Asthma

& Wheezing in the First Years of Life

An information paper for health professionals

FOR HEALTH PROFESSIONALS

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Contents

Key messages

Wheezing in infancy and childhood is a common condition, however it is not a single disorder and can be due to causes other than asthma.

Not all wheezing is asthma. In more than half of the children who wheeze within their first three years, the wheezing is transient and does not increase the risk of later asthma.

Presence of allergic sensitisation (atopy) is associated with an increased risk for persistent wheeze, reduced lung function at 6 years of age, and is more likely to be an indicator of asthma. The role of atopy in the development of asthma is not yet clear.

There is a clear association between parental asthma or atopy, sibling persistent wheezing, and asthma.

Exposure to tobacco smoke (including in-utero) increases the risk of childhood wheeze and asthma; therefore, it should be avoided.

Environmental conditions that increase the rate of bacterial and viral infections are risk factors for transient wheezing, but its relationship to asthma remains unclear.

Children with frequent simple colds and other common childhood infections in infancy, are less likely to develop persistent wheezing in later childhood. Many preschool children with viral induced wheezing will outgrow these symptoms, and do not have asthma.

Bronchodilators should be used for acute episodes of wheezing. Oral corticosteroids should not be prescribed for preschool children with mild to moderate episodes of wheeze, unless it is severe enough for hospital admission.

For ongoing prophylactic treatment, low dose inhaled corticosteroids (ICS) or montelukast is recommended.

Use of high dose ICS or combination therapy with a long-acting beta-agonist (LABA) is not recommended in those under 5 unless under specialist supervision. Medications should be administered via spacer.

Asthma & wheezing

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing – particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in bronchial hyperresponsiveness to a variety of stimuli, such as cold air and viruses.

Generally, asthma is identified by the presence of these symptoms, together with features of atopy (or a family history of atopy or asthma) and impaired lung function.[1] However, the diagnosis of 'asthma' cannot be made with certainty in a preschool child, because it is difficult to establish whether the underlying disease mechanism is airway inflammation in this age-group. Wheezing, coughing and breathlessness are common in young children, and can all be symptoms of conditions other than asthma.[1] Nevertheless, presence of atopy or other allergic conditions (e.g. eczema) increase the likelihood that wheezing in a young child may represent asthma.

Epidemiology of asthma

Asthma remains a significant health problem in Australia, with prevalence rates that are high by international standards. In 2007–2008, the prevalence in Australia was about 1 in 10 – equivalent to about 2 million people.[2]

While the prevalence of asthma and atopy in children and adolescents was shown to be on the rise in developed nations throughout the 1980s and early 1990s, more recent epidemiological studies have shown a decline in these countries, including Australia. To date, there is no clear explanation for this change in prevalence.

There is increasing evidence that asthma may originate in the first few years of life and involves a complex interaction between in-utero factors, genetic factors, atopy, viruses and the environment.[3]

What is wheezing?

Wheeze is a non-specific sign caused by narrowing of intrathoracic airways leading to expiratory flow limitation, irrespective of the underlying mechanism.[4] It is characterised by a continuous high-pitched sound emanating from the chest during expiration.[4,5]

In westernised countries, wheezing affects about one-third of babies in their first year.[1]

Wheezing-associated respiratory illnesses in children are often described as asthma,[6] however while most children with asthma show symptoms of wheezing, not all wheezing is related to asthma. Wheezing in infancy and childhood is not a single disorder[4], and is just as likely to be due to causes other than asthma.[7]

Many studies are investigating the relationship between wheezing and asthma to see whether wheezing phenotypes can be used as a predictor of asthma. So far there has been considerable progress in defining different wheezing disorders in childhood and identifying factors predictive of persistent wheeze and asthma. However, based on current evidence it is not yet possible to develop interventions to address likely causative factors.

Wheezing in childhood

Various forms of noisy breathing, including wheezing, are common among preschoolers.[4] Wheezing in infants up to 12 months old is most commonly transient, and is due to acute viral bronchiolitis or to the presence of relatively small and/or floppy airways which produces noisy breathing but no associated morbidity.

Parents/carers sometimes use the word 'wheeze' to mean different things, including cough, gasp or rattle, and a change in breathing rate or style of breathing. If based on parental report alone, children may be labeled as having wheeze when they do not,[4] therefore it is important to properly assess the child.

Wheezing in preschool children is usually associated with viral upper respiratory tract infections, which recur frequently in this age group.[4,5] Many children wheeze when they have viral respiratory infections, even if they do not have asthma.[5]

Wheezing can be due to many conditions, including anatomical abnormalities of the airways, cystic fibrosis, and bronchomalacia.[4]

Pathophysiology of wheeze in early childhood

Inflammation of airways may be absent in very young children with wheeze.[4]

There is not enough evidence to know whether the pathophysiology of recurrent wheezing and asthma-like symptoms in preschool children is the same as that of asthma in older children and in adults.[4] Therefore, the term 'asthma' should be used with caution in preschool children.

