Asthma in children: current thinking and future directions

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Asthma in childhood is common, with the UK having one of the highest prevalence rates in the world. This article describes the current stepwise management of asthma in children, outlines some of the steps being taken to tackle persistently poor asthma control and discusses new treatment approaches that may lead to improved control in the future.

We may wish for our children to run, play or stroke a pet unencumbered, but for some, sadly, this cannot always be the case. On average there are three pupils with asthma in every classroom in the UK, according to Asthma UK1 – one of the highest prevalence rates in the world. And behind the basic statistic of a child being admitted to hospital every 20 minutes with an asthma attack, is the very real trauma of a young person struggling to breathe.

In general, the earlier the onset of wheeze, the better the prognosis. Cohort studies show a break point at around two years old; most children who present before this age become asymptomatic by mid-childhood. Unfortunately for girls, female sex is a risk factor for the persistence of asthma in the transition from childhood to adulthood. Boys with asthma are more likely to grow out of their asthma during adolescence than girls.

Diagnosis

Of course, the correct diagnosis of childhood asthma is the necessary precursor step in managing it well. A step-by-step protocol to enable doctors to successfully do so is detailed in the 2014 British Thoracic Society /Scottish Intercollegiate Guidelines Network (BTS/SIGN) Asthma Guidelines.2

“A difference between diagnosis in children and adults is that in children the asthma guideline acknowledges that diagnosis often has to be made on history and examination alone, as lung investigations like spirometry are not possible in young children,” explains Dr James Paton, consultant in paediatric respiratory medicine at Glasgow’s Royal...
Hospital for Sick Children. “If a careful clinical assessment indicates that a diagnosis of asthma has a high probability, a trial of asthma treatment may be started straight away and its effect carefully assessed. Part of the diagnostic assessment includes a careful consideration of alternative diagnoses.” These alternative diagnoses could include anything from cystic fibrosis or reflux, to a foreign body or vocal cord dysfunction.

Though antiwheeze treatments are likely to be given regardless, some health professionals are less than keen to lumber a young child with the asthma label straight away. As Dr Charles Godden, an honorary medical adviser for the British Lung Foundation who specialises in paediatrics points out, childhood asthma is essentially a diagnosis that is arrived at by exclusion.

“When I’m attending international conferences on asthma someone will inevitably ask ‘what is asthma’ and we’ll all have a bit of an embarrassed chuckle but actually it’s not too easy to define,” he says.

“Over 20 years of my practice I’ve seen the labels changed so many times that I now hesitate to make a firm diagnosis of asthma in an under five year old as 50 per cent of this age group will wheeze, but they aren’t all asthmatics. In situations where there isn’t a clear-cut case to call it asthma I’d classify it as either virus-induced wheeze or multitrigger wheeze (if things other than having a cold are a factor), and monitor from there.”

According to the February 2013 NICE quality standard for asthma (QS25),3 it is important that the basis on which a diagnosis of asthma is suspected is clearly recorded because this process may have implications for the future management of the condition.

**Stepwise management**

The current BTS/SIGN asthma guideline2 details a management programme for asthma treatment in children aged 5–12 years that has gradually evolved, but has contained the same basic five steps since 2001 (see Figure 2). The idea is that children can move between steps, moving up to improve control as needed and down to find and maintain the lowest controlling step.

At step 1 (mild intermittent asthma) the prescription is simply for a short-acting beta_2 agonist (blue reliever inhaler) to ease symptoms of cough or wheeze whenever they occur. If a child needs to...

