



# Investigating wheeze in children

In this series of articles we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

## RAY NETHERCOTT

MD, MRCP

## CRAIG MELLIS

MD, MPH, FRACP

Dr Nethercott, Respiratory Research Fellow, Department of Respiratory Medicine, The Children's Hospital at Westmead, NSW. Professor Mellis, Head, Discipline of Paediatrics and Child Health, University of Sydney, The Children's Hospital at Westmead, Westmead, NSW. [Professor Mellis' current appointment is Foundation Head of Medicine, Bond University, Gold Coast, Qld.]

Series Editor

## CHRISTOPHER S. POKORNY

MB BS, FRACP

Dr Pokorny is a Member of the Board of Continuing Education, Royal Australasian College of Physicians, and a Gastroenterologist in private practice, Sydney, NSW.

This is the first of a two-part series of articles on wheeze in young children. This article focuses on the appropriate investigations for children with wheeze; the second article discusses the management of the more common conditions causing wheeze in infants and preschool children (see next month's issue of *Medicine Today*).

Wheeze is extremely common in infancy and early childhood, occurring in up to 30% of children before the age of 3 years. Most of these children have minimal morbidity and only a small percentage (i.e. those with significant breathlessness) require hospitalisation. Wheeze is defined as a high pitched, expiratory sound arising from the lower respiratory tract.

There are multiple potential causes of wheeze, and it is useful in paediatric practice to divide the differential diagnoses of wheezing into broad age categories before considering the appropriateness of investigations.

These broad categories are:

- infants (under 1 year of age)
- toddlers to preschool children (1 to 5 years)
- school-aged children (over 5 years).

The key differential diagnoses in these age categories are summarised in Table 1.

## The mechanism of wheeze

Wheeze signifies turbulent airflow due to expiratory airflow obstruction somewhere within the intrathoracic airways. While obstruction may originate at any level from the small peripheral bronchioles to the trachea, the vibrating air column that is audible as a 'wheeze' on auscultation arises from the larger airways. Thus, if there is extensive and severe bronchiolar obstruction (e.g. as in acute viral bronchiolitis) the bronchiolar pathology will generate widespread inspiratory crackles, whereas the expiratory wheezing is due to secondary dynamic obstruction of the larger airways. This results from the infant compressing larger airways in an attempt to expel air from the alveoli and through the extensive small airway obstruction during expiration (see Figures 1a and b).

Narrowing of the intrathoracic airways can occur by several mechanisms, including smooth muscle contraction (bronchospasm), mucosal oedema, external compression, intraluminal obstruction, or a combination of these.

## Investigating infants with wheeze

The key message is that most infants who wheeze do not have asthma. Infants with a single, acute

### IN SUMMARY

- Wheeze in infancy is not usually due to asthma.
- A thorough history and physical examination will generally determine the cause of the wheeze.
- Pulmonary function testing (FEV<sub>1</sub> and PEF) can be performed reliably in most children over 5 to 6 years of age and is useful if there is uncertainty regarding diagnosis or disease severity.
- In toddlers and preschool children always consider the possibility that an inhaled foreign body is the cause of wheezing.
- While not a routine investigation, a chest x-ray can be useful in all age groups to exclude most rare and serious causes of wheeze.

bout of wheezing usually have acute viral bronchiolitis and are unlikely to wheeze again.

### Transient early wheeze

Most infants with recurrent or persistent wheeze have transient early wheeze. Babies with transient early wheeze simply have relatively narrow and/or relatively floppy intrathoracic airways. Therefore, they are prone to wheezing, particularly in the first year of life. This wheezing is not normally associated with morbidity, such as shortness of breath, hospitalisation, or troublesome cough. Babies with transient early wheeze are healthy, thriving infants who wheeze, but are not troubled by the noisy breathing. The wheeze is unresponsive to bronchodilator therapy and preventer medication (such as inhaled corticosteroids). This is not surprising since the abnormality is structural rather than being due to smooth muscle spasm or airway inflammation.

The natural history of this syndrome is favourable because the wheezing progressively subsides as airway dimensions increase and airway stability improves with age and lung growth. Generally, the wheezing of transient early wheeze ceases in the second year of life.

