Management of asthma in children

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This review on childhood asthma focuses on acute and chronic management in relation to the asthma phenotypes reviewed in our previous article.¹ It includes when to refer to hospital services and updates on new and emerging treatments.

Managing asthma requires not only an understanding of specific treatments but also a commitment to supporting the child and family as they learn to deal with this long term illness. Key areas of management include acute asthma management plans, day to day “preventer” treatments, monitoring for side effects, and an emphasis on trying to achieve a normal level of functioning. For young children and those with atypical features, repeated review also provides an opportunity to revisit the diagnosis.

What is the acute management of asthma and episodic viral wheeze?

An exacerbation of asthma can occur at any time and in childhood is most commonly precipitated by viral upper respiratory tract infections. The British Thoracic Society/Scottish Intercollegiate Guidelines Network guideline recommends that all patients with asthma should have a written, individualised asthma management plan that includes clear and easy to follow instructions on acute management and guidance on daily treatment and when to call emergency services (fig 1).²

The management of episodic viral wheeze is controversial. Many doctors still favour an acute wheeze management plan similar to that used in acute asthma, with the use of regular bronchodilators and corticosteroids. Little evidence exists in the literature to support this approach, however. A Cochrane review of short acting β_2 agonists found eight studies involving 229 patients and found no benefit in episodic viral wheeze and persistent wheeze in children under the age of 2 years.⁴ The benefit of anticholinergics in the

management of episodic viral wheeze is similarly unclear. A Cochrane review of six studies involving 321 infants under the age of 2 years showed no impact on symptoms or clinical course of the acute illness.⁵ The studies were heterogeneous, however, leaving the possibility of a subgroup that may benefit. Currently, the indiscriminate use of anticholinergics and short acting β_2 agonists in the management of acute episodic viral wheeze is not recommended. Although these agents are still used for young children with wheeze, the doctor should ensure that a clear clinical benefit is achieved before they are regularly prescribed.

A short course of systemic corticosteroids at the onset of symptoms of episodic viral wheeze has been shown to reduce the need for additional drugs in infants admitted to hospital,^{6,7} and the use of high dose (1.6-2.25 mg/day) inhaled corticosteroids may also have some benefit if given at the onset of symptoms of upper respiratory tract infection in children known to have episodic viral wheeze.⁸

What is the long term management of atopic asthma?

The British Thoracic Society/Scottish Intercollegiate Guidelines Network guideline has clearly defined the long term management of atopic asthma,² with variations according to the age of the child (figures 2 and 3). Treatment follows a stepwise approach until control is achieved, and patients are then maintained on the lowest level of treatment that still achieves control. The latest update to the guidelines in 2005 recommended changes in four key areas. (1) Inhaled corticosteroids should be introduced in milder cases than previously recommended. (2) Education should be offered to families, and each child should receive an individual asthma management plan. (3) Clinicians in primary care should have specific training in asthma management, as this improves diagnosis, prescribing, education, monitoring, and continuity of care. (4) Patients with asthma who are admitted to hospital should be reviewed by clinicians with particular expertise in asthma management, preferably within 30 days.

We will not repeat in this review all the advice given in the guideline. However, a few areas are worth specific comment.

Inhaled corticosteroids—friend or foe?

The introduction of inhaled corticosteroids has transformed the management of chronic asthma.⁹

Searches and selection criteria

This review draws on the chapter on asthma and other wheezing disorders in children in *Clinical Evidence*, search date October 2006. We searched Medline in January 2007 with the terms asthma, viral induced wheeze, childhood, prevalence, symptoms, diagnosis, management, corticosteroids, and adrenal suppression. We also used the British Thoracic Society/Scottish Intercollegiate Guidelines Network guideline on the management of asthma

Fig 1 | Information to be incorporated into an individual asthma management plan.

*Use of large volume spacer to deliver bronchodilator has been shown to be as effective as delivery through nebuliser,³ but adequate doses of bronchodilator must be administered

Considerable benefit for all major clinical outcome measures is seen with low and moderate doses (beclometasone to 400 µg/day or fluticasone to 200 µg/day). Beyond this, however, the dose response curve is relatively flat,¹⁰ and increases bring only limited improvement.