Early life origins of asthma & wheezing

The development of asthma involves a complex interaction of genetic factors and environmental influences. A family history of allergy and asthma can be used to identify children at increased risk of asthma.

There has been considerable interest in whether a child's likelihood of developing asthma may be reduced by changing the environment. Much of the evidence for benefits of proposed environmental modifications comes from epidemiological studies. Interventional studies have examined the effect of manipulating various environmental factors, but as yet there is little convincing evidence that specific interventions are highly effective in preventing the onset of asthma.[8]

At-risk children have compromised airways from birth, in addition to up-regulated or down-regulated (or both) immune responses and raised IgE levels during the first years of life. A prospective birth cohort study in the UK found that atopic and non-atopic children who had never wheezed, but had atopic parents, had poorer lung function than children without a family history of atopy or asthma.[9] This suggests that their airways could be pre-modelled, possibly in-utero, putting them at increased risk of developing respiratory diseases such as asthma.[9]

The identification of 'asthma genes' related to IgE synthesis and allergic inflammation indicates that a genetic susceptibility to develop asthma is present from conception. It may be that clinical expression of asthma then depends on environmental factors[10] that operate differently in susceptible individuals, interacting with the developing immune system to cause disease.[11] Recent evidence suggests that environmental factors mediate the onset of persistent wheezing in genetically predisposed children, so avoiding allergens and other associated factors may delay but not prevent the onset of childhood asthma.[12]

Is it possible to prevent wheezing and asthma in a young child with a genetic predisposition?

Based on current evidence, it is still not possible to answer this question. Decades of research have shed light on many aspects of asthma, but because of its complexity it remains difficult to identify causative risk factors and develop interventions to address them. For this to occur, we need to know much more, including:

- the environmental factors that interact with 'asthma genes' in the development of persistent wheezing and asthma
- which tools (e.g. phenotype assessment) can be used to distinguish young children who are at high risk of developing asthma from the larger group with transient wheezing
- which strategies can prevent deficits in lung function in very young children in whom the disease process is beginning
- the nature of the population at risk, so we can develop interventions that are effective in preventing different types of childhood asthma
- the timeframe in which to intervene with various approaches.

Wheeze and its relationship to asthma

Understanding the different wheezing disorders may help to identify young children whose wheezing is likely to be related to development of asthma.[7] It may also help to avoid inappropriate treatment of children with non-asthma-related wheeze.[9]

Among preschoolers with recurrent wheezing, only 30% will have asthma at age 6 years.[13]

Longitudinal studies have identified various patterns of wheezing in preschoolers (wheezing phenotypes)[4], such as the American Thoracic Society/European Respiratory Society (ATS/ERS)[14] and Tucson[15,16] phenotype classifications (see Table 1).

However, it is important to remember that phenotype classifications are epidemiological tools rather than clinical ones. Early childhood wheezing phenotypes cannot be recognised or applied clinically, because they are recognised retrospectively, and there is insufficient published evidence to enable clinicians to predict epidemiological phenotype from the clinical presentation in an individual child with episodic wheeze.[4]

Regardless of when symptoms occur, children with persistent wheezing are more likely to have developed atopy than children with transient early wheezing.[6] They already have raised serum IgE levels and diminished airway function within their first year, and have reduced lung function by the age of 6.[7] Therefore, in general, children should be treated based on atopic risk, not necessarily based on age range.

Persistent wheezing may have an early or late onset[6,7]:

- early onset – children who begin wheezing during their first 3 years and continue to wheeze up to school age
- late onset – children who do not wheeze in the first 3 years of life but begin wheezing around the age of 6 years.

Persistent and late onset wheeze that continues during preschool years is associated with an increased risk of asthma.[17] A diagnosis of asthma is more likely if there are other risk factors, such as a family history of asthma or atopy[1] (see *Risk factors associated with asthma and wheezing* below). Bronchiolitis or wheezy bronchitis requiring hospitalisation is also likely to be related to later onset of asthma.[1,18]

Table 1: Wheezing Phenotypes based on Tucson Children's Respiratory Study and Avon Longitudinal Study of Parents and Children (ATS/ERS classification used).