### Asthma

Infants with genuine asthma, on the other hand, will have significant morbidity in association with their wheezing. This includes severe wheeze with shortness of breath, distressing cough and possible need for hospitalisation and oxygen therapy. There may be a clear cut response to  $\beta$ -agonists (e.g. salbutamol) and/or anticholinergics (e.g. ipratropium bromide) given by inhalation. Although the efficacy of inhaled corticosteroids is not well documented in this age group, infants with obvious asthma and ongoing morbidity deserve a trial of asthma preventive therapy.

Infants with significant asthma should be referred to a paediatrician for further evaluation, particularly if they are not responding to therapy.

### History and examination

As with all age groups, history and physical examination are paramount in determining the origin of the infant's wheeze. In particular, enquiry should be made regarding family history of atopy and/or asthma, perinatal history, any history

## Investigating wheeze in children

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Up to 30% of children will have an episode of wheeze before they are 3 years old. Most of these children have minimal morbidity and only a small percentage require hospitalisation. In most cases, a thorough history and examination will determine the cause of the wheeze.

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suggesting inhalation of a foreign body, previous response to medications, and any prior history of significant breathlessness, cyanosis, apnoea, or feeding difficulties.

Physical examination should be comprehensive and include both respiratory, cardiac and neurodevelopmental assessment plus plotting of height, weight and head circumference on percentile charts. It is important to note on

## Investigating wheeze in children

continued

examination the signs of respiratory distress (e.g. chest wall and subcostal retractions, nasal flaring and tachypnoea). On auscultation any difference in wheeze between the right and left lungs, and any unusual cough or noises with respiration should be noted, as should any signs of poor weight gain.

**Table 1. Causes of wheeze in children**

Common causes	Uncommon causes
<b>Infant</b> Acute viral bronchiolitis Transient early wheeze Infant asthma	Bronchopulmonary dysplasia (chronic lung disease of prematurity) Aspiration secondary to gastro-oesophageal reflux or secondary to dysco-ordinate swallowing Anatomical abnormalities (e.g. primary tracheomalacia) Familial bronchiectasis (cystic fibrosis, primary ciliary dyskinesia, immune deficiency syndrome) Congenital heart disease/cardiac failure
<b>Toddler</b> Wheezing associated with respiratory infection Asthma Foreign body inhalation	Familial bronchiectasis (see above) Mediastinal mass (obstructing major bronchi or trachea)
<b>School-aged child</b> Asthma	<i>Mycoplasma pneumoniae</i> bronchitis Foreign body inhalation Hysterical wheeze (paradoxical vocal chord movement) Mediastinal mass (e.g. enlarged hilar lymph nodes)

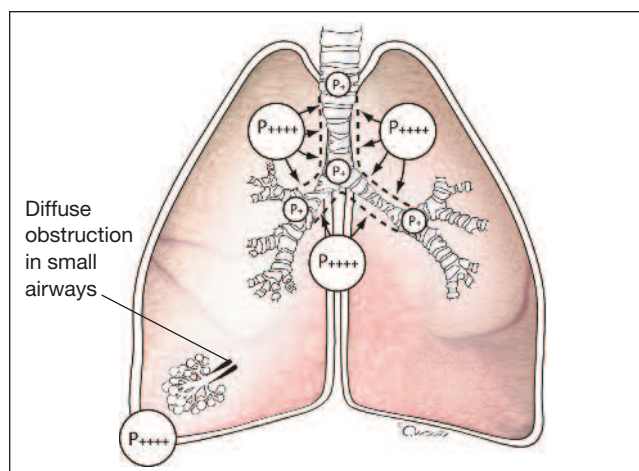
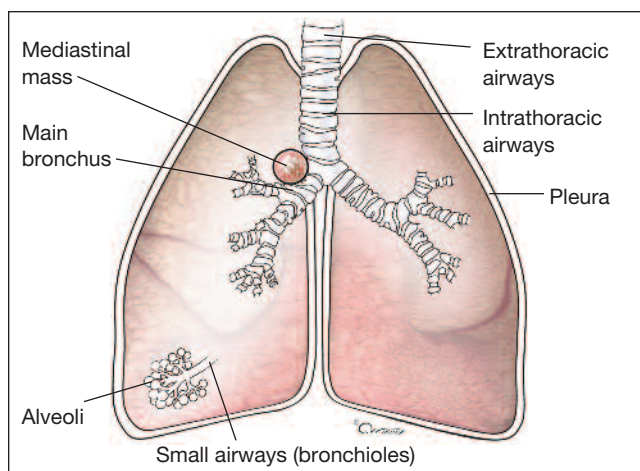
### Specific investigations