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**Step 1. Mild intermittent asthma**

| Inhaled short-acting beta_2 agonist as required |

**Step 2. Regular preventer therapy**

| Add inhaled steroid 200-400µg per day* (other preventer drug if inhaled steroid cannot be used) 200µg is an appropriate starting dose for many patients Start at dose of inhaled steroid appropriate to severity of disease |

**Step 3. Add-on therapy**

| 1. Add inhaled LABA 2. Assess control of asthma: • good response to LABA – continue LABA • benefit from LABA but control still inadequate – continue LABA and increase inhaled steroid dose to 400µg per day* (if not already on this dose) • no response to LABA – stop LABA and increase inhaled steroid to 400µg per day* if control still inadequate, institute trial of other therapies, eg leukotriene receptor antagonist or sustained-release theophylline |

**Step 4. Persistent poor control**

| Increase inhaled steroid up to 800µg per day* |

**Step 5. Continuous or frequent use of oral steroids**

| Use daily steroid tablet in lowest dose providing adequate control Maintain high-dose inhaled steroid at 800µg per day* Refer to respiratory paediatrician |

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Figure 2. BTS/SIGN guideline – Summary of stepwise management of asthma in children aged 5–12 years. Patients should start treatment at the step most appropriate to the initial severity of their asthma. Move up to improve control as needed, or move down to find and maintain lowest controlling step.2 LABA, long-acting beta_2 agonist; *beclometasone dipropionate or equivalent
use their reliever inhaler more than a few times a week they may move to step 2, which sees the addition of a anti-inflammatory corticosteroid preventer inhaler (brown inhaler) usually at a dosage of 200-400μg beclometasone dipropionate (BDP) daily or equivalent.

Step 3, should the child’s asthma still be uncontrolled, is potentially the most complex, initially involving the addition of an inhaled long-acting beta2 agonist (LABA). Sonia Munde, head of Helpline and nurse manager at Asthma UK explains: “What happens after the addition of LABA depends on the child’s response to it. The guidelines say that LABA should be continued if there is at least partial improvement along with an accompanying increase in dose of inhaled corticosteroid to 400μg (if needed and if the child is not already at this dose). However if the LABA makes no difference, it will be discontinued and the child is likely to be sought earlier. In cases where daily corticosteroids are unsuitable, a respiratory paediatrician is warranted.

In children under five years old, there are only 4 steps and referral to a specialist is likely to be sought earlier. In cases where daily corticosteroids are unsuitable due to difficulties with administration, chewable leukotriene-receptor antagonist tablets (montelukast) may be the primary choice of preventer medication in this younger age group.

For many specialist asthma clinicians and nurses though, the guidelines are just that – a guide. “They are useful to refer to but are very much a consensus document,” says Dr Godden. “They’re a useful framework for doctors who aren’t dealing with asthma on a daily basis, but aren’t the answer to all clinical situations by any means.”

Dr Steve Cunningham, a consultant and honorary reader in paediatric respiratory medicine at Edinburgh’s Royal Hospital for Sick Children, adds: “Many GP surgeries could not be expected to have the depth of asthma expertise to manage patients at step 5 and so would refer to a specialist; some would refer earlier than step 5, particularly for younger children.”

Solving persistently poor asthma control

There can be many and complex reasons as to why a child’s asthma remains poorly controlled, but the child’s environment – for example whether a parent smokes or not – is an important factor.

Sonia Munde says: “The health impact of passive smoking on children with asthma is enormous: it causes asthma, gives children with asthma more severe asthma symptoms and puts them at greater risk of potentially life-threatening asthma attacks so any parents or parents-to-be should be advised of this and encouraged to stop smoking if they already do so.”

For persistent and severe allergic asthma that remains intractable at step 5 in the treatment pathway, NICE has approved the use of omalizumab – a monoclonal antibody that binds to immunoglobulin E (IgE) so that it cannot react with allergens such as pollens, moulds and dust mites. It has a UK marketing authorisation as add-on therapy to improve control of severe allergic asthma in children from the age of six years. Despite the absolute minimum cost of treatment being estimated at £1665 per child per year (excluding VAT), it is considered a cost-effective treatment.

As Dr Paton points out: “Omalizumab is an injectable treatment, administered by a specialist in a tertiary care setting, so we can at least ensure that it is properly and cost-effectively administered.”

Sometimes, though, the solution for difficult childhood asthma may not be upping the ante with more potent and expensive drugs, but working with parents and children to ensure that youngsters are compliant with their current regimen. One of the key ways to improve success – and a key recommendation from last year’s Royal College of Physicians’ Why Asthma Still Kills report – is for all asthma patients including children to have a personal asthma action plan.