Although side effects are unlikely at doses of 400 µg/day of beclometasone equivalent,¹¹ they have become apparent at the higher doses. A Cochrane review of the effect of inhaled corticosteroids on height has suggested that height velocity in the short term is reduced with doses of over 400 µg/day beclometasone (0.8 cm/year),^{12,13} but longer term studies have shown that children do in fact attain a normal adult height.¹⁴ A more worrying concern in recent years has been reports of adrenal suppression in children taking higher dose inhaled corticosteroid,^{15,16} several reports with clinical evidence of acute adrenal crisis with hypoglycaemia,^{11,17} and one reported death in 2001.¹⁸ These reports have prompted some asthma specialists

to recommend that all children on “off licence” doses of inhaled corticosteroid (licensed doses for children are up to 800 µg/day beclometasone or budesonide, which is equivalent to 400 µg/day fluticasone) should have a low dose short adrenocorticotrophic hormone stimulation test.¹⁵ Caution is needed in interpreting the results of this test, however, as the repeatability in children with asthma has recently been questioned.¹⁹

Practically, if a child seems to need higher doses of inhaled corticosteroid than those recommended by the manufacturer, questions that need to be considered are:

- Is the diagnosis correct?
- Is the asthma genuinely severe?
- Are avoidable triggers present?
- Is concordance and delivery adequate?
- Are other treatments available that could be added to reduce the dose of inhaled corticosteroid needed?

This will ensure that all treatment options are maximised and alternatives considered before the dose of inhaled corticosteroid is increased to one that may result in serious adverse effects.

Long acting β_2 agonists in asthma

One method of achieving better asthma control without increasing the dose of inhaled corticosteroids is the addition of long acting β_2 agonists. These offer a longer duration of bronchodilation in children when used intermittently as a single dose,²⁰ and in adolescents and adults the addition of a long acting β_2 agonist to regular inhaled corticosteroids provides better control of symptoms than does doubling the dose of inhaled corticosteroids.²¹ The British Thoracic Society/Scottish Intercollegiate Guidelines Network guideline advocates a trial of the addition of short acting β_2 agonists in patients not controlled sufficiently on inhaled corticosteroid alone. However, in the paediatric population, no evidence exists of a bronchodilator effect or protection against exacerbations with the addition of short acting β_2 agonists to inhaled corticosteroids.²² Moreover, several studies have shown an increased risk of exacerbation and hospital admission in children on this combination.²² Evidence also exists of reduced protection against

Features that warrant referral to a specialist clinic

Feature	Comment
Poor response to 800 µg/day beclometasone (or equivalent)	Patient has reached step 4 of BTS/SIGN guideline and should be on other asthma treatments; concordance and drug delivery need careful assessment
Poor response to 400 µg/day beclometasone (or equivalent) and needs add-on treatments that general practitioner is unfamiliar with	
Young child (<5 years); uncertainty about drug delivery	Needs careful assessment of inhaler techniques and expertise of specialist asthma nurse
Young child (<1 year); often doubt about diagnosis	
Features that point to another diagnosis	
Recurrent admission to hospital	Suggests dangerous pattern of asthma
Particularly severe acute asthma, such as needing intravenous treatments or intensive care	These high risk patients should always be referred

BTS/SIGN=British Thoracic Society/Scottish Intercollegiate Guidelines Network.

Fig 2 | Summary of British Thoracic Society/Scottish Intercollegiate Guidelines Network guideline on management of asthma for children aged 5-12 years. LABA=long acting β_2 agonist.

*Or equivalent dose

exercise induced asthma with regular short acting β_2 agonists. Recent studies in adults have shown an increase in the relative risk of death from asthma with the use of salmeterol.

These findings have raised concern about the use of short acting β_2 agonists as regular preventive treatment in the paediatric population. A subgroup of paediatric asthma patients who benefit from the addition of short acting β_2 agonists to inhaled corticosteroids may well exist, but until appropriate studies are done the safety of these drugs remains unclear.²³ A short term trial in patients poorly controlled on short acting β_2 agonists and inhaled corticosteroids alone should therefore be followed by regular review and careful assessment of the response to treatment, so that treatments can be stopped if no clear benefit is shown.

Can inhaled corticosteroids help to prevent asthma developing?

The development of asthma often starts with recurrent discrete wheezy episodes.²⁴ Early intervention in the form of either episodic or regular inhaled corticosteroids has been suggested to prevent these infants developing asthma in later life. However, several studies have shown no disease modifying effect in this group of patients.²⁴⁻²⁶ The current recommendations

Fig 3 | Summary of British Thoracic Society/Scottish Intercollegiate Guidelines Network guideline on management of asthma for children aged under 5 years.

