



CLINICAL REVIEW

Diagnosis and management of asthma in children

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Asthma is a condition characterised clinically by recurrent episodes of wheeze, cough, and breathlessness, and physiologically by variable airflow obstruction. Airway inflammation is sometimes added to the definition, but it is rarely measured in clinical practice; some groups would consider episodic viral wheeze in preschool children as a separate condition. This review gives a practical perspective on the basic steps of diagnosis and management of asthma in school age children for non-specialists in primary and secondary care.

Who gets asthma?

There is wide geographical variation in the prevalence of asthma, with wheeze in 13 and 14 year olds varying from less than 1% (Tibet) to more than 30% (New Zealand), and in 6 and 7 year olds from less than 3% (India) to nearly 40% (Costa Rica).¹ Whereas in the United Kingdom atopy is a major factor associated with asthma, this is not the case in resource poor areas. In the developed world, the risk of asthma is increased by a positive family history of asthma and atopy, maternal smoking in pregnancy, and early sensitisation to aeroallergens. Numerous “asthma genes” have been discovered, and clearly asthma is a complex polygenic disease. In the developing world, atopy is often not associated with asthma; instead, the use of biomass fuels, tobacco smoking, and viral infections seem to be more important.

What are the clinical features?

All children have intermittent respiratory symptoms, but most do not have asthma. The first prerequisite for managing asthma is knowledge of the range of normal childhood illnesses. Typically, children may have more than 10 viral related colds a year, with symptoms lasting for more than two weeks; non-specific respiratory infections may also last for two weeks or more.

The process of establishing a diagnosis of asthma should extend over at least two consultations. The first step is to take a detailed history and carry out a physical examination, focused on excluding other causes of respiratory symptoms (box 1). Asthma

is suggested by reports of wheeze, dry cough, and breathlessness. Symptoms are typically worse at night and in association with specific triggers such as viral upper respiratory tract infections, exercise, and exposure to smoke and aeroallergens. Parents use the word “wheeze” to describe a wide range of respiratory noises.² Parental report of wheeze correlates poorly with objectively recorded wheeze.³ Thus until a doctor has heard and documented the presence of true polyphonic (musical) expiratory wheeze, an open mind should be kept about the nature of the sound described. A video questionnaire may be helpful to clarify what is being described.⁴

“Cough variant” asthma is a controversial topic. Although a few children may have cough and no wheeze as a manifestation of asthma, these presentations are rare. Isolated chronic dry cough in a community setting is rarely if ever due to asthma.⁵ We will not diagnose asthma unless there is a history of considerable breathlessness, as well as either or both of cough and wheeze.

Box 2 lists the indications for referral to secondary care. If there are features suspicious of a non-asthmatic condition, then referral to secondary care is indicated. Referral should be expedited when children are systemically unwell or there is concern about a serious condition.

How is the diagnosis confirmed?

The figure[↓] shows a proposed diagnostic algorithm. If asthma is suspected, it is good practice to document variable airflow obstruction with a peak flow meter using the best of three attempts:

- If peak flow is below age appropriate normal ranges (www.lungfunction.org/), then improvement by 12% or more 20 minutes after administering a short acting β_2 agonist (for example, 400 μg salbutamol given with a metered dose inhaler and spacer) is a useful test to confirm variable airflow obstruction.
- If peak flow is normal, then a two week period of home monitoring may confirm the diagnosis; if the peak flow

The bottom line

In problematic cases of childhood asthma, rather than escalating treatment, a systematic approach is needed, including a review of the diagnosis; adherence, including ability to take drugs correctly; and the child's environment

If diagnostic doubt still exists, including a failure to respond adequately to a low to medium dose of inhaled corticosteroids, referral should be made to a specialist team

Asthma is a disease that kills, even in children with "mild" asthma, and care must be seen in that context

Any emergency visit to hospital, regardless of whether admission occurs, is a marker of future risk, and should prompt a focused and urgent review of what trigger factors led to the attack and whether the attack was appropriately managed

Non-adherence to treatment, overuse of bronchodilators, and underuse of inhaled corticosteroids are common problems that should be routinely tackled

Failure of annual asthma review is a factor in asthma related deaths and for children a review should be routine at least every three months; these should be conducted by doctors or nurses with training in asthma and not seen as "tick box" exercises

When specialist services are also involved, good communication is essential; this is particularly true after an acute asthma attack

Sources and selection criteria

We performed a search of PubMed using the terms "asthma" or "wheeze", with the filters "clinical trial", "published in the last 5 years", "humans", "English" activated, with the subject age range "child: birth-18 years". Additionally, we searched the Cochrane database of systematic reviews and Clinical Evidence, as well as our personal archives of references, and checked the reference lists in all the manuscripts. We selected only those manuscripts related to the diagnosis and practical management of asthma and eliminated those that studied preschool aged as well as school aged children, because the pathophysiology of wheeze and the treatment algorithms are different in these two age spans. We excluded small trials and case series if the findings had been subsumed into a meta-analysis or Cochrane review.