For most infants with wheezing no investigations are necessary to make the diagnosis. However, if the wheeze is recurrent, severe, or persistent, further investigation may be warranted, particularly if there is an associated history of significant breathlessness, troublesome cough, failure to thrive, cyanotic episodes or apnoea. An appropriate initial investigation in this situation is a chest x-ray. If the chest x-ray is normal, this rules out chronic lung disease of prematurity, acute viral bronchiolitis, and most of the severe, anatomic congenital malformations that can produce expiratory wheezing. If the chest x-ray suggests a mass lesion or lobar emphysema, a CT scan of the chest is indicated.

If recurrent vomiting, feeding difficulties and/or possible aspiration are prominent historical features, a barium swallow may be indicated.

Enquiry regarding the infant's newborn screening tests for cystic fibrosis should be made, although a negative screening test does not totally preclude a diagnosis of cystic fibrosis.

Direct visualisation of the airways (laryngoscopy and bronchoscopy under



Figures 1a and b. Mechanism of wheeze. a (left) A large mass in the region of the right main bronchus and carina causing obstruction of large, central airways and an expiratory wheeze. Wheeze occurs at the site of the obstruction and may be localised to one side of the chest. b (right). Widespread narrowing of small, peripheral airways (e.g. viral bronchiolitis). During expiration large, central airways are compressed due to high positive pleural ( $P++++$ ) pressures and low intra-airway pressure ( $P+$ ). This results in diffuse wheeze from large airways narrowing during expiration.

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general anaesthesia) is indicated only in infants whose wheeze is associated with apnoea or cyanotic episodes, or when chest x-ray or CT scan suggests an endobronchial or large airway compressive lesion.

If the noise is predominantly inspiratory (inspiratory stridor) then a laryngeal abnormality is likely, such as infantile larynx ('floppy' larynx or laryngomalacia).

Immune function testing is rarely indicated, except when there is a history of wheeze with recurrent pneumonia or x-ray changes suggesting suppurative airways disease (chronic bronchitis/bronchiectasis). Expert immunological opinion should be sought before extensive immune function testing.

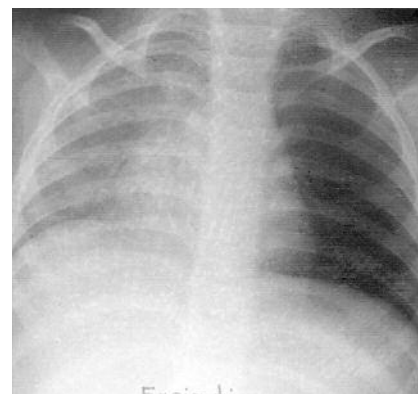
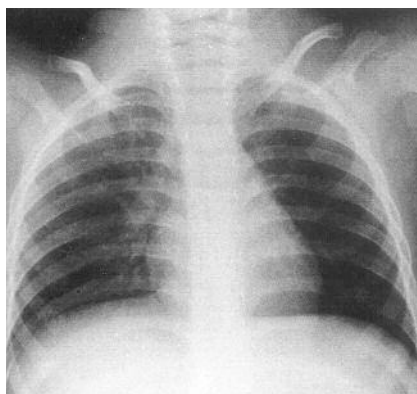
In summary, most infants with an acute, single episode of wheeze have acute viral bronchiolitis, while infants with recurrent or persistent wheeze have either transient early wheezing or, less often, infantile asthma.

### Investigating toddlers and preschoolers with wheeze Wheezing associated with respiratory infection

Toddlers and preschoolers have a high rate of wheezing in association with viral respiratory tract infections (wheezing associated respiratory infection or WARI). The distinction between wheezing associated with respiratory infection and episodic asthma is subtle, but current consensus is that wheezing associated with respiratory infection simply represents the mildest end of the spectrum of classic childhood asthma. Most toddlers who wheeze only with viral upper respiratory tract infections cease to wheeze in later childhood.

