Diagnosis of asthma in children under five

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A child presenting with chronic and relatively non-specific symptoms, such as cough or 'wheeze', needs to be placed in one of three categories:

- Normal child (the diagnosis which requires the most skill and experience)
- A child with a serious illness such as cystic fibrosis (CF) or tuberculosis (rare, but essential to get right)
- A child with asthma.

If the child is thought to have 'asthma', is it the result of T-cell driven, eosinophil mediated, airway inflammation, or as a result of intra-uterine disturbance of airway growth? Resolving this question is fundamental to planning treatment. This paper assumes the child is not capable of performing lung function tests, but if a child is capable, it is inexcusable to make a diagnosis of asthma without having documented the presence of airflow obstruction which is variable with time and treatment. The specific conditions, and their diagnoses, which may require specialist assistance, will only be covered briefly as the aim of this paper is to highlight indications for referral.

HISTORY TAKING

Wheezing due to airway narrowing sounds like a high-pitched, musical whistle. However, many parents use 'wheezing' to describe other noises, for example a palpable crackling in the chest or even nasal snuffling. Time must be spent on the history to determine exactly what is meant by 'wheezing'. Differentiating stridor from wheeze in the tachypnoeic child may be difficult for parents. Coughing is universal in childhood, at least at the time of viral upper respiratory infections. There is only poor correlation between objective measures of cough such as diary cards and perception of severity by observers.[1,2] Ambulatory cough monitoring has been used predominantly in older children,[3-5] but is not routinely available in clinical practice.

Table 1: Points to seek in the history suggesting an underlying serious diagnosis

- Are the child / family really describing wheeze?
- Upper airway symptoms – snoring, rhinitis, sinusitis
- Symptoms from the first day of life
- Very sudden onset of symptoms
- Chronic moist cough / sputum production
- Worse wheeze or irritable after feed, worse lying down, vomiting, choking on feeds
- Any feature of a systemic immunodeficiency
- Continuous, unremitting or worsening symptoms

Table 2: Points to seek on examination suggesting an underlying serious diagnosis

- Digital clubbing, signs of weight loss, failure to thrive
- Upper airway disease – enlarged tonsils and adenoids, prominent rhinitis, nasal polyps
- Unusually severe chest deformity (Harrison's sulcus, barrel chest)
- Fixed monophonic wheeze
- Stridor (monophasic or biphasic)
- Asymmetric wheeze
- Signs of cardiac or systemic disease

Having established whether the child truly wheezes, and whether there is excessive cough, the next step is to identify the pattern and severity of symptoms. The key distinction is whether the child has symptoms solely during a viral cold (virus associated wheeze; VAW), or additional symptoms between colds. If the latter, symptom frequency and triggers should be determined. Triggers may include excited emotional behaviour, dust, exercise, exposure to animal fur, weather or environmental temperature change, strong perfumes or aerosol sprays, and smoke from cigarettes or open fires. The therapeutic approach to VAW is completely different to that to the child with chronic symptoms in between viral colds.

The severity of symptoms should next be determined, both in terms of the disruption to the child and also to the family. The family of a child who coughs intermittently, but is not particularly breathless may merely be seeking reassurance that there is no serious underlying disease, rather than seeking a prescription for regular medication. Other factors influencing treatment decisions are a history of atopy in the child or first degree relatives, which may make the giving of prophylactic treatment more likely. The specific questions which should be asked of the child with symptoms between colds are summarised in Table 1. The upper airway can be the forgotten area of paediatric respirology.[6] The most common cause of chronic cough is the catarrhal child with postnasal drip. Symptoms suggestive of obstructive sleep apnoea should be sought, including snoring, apnoeic pauses, restlessness, daytime somnolence and poor concentration. Adenotonsillectomy may be completely curative of the chronic cough, and prevent the (rare) dangers of night-time respiratory failure. In general, the earlier the onset of symptoms, the more likely that an important diagnosis will be made. Symptoms starting at a few weeks of age may be due to asthma, but if the problem started literally from day one of life, structural abnormalities of the airway should be excluded. If there is prominent and persistent rhinitis from birth (almost inevitably and fatuously diagnosed as the baby being born with a viral cold), then primary ciliary dyskinesia (PCD; Kartagener's syndrome) should be considered.[7] A very sudden onset of symptoms is strongly suggestive of endobronchial foreign body, which requires referral by telephone for immediate investigation. Parents may not volunteer the history, and should be asked whether choking on a foreign body is a possibility.[8] Babies too young to bring their hands to their mouth may have had small objects pressed onto their face by siblings.