Box 1 Features suggestive of a non-asthma diagnosis*History*

Absence of true polyphonic (musical) wheeze

Presence of prominent upper airway symptoms such as rhinitis, snoring, and sinusitis

Symptoms from the first day of life—these are never due to asthma, and a serious condition such as primary ciliary dyskinesia, aspiration due to incoordinate swallow, and congenital lung and airway malformations must be excluded

Sudden onset of symptoms—suggestive of foreign body aspiration and requires immediate management. Anaphylaxis may also be a consideration, but other features such as urticarial rash and focal swelling would be expected to give clues to this diagnosis

Presence of chronic moist cough or sputum production—if present daily for more than six weeks and has not resolved with one course of antibiotics, referral is indicated

History of systemic illness or suggestive of immunodeficiency: severe, persistent, unusual, or recurrent infections (SPUR)

Continuous, unremitting symptoms with no symptom-free days

Physical examination

Systemic signs such as clubbing, weight loss, failure to thrive

Upper airway disease—tonsillar hypertrophy, noticeable rhinitis

Unusually severe chest deformity

Unexpected signs on auscultation (fixed monophonic wheeze, stridor, asymmetrical signs)

Chest palpation during coughing or forced expiratory manoeuvres—palpable secretions revealed

Signs of cardiac or systemic disease, such as a cardiac murmur, abnormalities in heart sounds or precordial impulses, abnormal peripheral pulses, weight loss, and unusual systemic infections such as pyogenic arthritis or meningitis

Box 2 When to refer to secondary care

The diagnosis is in doubt

An age appropriate level of treatment is not working despite apparently satisfactory adherence; specifically if the child has received more than two courses of systemic corticosteroids in a year, or has not responded to British Thoracic Society Step 3 treatment (inhaled corticosteroid 400 µg/day plus long acting β₂ agonist)

Any involved people (doctor, child, family) are unhappy with outcomes

chart is a flat line (or variability is within normal limits) despite ongoing symptoms, it is difficult to attribute the findings to asthma. Peak flow variability of 15% or more is strongly suggestive of asthma; likewise, if children are given a β₂ agonist at home, an improvement by 12% or more 20 minutes later is also supportive of a diagnosis of asthma. However, it is acknowledged that compliance with peak flow monitoring is often poor.

- If peak flow is normal, consider getting children to run for 10 minutes, either on the flat or up and down steps.

None of these tests is sensitive to the diagnosis of asthma; however, it is a safe principle that the more practitioners try and fail to identify airflow obstruction, the less likely is a diagnosis of asthma. Routine chest radiography is not needed; and indeed a normal radiograph cannot exclude a serious condition.

Occasionally a blind trial of asthma treatment may be considered justifiable; in that case it is essential to have a trial period of discontinuation of treatment to ensure that any apparent benefit is related to the treatment rather than arising spontaneously. No evidence base exists to recommend a particular trial regimen;

we would use a three stage protocol, preferably combined with peak flow measurements at home to document improvement:

- Initiate treatment with beclomethasone equivalent 200 µg twice daily using a metered dose inhaler and spacer
- Reassess at six weeks; if no benefit then the diagnosis is unlikely to be asthma, stop treatment and consider referral for investigations; if the symptoms have disappeared, stop treatment and reassess six weeks later
- If symptoms have recurred by six weeks, restart inhaled corticosteroid in a low dose (100 µg beclomethasone equivalent twice daily using a metered dose inhaler and spacer), and continue to adjust dose depending on response.

How is it managed?

A recent report of asthma related deaths in adults and children in the United Kingdom has highlighted that nearly half of those who died from asthma could have been saved by attention to several components of basic management (box 3).⁶

Pharmacotherapy

The basic management steps for asthma are well summarised in national and international guidelines.⁷⁻⁸ All guidelines agree that first line preventive treatment should be with inhaled corticosteroids. There is no evidence to support the use of combination inhalers as first line treatment in children, indeed the reverse is the case,⁹ and their increasing prescription in this role is to be discouraged. Importantly, the Best Add-on Therapy Giving Effective Responses (BADGER) study showed that the plateau of the dose-response curve to inhaled corticosteroids for most children with asthma is 200 µg/day fluticasone or equivalent, and few children benefited from a step up to 500 µg/day.⁵⁻¹⁰ The best response was adding a long acting β₂ agonist, and some children also responded to a leucotriene receptor antagonist. We recommend that those children with asthma who do not respond to fluticasone 200 µg/day plus any one additional treatment should be managed as treatment failures and not by escalating pharmacotherapy.