### Asthma

If the child has additional risk factors for asthma, such as coexistent atopy (eczema or allergic rhinitis) or a strong family history of atopic disease, recurrent wheezing may well be due to genuine, ongoing



Figures 2a and b. Normal inspiratory chest x-ray (a, left). Expiratory chest x-ray (b, right) shows 'air trapping' in the left lung. A fragment of peanut was removed from the left main bronchus at bronchoscopy.

asthma. Most children with asthma develop wheeze symptoms by their second or third birthday. An historical feature that strongly supports the diagnosis of asthma is a clear cut, immediate response to a bronchodilator such as inhaled salbutamol.

### Foreign body inhalation

Children in this age group are particularly prone to inhalation of foreign bodies – especially nuts. A history of acute aspiration is often absent, as the parents may not have witnessed the inhalation episode. The classic physical signs of an acute foreign body aspiration are asymmetry of wheeze, breath sounds and air entry. Most foreign bodies will travel through the trachea and lodge into one or other main bronchus where they initially cause a 'ball valve' (air-trapping) obstruction. On auscultation there will be diminished breath sounds and localised wheezing on the side where the foreign body has lodged. The typical chest x-ray appearance is one of unilateral air trapping on the expiratory film, with a relatively normal inspiratory film (Figure 2).

If a foreign body has been retained in the airways for some time (weeks) it can cause total obstruction of a bronchus. Subsequent resorption of air from the lung will result in atelectasis of the lung,

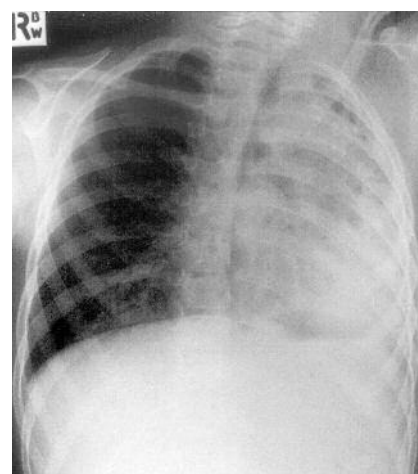


Figure 3. Typical chest x-ray of child with a retained foreign body in the left lung, which is totally collapsed. A large grass seed plus extensive granulation tissue were removed. The patient had experienced fever, cough and sputum production for many months.

and a loose productive cough. If a foreign body has been retained the chest x-ray will show extensive unilateral collapse of the obstructed lung with displacement of the mediastinum towards that side; this is quite unlike the x-ray of acute foreign body inhalation (Figure 3).

However, a foreign body in an airway cannot be ruled out on history, physical examination, or chest x-ray alone. Thus, if the clinical or radiological scenario

suggests foreign body aspiration, and there are ongoing symptoms (particularly cough and wheeze of relatively abrupt onset that is unresponsive to treatment) specialist referral should be arranged and a bronchoscopy (under general anaesthesia) considered.

### Specific investigations

As with infants, most toddler and preschoolers with wheezing can be managed without the need for any investigation, other than a good history and physical examination. A trial of asthma treatment may be appropriate, although in this age group formal lung function testing (spirometry) to objectively diagnose asthma is impossible. A normal chest x-ray will rule out most of the rare and unusual causes of wheeze in this age group.

In summary, most toddlers and

preschoolers with wheeze have either wheeze associated with respiratory infections or episodic asthma. If the wheeze is persistent, progressively worsening, unresponsive to therapy, or associated with significant morbidity (e.g. distressing cough or breathlessness) further investigation and referral to a paediatrician is warranted.

### Investigating school-aged children with wheeze

#### Asthma

In school-aged children, wheeze is generally due to classic childhood asthma; however, not all that wheezes is asthma (Table 1). Fortunately, in the school-aged child with wheeze, lung function testing (including response to bronchodilators) can be used to give objective support for a diagnosis of asthma. Only those children with more troublesome asthma or in whom diagnostic difficulty is an issue require formal spirometry. This is particularly helpful if performed when the child is wheezing to enable measures both before and after a bronchodilator (such as salbutamol), a 10 to 15% improvement in FEV<sub>1</sub> being diagnostic of asthma.

Childhood asthma is broadly divided into episodic and persistent disease, based on the frequency of symptoms (Table 2). Since most children have episodic rather than persistent asthma, spirometry is generally normal between attacks. Thus, finding abnormal spirometry between attacks is strong evidence for persistent asthma, of at least moderate severity.

Although rarely indicated, asthma can be confirmed with bronchial provocation testing, such as 6 minutes of vigorous exercise. A positive bronchoconstrictor response (more than 10 to 15% drop in

FEV<sub>1</sub> or peak flow) is diagnostic of bronchial asthma. However, a negative response does not rule out the possibility of underlying episodic asthma.