*Or equivalent dose

are that inhaled corticosteroids should be reserved for children with persistent symptoms.

How can drug delivery be optimised, both at home and school?

To achieve optimum inhaled drug delivery for children with asthma, the correct device must be prescribed alongside education on how to use it, as poor inhaler technique can mean that more than 80% of the drug is swallowed, thus reducing effectiveness.²⁷ The National Institute for Health and Clinical Excellence has published guidance on recommended inhaler devices for children aged under 5 and 5-15 years.^{28,29}

Receipt of asthma inhalers by children at school can often be of concern to parents. School staff are not required to administer asthma drugs to pupils except in an emergency situation, but many staff are happy to help. School staff should have education on managing pupils with asthma readily available, along with instruction on the correct ways to administer inhaled drugs. This can be done through the school health adviser. All schools should have their own policy on asthma. Asthma UK (www.asthma.org.uk) has published comprehensive guidelines for the management of pupils with asthma and recommendations for policy development to which head teachers should be directed.

Do effective treatments for long term management of episodic viral wheeze exist?

No regular drugs are currently recommended for the prevention of episodic viral wheeze. Unlike atopic asthma, regular low dose inhaled corticosteroids offer no benefit in the prevention of episodic viral wheeze.⁸ Recently, leukotriene receptor antagonists have shown some promise in the prevention of episodic viral wheeze. One multicentre double blind study showed that regular treatment with montelukast reduced the rate of exacerbations by 32% and corticosteroid use by 30%,³⁰ but larger independent trials are needed to support this.

When is referral to tertiary services warranted?

The point of referral to a specialised clinic depends on many variables, including the expertise of the primary care team, the support they have from nursing staff, their locality, and ease of access to a specialised service. Most general paediatricians will have good knowledge and expertise in assessing and managing childhood asthma and can provide a useful second opinion. However, not all have access to specialist asthma nurses or investigations that might help to secure the diagnosis or

TIPS FOR GENERAL PRACTITIONERS

- Establishing the asthma phenotype will help to guide long term management
- Consider the possibility of an alternative diagnosis in a child with difficult to control asthma
- Information about asthma treatment at school is available from the Asthma UK school policy guidelines (2006)

SUMMARY POINTS

Inhaled corticosteroids, although safe if given at the recommended dose, can have important adverse effects if given above it, including adrenal suppression

Long acting β_2 antagonists can be used as add-on treatment to avoid further increases in the dose of inhaled corticosteroid but can be associated with increased risk of exacerbations and hospital admission

Long acting β_2 antagonists should therefore be continued only if a demonstrable response to treatment occurs

Inhaled corticosteroids do not prevent the development of asthma

Low dose inhaled corticosteroid should not be used as preventive treatment for episodic viral wheeze

Referral to a specialist centre should be considered when a child reaches step 4 of the British Thoracic Society/Scottish Intercollegiate Guidelines Network guideline or earlier, depending on the expertise of the general practitioner and the resources available

explore differential diagnoses. The British Thoracic Society/Scottish Intercollegiate Guidelines Network guideline recommends referral to a paediatrician with specialised expertise in childhood asthma when a child reaches step 4 (patients needing an increase in inhaled beclometasone up to 800 $\mu\text{g}/\text{day}$ or equivalent).² However, if the general practitioner is unfamiliar with treatments that are added on to inhaled corticosteroids an earlier referral is sensible; indeed most asthma specialist services will wish to receive referrals if 400 $\mu\text{g}/\text{day}$ of beclometasone or equivalent is not achieving control. The table shows features that might warrant referral.

ADDITIONAL EDUCATIONAL RESOURCES

British Thoracic Society, Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma: a national clinical guideline. Revised edition November 2005 (www.brit-thoracic.org.uk/Guidelinesince%201997_asthma.html)

Lung and Asthma Information Agency (www.laia.ac.uk/)—Provides epidemiological data on asthma

Information resources for patients

Asthma UK (www.asthma.org.uk)—Comprehensive information resource on asthma for parents and children, including chat rooms and information on educational holidays

Patient UK. Asthma (www.patient.co.uk/showdoc/23068680/)—Provides information on what asthma is and on the different treatment options available

Scottish Intercollegiate Guidelines Network (www.sign.ac.uk/)—Provides a link to the updated guidelines on the management of asthma and the evidence behind the guidelines

British Thoracic Society (www.brit-thoracic.org.uk/)—Provides a link to the updated guidelines on the management of asthma and the evidence behind the guidelines

What are the therapeutic options in severe asthma?