No inhaled drug is effective unless delivery to the airways is optimised. Children must be shown how to use inhalers and their technique checked repeatedly. The use of spacers is particularly problematic in adolescents—the devices are often considered “babyish” and so the young person puts the metered dose inhaler straight in the mouth, with usually poor delivery of drug to the lower airway in consequence. In this case a breath actuated or dry powder device would be preferable. Spacers for school aged children should always be used with a mouthpiece, not with a mask.

Adverse environmental factors

It must be highlighted that any tobacco smoking has an adverse effect on asthma outcomes.⁴⁻¹¹ Cotinine levels (an objective measure of exposure to nicotine in tobacco) are just as high in those who smoke “but not in front of the children.”¹² Exposure to household mould is also likely to be detrimental.¹³ Skin prick testing to identify allergy to household pets should be considered. Whether sensitised people benefit from avoidance of house dust mite is controversial¹⁴ and in the United Kingdom is not recommended in the most recent guidelines from the British Thoracic Society/Scottish Intercollegiate Guidelines Network.⁷ However, multifaceted interventions may be considered in those with severe disease.¹⁵

Comorbidities

In childhood, comorbidities such as obesity, rhinosinusitis, food allergy, dysfunctional breathing, and psychosocial problems may contribute to respiratory symptoms. Gastro-oesophageal reflux is often found if sought, but treatment does not affect asthma outcomes.¹⁶ It is much easier to identify obesity than to treat it; obesity may lead to breathlessness, which is not asthma related, causing confusion about the diagnosis. Whether treatment of rhinosinusitis improves lower airway inflammation is controversial, but upper airway symptoms certainly should be treated on their independent merits.¹⁷ Food allergy is associated with severe asthma in particular; whether allergy causes increased asthma severity.¹⁸ Dysfunctional breathing (vocal cord dysfunction, exercise induced laryngeal obstruction) is a really important and often under-appreciated problem. It may cause stridor, and be associated with paraesthesia, sore throat, and hoarseness of the voice. It never occurs during sleep. The diagnosis may be obvious from a video of an attack; parents should be able to make a recording on their mobile phone (but clearly if children are thought to need urgent medical attention, this takes priority). Confirmation of doubtful cases can be made in specialist centres by experienced physiotherapists and laryngoscopy during exercise. Finally, psychosocial problems were identified in 26% of people with asthma who died,⁶ and from our experience these are common in children with severe asthma.¹⁹

Provision of an asthma treatment plan

Asthma treatment plans are underused and thought to be associated with poor outcomes.⁶ The purpose of a treatment plan is to guide young people and parents on maintenance treatment, asthma triggers and how to avoid them, and what to do in the event of worsening symptoms, particularly an acute asthma attack. Numerous proformas are available, and whichever is chosen should be regularly reviewed or updated. Long term, children largely do not reliably measure their peak flow twice a day, but measurement at the time of a viral cold or increased symptoms can be used to drive treatment changes and the need to seek medical attention. A major challenge is to ensure that, without causing distress, families understand that asthma can be serious. Phrases that may be helpful include “asthma is one of those conditions which can be very serious, but if properly managed should not impact on your child’s life. However, if treatment is neglected, your child can become seriously ill or even worse, and we all need to remember this.” An obvious adverse effect of prescribing inhalers to all patients with asthma, many of whom have a diagnosis on the weakest of grounds, is that the condition is trivialised.

Regular follow-up

As with all conditions in childhood, regular and focused follow-up is essential. Basic child health should be assessed, including height and weight, and immunisations, especially against influenza. Growth failure may be related to over-treatment with inhaled corticosteroids, poorly controlled asthma, or an unsuspected coincidental diagnosis. Day to day asthma control should be assessed, including the number of dispensed prescriptions for short acting β₂ agonists and whether the child has had an emergency visit for asthma. The possibility of a missed or wrong diagnosis, no matter how eminent the health professional who initiated treatment, should always be considered. Above all, adherence to treatment, including adequacy of inhaler technique, should be checked. Assessing

Box 3 Components of asthma management

- Institution of appropriate pharmacotherapy administered using an age appropriate inhaler device
- Attention to adverse environmental factors, especially exposure to tobacco smoke
- Attention to any comorbidities, especially dysfunctional breathing
- Provision of an asthma treatment plan
- Regular follow-up and assessment of progress

adherence is difficult and needs to be done with sensitivity (box 4 lists some approaches that may be useful).