It is also possible to detect clinically provoked bronchoconstriction by auscultation of the chest before and after provocation (such as repetitive coughing or a short sprint up and down a corridor or a flight of stairs). This can be done relatively easily in a general practice setting. The development of generalised wheezing after such provocation would be strong supportive evidence of underlying asthma.

An alternative to bronchial provocation is to measure 'variability' of peak expiratory flow (PEF) over one to two weeks, with the child measuring his or her own PEF twice daily. Although there is normally a variability in peak flow, if this exceeds 25 to 30% it is abnormal and strong evidence for asthma. The normal method of calculating the variability of peak flow is shown in the box on this page. Measurement of PEF is highly effort-dependant, therefore, if the effort varies so too will the measured peak flow.

Other clinical information supporting a diagnosis of asthma includes:

- a family history of asthma and atopic diseases (in first degree relatives)
- a personal history of other atopic disease (eczema or allergic rhinitis)
- the presence of multiple positive allergen skin tests or radioallergo-sorbent tests (RAST) – i.e. atopy
- a clear cut clinical response to a bronchodilator agent
- a sustained remission of symptoms on long term preventive therapy (such as inhaled corticosteroids).

As mentioned above, allergen skin prick testing or RAST for specific IgE to common food or airborne allergens can provide additional evidence to support an asthma diagnosis. Although not all children with atopy will have asthma, almost all school-aged children with significant asthma will have one or more positive skin tests or RAST. Thus, the absence

### Table 2. Classification of childhood asthma severity

#### Persistent asthma

Occurs in 5% of children with asthma  
Symptoms (cough or wheeze) most days or nights  
Episodes frequent and often severe

#### Episodic: frequent

Occurs in 20% of children with asthma  
Episodes at least every 4–6 weeks  
Episodes moderately severe

#### Episodic: infrequent

Occurs in 75% of children with asthma  
Episodes less than every 4–6 weeks  
Episodes mild  
Generally triggered by viral upper respiratory tract infection

### Calculating peak expiratory flow variability

$$\text{Peak expiratory flow variability} = \frac{(\text{highest peak flow}) - (\text{lowest peak flow})}{(\text{mean peak flow})} \times 100$$

continued

of atopy would be unusual in an asthmatic child, particularly in an older school-aged child, and should prompt a re-evaluation of the diagnosis of asthma.

### Uncommon causes of wheeze

A school-aged child with a sudden acute bout of wheezing and no past history to suggest asthma needs to be carefully evaluated, especially regarding possible inhalation of a foreign body.

In the child with persistent wheezing that is proving unresponsive to anti-asthma medications, other diagnoses need to be considered. These include a 'fixed' obstruction within the intrathoracic airways (such as tracheal or bronchial stenosis) or compression of the tracheobronchial tree due to a mediastinal mass. These unusual causes of wheeze will have other symptoms and signs of the underlying pathology.

### Other investigations

A chest x-ray may be indicated at the first presentation of a school-aged child with a history of significant wheeze, particularly if there are any unusual features. A normal chest x-ray rules out most of the rare but serious causes of wheezing in all age groups. Children with asthma usually have a normal chest x-ray, but in the presence of airflow obstruction due to acute asthma, the chest x-ray will show generalised hyperinflation, air trapping and/or patches of subsegmental collapse. Repeated chest x-rays with each episode of acute asthma are totally unwarranted.

### Summary

Wheezing is a very common symptom in childhood, particularly during infancy. A thorough history and physical examination will normally suffice for diagnosis and management.

In infants acute wheeze is usually due to acute viral bronchiolitis, while persistent or recurrent wheeze in infants is most often due to transient early wheezing rather than asthma. In preschoolers and toddlers wheezing is generally due to wheeze in association with respiratory infections (WARI), which probably represents the mildest end of the episodic asthma spectrum. Most will cease wheezing as they progress through childhood and have fewer viral respiratory tract infections. In school-aged children wheezing is usually due to classic childhood asthma, which can be diagnosed objectively and treated conventionally.

A normal chest x-ray effectively rules out most of the rare and serious causes of wheeze in all age groups; however, chest x-rays should be performed only when the history, examination or progress is unusual or confusing. **MT**