Classification system/source	Phenotypes identified	Description
Tucson Children's Respiratory Study [15, 16]	Transient early wheeze	Wheezing begins and ends before age 3 years (approximately 20% of children) Associated with premature birth and parental smoking
	Persistent early-onset wheeze	Wheezing begins after age 3 years (approximately 14% of children) Typically child has recurrent episodes of wheeze during upper respiratory tract viral infections. In those under 2 years old, usually Respiratory Syncytial Virus (RSV)
	Late-onset wheeze	Wheezing begins after age 3 years (approximately 14% of children) Not associated with atopy or family history of atopy
Avon Longitudinal Study of Parents and Children (ATS/ERS classification used) [14]	Transient early wheeze	Wheezing mainly occurs before 18 months, then mainly disappears by age 3.5 years (approximately 16% of children) Not associated with allergies to airborne antigens
	Prolonged early wheeze	Wheezing occurs mainly between age 6 months and 4.5 years, and is mainly gone before the child's 6th birthday (approximately 9% of children) Not associated with allergies to airborne antigens Associated with a higher risk of airway hyperresponsiveness and reduced lung function at age 8–9 years, compared with never/infrequent wheeze phenotype.
	Intermediate onset wheeze	Wheezing begins sometime after age 18 months before 3.5 years (approximately 3% of children). Strongly associated with atopy (especially house mite, cat allergen), higher risk of airway hyperresponsiveness and reduced lung function at age 8–9 years, compared with never/infrequent wheeze phenotype.
	Late onset wheeze	Wheezing mainly begins after age 3.5 years (approximately 6% of children) Strongly associated with atopy (especially house mite, cat allergen, grass pollen)
	Persistent wheeze	Wheezing mainly begins after 6 months and continues through to primary school (approximately 7% of children) Strongly associated with atopy

Risk factors associated with asthma & wheezing

There are many risk factors associated with asthma and wheezing. The type of risk factor is likely to depend on the type of wheezing disorder acquired in childhood.[6]

Family history

There is a strong link between family history, wheezing and asthma. A family history of atopy or asthma (or other lower airways disease) is a risk factor for all types of wheezing, but significantly more of a risk for persistent wheezing.[6] Maternal atopy and asthma in particular increase the risk of persistent wheezing.[7]

Family studies have demonstrated the genetic contribution to atopy, persistent wheezing and asthma.[6] Familial contribution to transient early wheezing is likely to take the form of congenitally small airways.[6]

All types of wheezing are significantly more frequent in boys than girls during childhood[6] and boys tend to have lower airway function than girls during infancy and childhood.[19]

Environmental tobacco smoke

Exposure to tobacco smoke increases the risk of childhood wheeze and asthma and therefore should be avoided.

A longitudinal study of asthma and allergic diseases in schoolchildren (in Northern Sweden since 1996) found that both environmental tobacco smoke and personal smoking were significantly related to asthma and wheeze in teenagers.[20]

A recent systematic review of all prospective epidemiological studies assessing the association between passive smoking and asthma incidence found that exposure to pre- or postnatal passive smoke was associated with 21–85% increase in incidence of asthma. The strongest effect from prenatal maternal smoking on asthma was found in children aged ≤ 2 years.[21]

Maternal smoking in pregnancy is a risk factor for all types of wheezing.

It is well accepted that maternal smoking increases the risk of transient early wheezing and impaired lung function in infancy.[22] Exposure to smoking appears to affect lung development, resulting in reduced lung capacity and smaller airways. This in turn makes wheezing with viral illness more likely, as well as increasing the risk of prematurity and low birth weight.[6]

Exposure to maternal smoking in-utero has been associated with long-term deficits in lung function that, together with the lung impairment produced by asthma, may increase the risk of chronic respiratory diseases later in life.[23] These adverse outcomes in babies can also potentially increase the likelihood of wheezing and asthma in children.

Evidence suggests that reducing maternal smoking would decrease wheezing illnesses in young children, and reduce the long-term effects of tobacco smoke on children with asthma.[23] Therefore, health professionals have a particular responsibility to address smoking cessation options with parents/carers.[24]

Allergic sensitisation

Allergen sensitisation does not appear to be a direct risk factor for persistent wheezing and asthma. It is likely that other, as yet unknown, factors are responsible for both allergen sensitisation and the onset of persistent wheezing and asthma.[11]

Allergic conditions such as allergic rhinitis and eczema are associated with persistent wheezing but not transient wheezing.[6] There is also a direct relationship between risk of persistent wheezing and serum IgE level during the first year of life, just as there is a link between asthma and IgE level in older children and adults.[7]

Despite the strong association between atopy, persistent wheezing and asthma, the role of sensitisation in the development of asthma is far from clear. There have been conflicting results from studies examining the effects of common allergens such as house dust mite and pets on the development of asthma.[25]

Evidence from a growing body of research indicates that the prevalence of asthma is independent of allergen exposure in early life.[25] Interventions to reduce exposure to allergens (such as house dust mite) can reduce wheezing in babies but do not appear to alter the development of wheezing or asthma in later childhood.[11]