Role of biomarkers

Interest is increasing in the role of biomarkers to drive asthma treatment. In children, there is as yet no evidence that any biomarker should be used to determine management. Blood eosinophil levels do not correlate well with airway eosinophilia,²⁰ unlike in adults; exhaled nitric oxide and airway eosinophilia have inconsistent relations over time, even within an individual²¹; and no study has yet determined a convincing role in routine practice,²² although undoubtedly, biomarker driven treatment remains an important aspiration.

How are acute asthma attacks managed?

Asthma attacks can be immediately fatal, can be predictive of future clinical course and subsequent attacks, and may be associated with impairment in normal airway growth.²³ The term “exacerbation” has been criticised as too benign.^{24 25} Box 5 summarises the key steps in recognising and managing an acute asthma attack.

Evidence in the United Kingdom suggests that most deaths related to asthma occur in those who are not receiving specialist care.⁶ Primary care clinicians must be alert to detecting patients with high risk “mild” asthma (box 6), and those with unscheduled hospital visits and admissions.

How is treatment failure managed?

A serious error of judgment is to escalate treatment in those children with asthma who are unresponsive to basic management, without due consideration of possible reasons for why this might be the case. Broadly, treatment failures can result in persistent symptoms on a daily basis or recurrent acute asthma attacks requiring oral corticosteroids, or both. The threshold for referral to specialist care depends on the experience of the treating doctor and the expertise in the clinical setting; suggested indications are given in box 2.

Persistent symptoms

The commonest causes of treatment failure are wrong diagnosis and poor compliance with treatment, and both should be reviewed, including checks of adherence and inhaler technique (box 4).¹⁹ It is particularly important to remember symptoms of dysfunctional breathing. A check on prescription uptake is often revealing, and indeed electronic alerting of excessive β_2 agonist and inadequate preventer prescription is another key recommendation of the National Review of Asthma Deaths in the United Kingdom.⁶ The home environment also should be considered; a home visit by an experienced nurse, if possible, can often be illuminating.¹⁹ The possibility that symptoms are being over-reported, and there are hidden gains, should not be forgotten.

Acute asthma attacks

A review after an acute asthma attack requires a focused response to determine whether there are ongoing reversible problems that contributed to the episode, and whether the attack itself was correctly managed.

The combination of allergic sensitisation, exposure to allergens, and viral infection is strongly predictive of asthma attacks, of which only exposure to allergens can be modulated.²⁶ Inhaled corticosteroids are protective of attacks in people with atopic asthma. Attention to adherence, optimising the dose of inhaled corticosteroids, and reducing exposure to environmental allergens to which the child is sensitised is essential. Poor baseline control is associated with risk of attacks, and every effort should be made to reduce this risk.

The management of the acute attack should be reviewed, regardless of whether the child was admitted. Was there an action plan in place, with documented triggers, and was it followed? Does the plan need revision in light of the attack? Has there been regular review? Was the spacer and short acting β_2 agonist readily available and neither underused nor over-used? Prescription of more than one canister of a short acting β_2 agonist a month, failure to prescribe or collect adequate prophylactic drugs, and prescription of long acting β_2 agonists as sole treatment are red flags.

Although it is not possible to abolish asthma attacks totally, risk can be reduced and management optimised to control them.

How is episodic viral wheeze managed?

By school age, most children with asthma have many triggers leading to wheeze, including exercise, viral colds, exposure to allergens and cold air. Wheeze with viral colds as the sole trigger and with no symptoms between colds is most common in preschool children, but may occasionally be seen in school aged children. In these rare circumstances, intermittent rather than continuous treatment is permissible, but clinicians should be sure that there are no important interval symptoms.²⁷ If attacks are frequent and severe, then a trial of regular inhaled corticosteroids should be given. This may highlight that interval symptoms have been missed. This group needs equally careful follow-up, in particular to detect a change of symptom pattern.

How is asthma managed in adolescents?