Occasionally, children do not respond well to conventional treatments and continue to have symptoms or even have severe, acute, or life threatening episodes of asthma. These children are managed with long term oral prednisolone and need frequent visits to the specialised asthma clinic, where symptoms and side effects can be monitored. The most common cause for a poor response to oral corticosteroids is non-compliance.³¹ If symptoms persist despite regular steroid treatment, monthly subcutaneous injections of steroid can be given to ensure compliance. For those who continue to have poor control, additional immunosuppression, such as ciclosporin or methotrexate, may be tried. Although little evidence exists for benefit in children, this option is used in those who have severe side effects from oral corticosteroids or continue to have severe asthma despite exhausting all alternatives.

Alternative treatments include continuous subcutaneous terbutaline, which has been used with success in the past and can be well tolerated.³² More recently, the anti-IgE monoclonal antibody omalizumab has been used in children with asthma as an alternative to methotrexate. It binds to the IgE epitope that binds the IgE receptor, thus preventing IgE mediated mast cell degranulation. Several trials have shown clinical benefit from omalizumab in the form of significantly fewer exacerbations per patient and a significantly lower percentage of patients having exacerbations.³³ The two weekly or four weekly subcutaneous injections seem to be well tolerated, and some specific benefit seems to be achieved, with measurable reductions in the dose of oral prednisolone needed.

Some specialists advocate detailed invasive investigations in these difficult to treat patients, including measurement of airway eosinophils and neutrophils in broncho-alveolar lavages. They hypothesise that different mechanisms are responsible in individual cases and that targeting treatment to recognised subgroups—for example, ciclosporin for persistent eosinophilic inflammation or azithromycin for persistent neutrophilic inflammation³¹—is a more effective strategy. Much still remains to be learnt, however, about specific treatments in this difficult group of patients.

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My “memorable patient” story

When it comes to medical interviews, there are a few classic questions, including “Tell me about a memorable patient.” I used to hate this question. As a senior house officer, I took “memorable” to mean the complex, clever medical diagnosis or the difficult case that required clever handling. Most people I knew, myself included, would make up impressive sounding cases tailored to fit the interview. Occasionally, I would use a real patient, as long as there was something about their case that demonstrated my skills or my ability to improve myself. As I was generally successful at interviews, I assumed this was a good approach.

One evening on call, I was idly chatting with the consultant. He mentioned that “Tell me about a memorable patient” was his favourite question. He felt that the type of patient the candidate deemed memorable was far more important than the details of the case, and that this choice of patient told him more about the candidate than any other question. I paid little attention at the time, but, two years later, I still remember this remark.

As I've progressed through my training, my attitudes and opinions have changed. Memorable no longer means challenging or complex. Of course, I've not been asked the question since, but I wish someone would. If you asked me today, I would not tell you about the clever diagnoses I have made or the newborns I have successfully resuscitated; I would tell you about just one child—my favourite patient. I'd tell you about this boy who was happy, well adjusted, and polite despite debilitating chronic disease. I'd tell you how he never minded any examination or test and how he had the wonderful gift of

making everyone around him feel happy and relaxed, myself included.

With so many of my colleagues anxiously preparing for interviews for specialist training posts, I am constantly being asked for advice. While I try to help them formulate answers, I remember my conversation with the consultant and my memorable patient. I tell my colleagues that interviews are not just about you the doctor; they're also about you the person. Tell the interviewers about the silliest, funniest, nastiest, or nicest children or parents you have ever met: this reflection on your personality is just as valid as, and probably more interesting than, a medical diagnosis. And incidentally, although I remember the child's name, face, and personality perfectly, I can't remember his diagnosis.

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We welcome articles up to 600 words on topics such as *A memorable patient*, *A paper that changed my practice*, *My most unfortunate mistake*, or any other piece conveying instruction, pathos or humour. Please submit the article on <http://submit.bmj.com>. Permission is needed from the patient or a relative if an identifiable patient is referred to. We also welcome contributions for “Endpieces,” consisting of quotations of up to 80 words (but most are considerably shorter) from any source, ancient or modern, which have appealed to the reader.