Sonia Munde comments: “Research shows that if a patient uses a written asthma action plan they are four times less likely to be admitted to hospital for their asthma. That’s because it works as a step-by-step guide, which a patient or carer fills in with their GP or asthma nurse to help them stay on top of their asthma. An action plan works as a personalised written record of what medicines patients need to take, what symptoms to look out for and what they need to do if their asthma gets worse.” Action plans for children and adults can be downloaded from www.asthma.org.uk.

There’s also evidence that school-based asthma interventions delivered by adults (usually health professionals) to children may also be useful. Of all the school-based interventions tested, the Asthma Self-Management for Adolescents programme, created by Dr Jean-Marie Bruzzese of New York University School of Medicine, seems to have the most impact, improving symptoms, quality of life, emergency department use and hospitalisation. It must be noted, however, that most evaluations with this programme have been done in the USA, often involving minority ethnic groups not directly applicable to the UK.

In the UK, a couple of research projects are investigating barriers to good asthma treatment in children. Dr Louise Fleming, clinical senior lecturer at Imperial College and paediatric respiratory consultant at the Royal Brompton Hospital says: “We previously found that at least half of all children referred to our difficult asthma service used their inhaled steroids far less than prescribed. Our current research seeks to improve the way we monitor adherence to enable us to identify children who need help taking their asthma medication. This will help us to understand why their adherence is poor and the ultimate aim is to craft a programme of appropriate support.”

In a similar vein, Professor Graham Roberts, a consultant paediatrician at...
the University of Southampton is currently carrying out a 36-month research project that aims to empower teenagers to self-manage their asthma better. “Teenagers are at increased risk of asthma death even more so than younger children,” explains Professor Roberts. “Previous research has demonstrated that patients with the best self-efficacy – the belief and the ability to self-manage specific tasks – have the best asthma control. We are therefore working with young people using self-efficacy theory, with the hope that we can develop a new adolescent approach that healthcare professionals can use.”

**Administering medication appropriately**

Even if you get a child or young person to be compliant with taking asthma medication at the right time and dosage, there are difficulties that can be encountered with giving inhaled drugs to young children, which means that the method of administration chosen is absolutely critical.

“For children up to five years, the guidelines say that routine preventer and reliever therapy is best delivered by a pressurised metered dose inhaler (pMDI) used with a spacer,” says Sonia Munde. “Spacers make aerosol inhalers easier to use, ensure the child gets more medicine into their lungs and also reduce the risk of oral thrush.

“It’s vital that a child’s inhaler technique is checked. Guidelines for children with asthma (up to the age of five) say when they are three years old, they can usually use a spacer device without a mask, which helps to get more of the medication into their lungs and reduces the risk of skin changes from steroids (a red rash). Patients should be advised that they should see their GP or practice nurse if symptoms flare up so that their technique can be checked.”

For children aged 5–12 years, a pMDI and spacer is also recommended for inhaling preventer medication, but for reliever medication, a breath-actuated inhaler (no spacer) is an alternative that could be used as it is more portable.

With nearly £1 billion being spent on respiratory inhalers in England, according to a 2011 NHS Prescription Cost Analysis survey, is there pressure on prescribers to choose the cheapest over the safest and most effective medications? “Of course how much you are spending is a consideration, but in paediatric asthma, treatment will always be determined by the medicine the child needs, and the child’s ability and willingness to use it,” says Dr Cunningham. “If after these factors have been taken into account there is more than one equally good treatment, we will then consider overall cost.”

Dr Godden adds: “If I was treating a child with high dosages of inhaled corticosteroids, I’d prefer to choose one with less potential to affect growth and cause adrenal suppression. I would be happy to choose a more expensive drug with a better safety profile.”

For most doctors it comes down to factors like dosage and length of time the drug is to be used. If ultimately the amount of drug the patient is going to be exposed to is very low, something costing less with a slightly higher side-effect profile could be perfectly acceptable and that is where the expertise of the prescriber comes in.