Adolescence is a difficult time, irrespective of the presence of asthma. Risk taking behaviour, including experimenting with tobacco, e-cigarettes, and other substances of misuse is common and affects asthma control.²⁸ Denial of illness and symptoms is also the norm, and adolescents can be reluctant to take any treatment regularly. Spacers are often discarded and it may therefore be better to prescribe dry powder or breath activated devices to ensure adequate drug delivery. Although evidence of efficacy in paediatric practice is lacking,²⁹ combined budesonide and formoterol is a safer option than short acting β_2 agonists as sole treatment. Time and patience are needed,

Box 4 Methods for assessing adherence

Check how many prescriptions for inhaled corticosteroids have been dispensed over the previous year

If feasible, and there is only one local pharmacist, check how many prescriptions have actually been dispensed

Ask the child to demonstrate how the inhaler is used

Ask questions sensitively, such as “Most patients and all doctors find it difficult to remember to take treatment; how often do you think you/your child forgets?” or “Most patients and all doctors find it difficult to remember to take treatment; do you think you forget at least once a day?”, acknowledging that adherence can be difficult and encouraging patients to share their experiences

Explore whether there are particularly difficult times for children or parents to remember the treatment, such as during the morning rush for school

In a sensitive way, find out if carers actually supervise their children taking the drug or if it is left to the children to remember

Consider home visits—have the drugs been removed from the wrapper, are they in date, and are they readily accessible?

Consider electronic monitoring of treatment uptake (usually in secondary care)

and the readiness to make compromises to help young people move to safe asthma self management.

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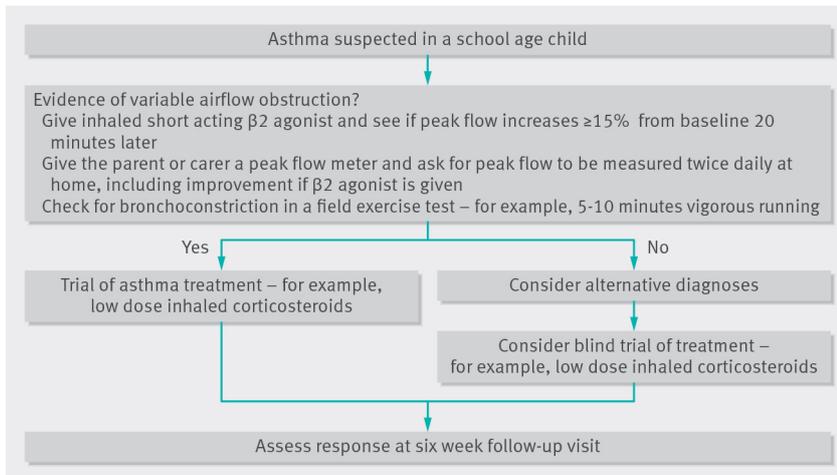
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Figure



Proposed diagnostic algorithm for asthma

Box 6 Key questions for identifying “at risk” children

The following information should easily be accessible electronically, and none requires special expertise. If any question cannot be answered satisfactorily, then an urgent review is mandatory

- Has the child been taken to an emergency department or admitted with asthma? If so, has there been follow-up?
- Does the child have an asthma plan and was the last annual review within the past year?
- How many prescriptions for preventive and reliever drugs are being collected for the child?
- Is the child brought to review appointments? When was the child last seen?
- Do you know what triggers this child's asthma?

Questions for future research

When a child at high risk has been identified (for example, by excessive β_2 agonist prescriptions), what is the best intervention package to reduce risk?

What is the best template for the annual asthma review?

When poor adherence is confirmed what is the best way to improve it?

Additional educational resources*Resources for healthcare professionals*

The European Respiratory Society e-learning resources (www.ers-education.org/publications/european-respiratory-monograph/archive/paediatric-asthma.aspx)—This is a link to a monograph on paediatric asthma published by the European Respiratory Society in 2012 (registration required)

World Allergy Organization (www.worldallergy.org/professional/allergic_diseases_center/treatment_of_asthma_in_children/)—Summary of different management recommendations, including GINA (the Global Initiative for Asthma)

British Thoracic Society Asthma Management Guidelines (www.brit-thoracic.org.uk/document-library/clinical-information/asthma/btssign-guideline-on-the-management-of-asthma/)—This URL links to the evidence based asthma management guidelines, which are the basis of best clinical practice

Resources for patients

Asthma UK (www.asthma.org.uk/advice-children-and-asthma)—This URL links to the patient's charity, Asthma UK, which has excellent resources for professionals and patients, including research updates and information leaflets

NHS Choices. Asthma in children (www.nhs.uk/conditions/Asthma-in-children/Pages/Introduction.aspx)—This website gives information about all aspects of the cause, diagnosis, and management of asthma, including a useful animation