Role of viruses

Role of viruses in the development of asthma

Recent studies indicate that certain viral infections in early life may lead to increased risk of developing asthma in childhood. This association is more likely in a child with atopy.[26-28]

Role of viruses in triggering asthma exacerbations

Although allergen exposure can trigger asthma exacerbations, this is not the most common cause. In both adults and children, the majority of asthma exacerbations are caused by respiratory virus infections of which rhinoviruses are by far the most frequent. For example, an Australian study has reported that 78% of acute asthma exacerbations were virus-associated, and of these, 83% were rhinoviruses. The marked increase in asthma exacerbations in both children and adults (occurring in the autumn, winter and early spring months) is predominantly virus-related, with rhinoviruses dominating.[29]

When is wheeze indicative of asthma?

It is not possible to predict with certainty whether a child who has wheeze will develop asthma, however it is possible to give an estimate of probability based on other contributing factors.

The probability that wheeze is a sign of asthma is more likely if a child presents with:

- other allergic diseases, such as atopic dermatitis (eczema) and allergic rhinitis
- evidence of atopic sensitisation (allergen specific IgE)
- family history of asthma and other allergic diseases
- late onset persistent wheeze

It is important to explain to parents/carers that wheezing in an infant or preschooler does not mean the child will have asthma or allergies by primary school age.

In preschool-aged children with recurrent wheeze (e.g. four or more episodes per year), consider using the Asthma Predictive Index[30] to estimate whether children are likely to have asthma during primary school years.

Management of asthma & wheeze

Acute exacerbation

Based on current evidence, for children aged 5 years or younger (particularly those with intermittent, viral-induced wheezing) acute exacerbations should be treated with short-acting bronchodilators (as needed), preferably administered with a spacer and face-mask.

Oral corticosteroids should not be routinely used, and be limited to those with severe wheeze who require hospital admission,[31] or those with moderate to severe asthma exacerbations with incomplete response to beta-agonists.

Ongoing prophylactic (preventative) therapy

In a child with frequent intermittent or mild persistent asthma, initial therapy options include low-dose ICS (<200mcg Beclomethasone dipropionate or equivalent) or montelukast. If adequate asthma control is not achieved after a trial period of 2–4 weeks[31] with montelukast, it should be replaced with low-dose ICS.

If asthma control is still not achieved, consider referral for specialist investigation. Use of high dose ICS or combination therapy with a LABA is not recommended in children under 5 years unless under specialist supervision.[32]

The use of a spacer when administering medication is recommended; it helps the medication to reach the right area of the lungs, ensuring that it doesn't end up in the mouth and throat where it can lead to oropharyngeal thrush and hoarseness.

Education & self-management

It is important to give the parent/carer some basic education on wheeze and how to manage it. If asthma is suspected, offer further asthma education. See the latest edition of the Asthma Management Handbook for guidance via our website: nationalasthma.org.au

When diagnosing a child with wheeze or asthma it is very important that he/she has access to:

- reliever medicine (e.g. *Salbutamol*) and that the parent/carer is educated on how to use it appropriately
- a spacer: a small-volume spacer with a face-mask is suitable for a child under 4 years old. Small and large volume spacers without a face-mask are suitable for children over 4 years old. See our how-to video- *Using your inhaler: puffer and spacer for kids* via our website: nationalasthma.org.au.
- an asthma action plan.

Consider preparing an asthma action plan for each patient with asthma and review it regularly. When preparing an asthma action plan, go through it with the parent/carer so they are clear on what they need to understand and do in certain situations; for example, being aware of the signs of an exacerbation, when their child should take oral corticosteroids, and when they should seek medical help.

If a child has visited hospital for treatment, ensure their parent/carer has everything they need to manage their child's wheeze or asthma, such as:

- a discharge letter for the child's doctor
- a short-term reducing medication plan
- asthma medications and/or scripts
- asthma action plan (new or updated)
- instructions on how to use the asthma medication device/s; for example a spacer device with a puffer
- asthma education from a health professional and/or referral to a health professional for asthma education.

It is recommended that the parent/carer makes an appointment with their child's family doctor within a week following discharge from hospital.

Further information

Visit the National Asthma Council Australia website at: **nationalasthma.org.au**

A matching patient resource is also available via the National Asthma Council Australia website.

Although all care has been taken, this information paper is only a general guide; it is not a substitute for assessment of appropriate courses of treatment on a case-by-case basis. The National Asthma Council Australia expressly disclaims all responsibility (including negligence) for any loss, damage or personal injury resulting from reliance on the information contained.

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References

References are listed in the online version of this information paper, on the National Asthma Council Australia website: nationalasthma.org.au

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leading the attack against asthma