“The bottom line is that you shouldn’t over- (or under-) treat,” says Dr Godden. “If I am treating an asthmatic child and they stop having any symptoms at all, I will generally feel I am overtreating them and would probably start edging doses downwards to a point where they still experience the occasional minor wheeze.”

**Future developments**

This year, the BTS/SIGN asthma guideline will receive another regular update, with minor changes to the diagnostic and pharmaceutical sections being expected. In addition, separate NICE guidelines will be released in July 2017 on asthma and its management for the first time.

Over the last 10–15 years, most of the changes in therapeutics for paediatric asthma could only reasonably be referred to as tweaks – for example slight changes to drugs (including the introduction of combination products), along with somewhat more substantial improvements in delivery devices. What the future might hold, therefore, is obviously of great interest.

One thing already available that is piquing the interest of some paediatric asthma specialists is Airsonett, previously known as Protexo. This drug-free medical device, which NICE suggests could be used beyond step 4 of the asthma treatment pathway, provides a temperature-controlled laminar flow of filtered air over the patient while they sleep. The idea is to reduce the level of allergens inhaled during the night allowing the lungs a period of time to recover from inflammation.

“There’s some clinical research to support its use and I have had patients who have used it, with varying results,” says Dr Cunningham. “One advantage is that it’s a drug-free treatment.”

Dr Godden agrees: “Some may dismiss it as a little wacky, but I think that’s unfair given how we haven’t really had much new in the last 10 years for paediatric asthma. I don’t have any patients using it at the moment, but it’s definitely on my radar.”

Getting access to Airsonett for a patient can be fairly convoluted, but not impossible – a first step would be for a clinician to check with their own CCG, which may already have a policy on the use of the device.

At various centres throughout the UK, a number of potential new drugs and treat-
Treatment for asthma are being developed, some or all of which could potentially impact on childhood wheezing going forward.

For example later this year, results from a final large-scale multinational clinical trial involving 1,409 people across nine countries is due to report on a cat allergy treatment, which might hold promise for children who suffer wheezing attacks around one of our commonest pets.

Pending successful trials, a new class of drugs called calcilytics (which were originally produced as a treatment for osteoporosis and act as antagonists at calcium-sensing receptor in the lungs reducing the inflammatory response to asthma triggers) might also be available within about five years. In addition, clinical trials of a new treatment for those whose asthma is triggered by house dust mites, appear to be around the corner, following the discovery by a UK-funded team at St George’s, University of London, of a way to prevent the allergy in the first place rather than to just treat the reaction.

More usable asthma diagnostic tests for young children are also in the pipeline, which can only be a good thing considering that the most common age group of children admitted to hospital with wheezing attacks are one to three-year-olds, who still cannot routinely have lung function measured (the techniques used need patient co-operation not possible in infants). One such child-friendly diagnostic test being evaluated in an Asthma UK-funded study is the adaptation of a breathing test that already exists for cystic fibrosis; some results can be expected soon.

Looking into the future, those clinicians working day to day to help asthmatic children hope they can look forward to a time when treatments can be more targeted toward an individual child.

“We’re some long way off, but it would be good to one day base the treatments we offer on an individual child’s genotype,” says Dr Godden.

Dr Paton suggests there might be a time when treatments that target the immune system could be much more refined. “The way I explain it is that we know that different immunological pathways are active in different patients like different wiring circuits in your house controlling different lights. For better asthma treatments, we’re looking for the equivalent in immune terms of knowing which switch to flick to turn off a particular light. You want to be able to turn off your own individual asthma lighting circuit rather than just tripping everything with the circuit breaker, which is more where we are at now.”

Unfortunately though, Dr Godden points out, we are not too good at peering into a medical crystal ball and differentiating between what is going to be useful as opposed to just interesting. As Dr Paton puts it: “I can’t predict exactly what the future of paediatric asthma holds, but I can tell you for sure we will definitely be doing things differently five years from now.”

References
1. Asthma UK. https://www.asthma.org.uk/about/media/facts-and-statistics/

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None to declare.

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