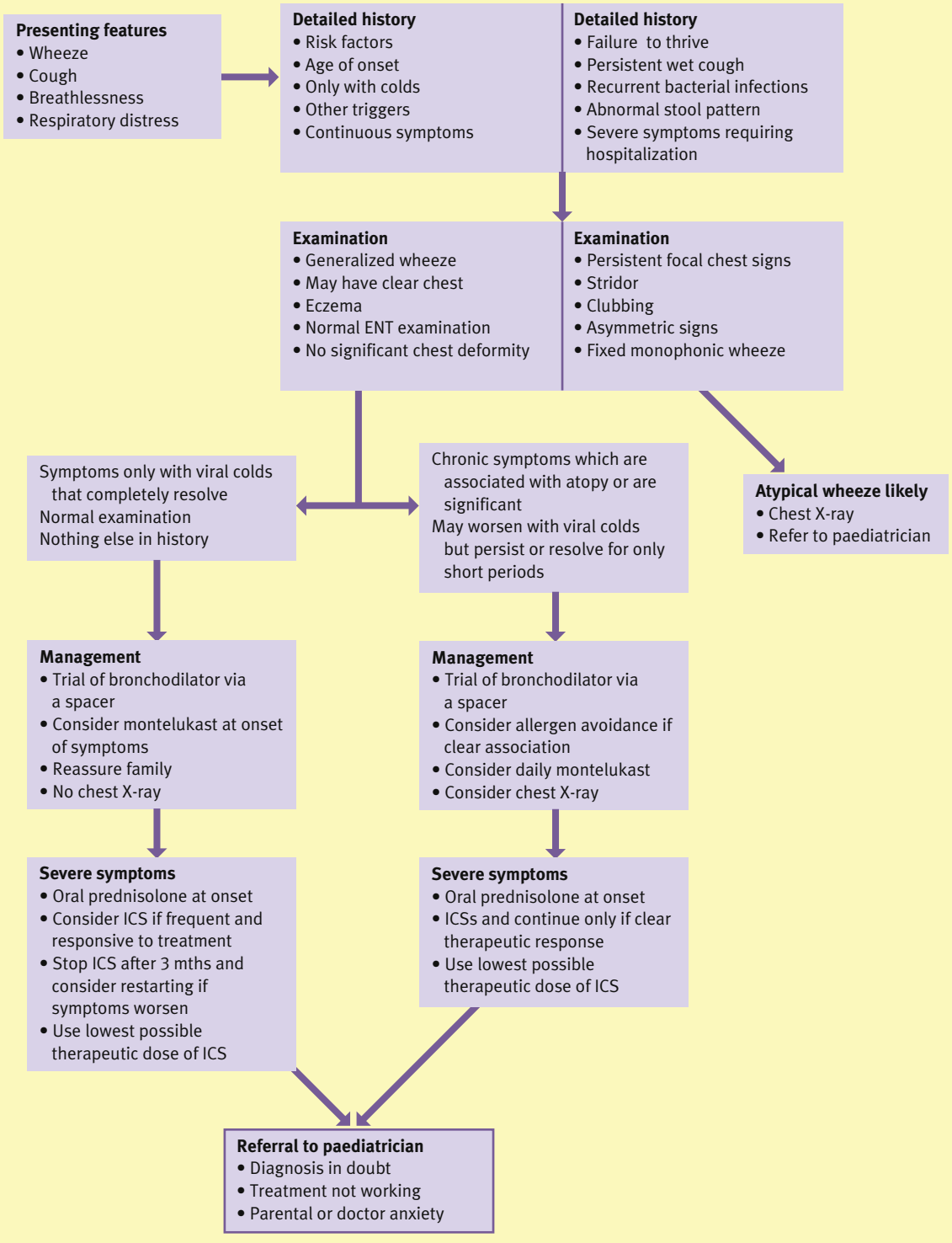
Treatment options

The pathophysiology of wheeze in young children may be multifactorial with bronchospasm, mucus oedema, mucus plugging, abnormal airway architecture and mechanics all contributing.[11] These mechanisms may not be receptive to pharmacological manipulation and so the response to conventional asthma treatments may be highly variable.

Preventative measures

Passive prenatal smoking results in underdevelopment of the fetal bronchial tree leading to diminished lung function from birth.[12] This is the most important preventable risk factor for early transient wheeze. Although parents rarely admit to smoking in front

Management of preschool wheeze in a primary care setting



ICS, inhaled corticosteroids.

Figure 3

of their child, urinary cotinine (a metabolite of nicotine) studies consistently reveal that wheezing children of parents who smoke are significantly exposed. Passive postnatal smoking constitutes a significant risk factor for infection, worsening asthma symptoms and decreased lung function in young children. Unfortunately interventions to decrease parental smoking are often unsuccessful.[13] Breastfeeding is associated with lower asthma rates during childhood.[14] Primary prevention by reducing the allergen burden in the environment has not been very successful. For secondary prevention it is clear that if the child is sensitized to an aeroallergen (e.g. cat) then it should be removed from their environment. There is evidence that environments rich in microbacteria, such as farms, protect against the development of allergies. Two bacterial species identified in cowsheds possess strong allergy protective properties.[15] Antibiotic use in the first 2 years of life may be implicated in the development of asthma and careful antibiotic prescribing is warranted.[16]

Bronchodilator therapy

There is good evidence that β_2-receptors are present in the airway from birth and there is definite physiological evidence that at least some children respond to inhaled β-agonists. However, a Cochrane review[17] published in 2002 looked at the efficacy of inhaled short-acting β-agonists for 'recurrent wheeze' in children under 2 years old and could not find clear evidence of benefit. The data from the 8 randomized trials was markedly heterogeneous which severely limited the performance of between-study comparisons. In clinical practice, it is worth undertaking a therapeutic trial of β_2-agonists to assess benefit. Ipratropium bromide is no more effective than β_2-agonists in preschool children. The younger the child the less likely a response to either agent but in reality it is difficult to predict who will respond. There is no evidence that drugs given by a nebulizer are any more effective than those given through a spacer and mask.

Inhaled corticosteroids and oral steroids

There is no doubt that inhaled corticosteroids (ICS) are beneficial for preventing daily symptoms and improving lung function in school children. Such effectiveness has not been proven in children with viral-induced wheeze.[18] ICS maintenance therapy is not effective in preventing or treating asthma exacerbations secondary to viral infections in older school children or adults with established, atopic asthma. In young children, the use of high-dose ICS at the onset of viral colds does not reduce the risk of hospital admission and need for oral steroids but does have a modest beneficial effect on severity of symptoms.[19]

In preschool children with persistent wheezing, the efficacy of ICSs is less clear. Some studies show clinical and physiological benefits, particularly if the child is atopic, whereas others show no benefit. The effect of high-dose ICS on growth is well known, but in animal models recent evidence suggests nebulized steroids can impair alveolar development[20] implying the need for increased caution in infants. There is recent evidence that long-term use of ICS has no effect on the natural history of asthma or wheeze in later childhood.[21] This important conclusion means ICSs should be prescribed only if the current symptoms are severe enough and then are only continued if shown to be beneficial.

The role of systemic corticosteroids is controversial. A recent randomized controlled trial of parent-initiated oral prednisolone at the time of viral infection showed no evidence of benefit.[22] However, another randomized trial showed that systemic steroids given to children presenting to the emergency department with preschool viral wheeze reduced the need for additional asthma medication in hospital and reduced length of stay from 3 to 2 days.[23] A trial of systemic steroids is sensible in a severely wheezing young child, especially when there are risk factors for atopic asthma and the child responds to bronchodilators.

Leukotriene receptor antagonists

The use of leukotriene receptor antagonists seems logical as there is increased production of cysteinyl leukotrienes at the time of viral infection, and viral infections are a major trigger in preschool children. Physiological studies of the oral leukotriene antagonist montelukast have shown bronchoprotection and a reduction in exacerbations in preschool children.[24] Montelukast has a rapid onset of action and a recent study of a 7-day course given from the day of onset of viral symptoms reduced symptoms by 14% and days off childcare or school by 37%.[25] A trial of montelukast is an appropriate first-line preventative strategy for young children with persistent wheeze and can be considered as an intermittent therapy for those with frequent viral exacerbations.

Prognosis

The most common parental question is 'will he grow out of it, doctor?' The long-term cohort studies provide some reassurance. Eighty per cent of children who wheeze during the first year of life do not wheeze after the age of 3 years. Sixty per cent of children who wheeze in the second year of life and 30–40% of those in the third year, have stopped wheezing by school age.[7] Children who are clearly atopic are more likely to continue with symptoms during childhood.

Conclusion

The pattern of wheeze in preschool children is an indicator of both likely treatment response and prognosis.

- For children with acute episodic wheeze and cough with no interval symptoms a trial of treatment during the acute episode is appropriate. These children are unlikely to benefit from prophylactic treatment with inhaled steroids but exacerbations may be ameliorated in some by the intermittent use of leukotriene receptor antagonists (montelukast).
- For children with chronic symptoms, therapy is dependent on severity. Mild symptoms that do not disturb sleep or feeding may not require treatment. For troublesome chronic symptoms and particularly where there is evidence of atopy it is reasonable to trial stepwise treatment with leukotriene receptor antagonists (montelukast) as first line followed by low-dose inhaled steroids. Therapy which is not helpful should be stopped. A referral to an expert in paediatric respiratory disease should be made before escalating therapy.

Some children may have a poor response to pharmacological treatment and avoidance of triggers, and supportive treatment for severe exacerbations (with oxygen ± oral steroids) may be mainstay of treatment. A management plan is outlined in Figure 3. There is room for new evidence-based therapy for preschool wheeze. ◆

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Practice points

- Wheeze is a very common symptom in preschool children
- Pre- or post-natal smoking is the single most important risk factor for wheeze in this age group
- Viral infections are the commonest triggers
- Bronchodilator therapy via a spacer should be the first-line treatment for acute symptoms
- Leukotriene antagonists can be effective and should be tried if prophylaxis is warranted
- Inhaled corticosteroids rarely improve symptoms and have no disease-modifying properties in the long run
- In all cases where inhaled corticosteroids are started, it is important to stop their use after several months to look for evidence of their efficacy