Chronic sputum production or a moist cough without a viral cold should always be a cause for concern. Although it may be due to postnasal drip or asthma, causes of chronic pulmonary sepsis (below) such as CF, PCD and agammaglobulinaemia, may need to be excluded.

Gastroesophageal reflux should be suspected in an infant who is worse after feeds, is an irritable feeder and vomits or possets easily. A therapeutic trial of thickening of feeds and, with appropriate warning to the parents, cisapride is reasonable on clinical suspicion without further investigation. Choking on feeds, particularly in a child with known neurodevelopmental handicap or neuromuscular disease, suggests incoordinate swallowing due to bulbar or pseudo-bulbar palsy. Laryngeal cleft or H-type tracheo-oesophageal fistula may present with symptoms at the time of feeding.

Although symptom-free periods do not exclude the possibility of a serious underlying disease, the child who has no

days free of symptoms certainly merits critical consideration of alternative diagnoses. Finally, a history of systemic infections or poor weight gain in the context of chronic respiratory disease should never be dismissed lightly.

PHYSICAL EXAMINATION

Often there will be no physical signs (Table 2). Digital clubbing is an obvious and important sign, but will not be found if not actively sought. My experience has been that children are not uncommonly referred with unnoticed obvious chronic clubbing. The upper airway should be inspected for rhinitis; nasal polyps are virtually pathognomonic of CF in this age group. Although a severe Harrison's sulcus and pectus carinatum can be due to uncontrolled asthma, the more severe the deformity, the greater the likelihood of another diagnosis. Palpation of the chest with the palms of the hands during quiet breathing or, in an older child, during blowing or huffing, may be a better way of detecting airway secretions than auscultation. However, careful auscultation may elicit unexpected findings such as crackles, fixed monophonic wheeze, asymmetric signs or stridor.

WHAT IS THE ROLE OF THE CHEST X-RAY?

Most hospitals rightly offer open access for chest X-ray (CXR) and the radiation dose using modern techniques is trivial (equivalent to one transatlantic trip in Concorde). Even so, I contend that a CXR is unnecessary in the vast majority of infants with chronic cough and/or wheeze seen in the community. Furthermore, many of the conditions listed in Table 3 cannot be excluded by this investigation and require further tests (Table 4). I would suggest that either the diagnostic situation is clear cut, in which case a CXR is unnecessary, or it is not, in which case the child needs to be referred. There will be exceptions, and it may be deemed proper to request a CXR to reassure parents.

WHAT TYPE OF 'ASTHMA'?

Not all that wheezes is asthma and not all that is labelled asthma is due to inflammation. Two areas of controversy are the pathophysiology of VAW and if cough variant asthma exists.

What causes VAW?

There is increasing evidence that the main problem is due to *in utero* airway maldevelopment. Summarising this evidence, three separate studies have shown that babies born to mothers who smoke, are atopic, or have hypertension in pregnancy, have abnormal lung function shortly after birth, presumably a reflection of an abnormal intra-uterine process.[9-11] Three prospective studies (Tucson, Boston, Perth) showed that in babies with VAW, lung function was abnormal prior to the first episode of wheeze.[12-14] Unlike in older children and adults, two studies showed no evidence of bronchial hyper-reactivity (BHR) in VAW.[15,16] A double blind trial showed that VAW does not respond to inhaled steroids.[17] In a study using blind broncho-alveolar lavage at the time of routine paediatric surgery, there were no eosinophils in the lavage of children with VAW, quite different from the atopic asthmatics.[18,19] Finally, a prospective study, which followed children until age 35 years, showed clearly that longterm outlook in terms of lung function in children with VAW was unaffected by steroid therapy.[20] One is forced to the conclusion that VAW is nothing to do with eosinophilic inflammation, and should not be treated the same way. Unfortunately, many infants do not fit neatly into the categories of either non-atopic, VAW or majorly atopic, interval and viral associated symptoms. Even many atopic wheezers will outgrow their symptoms within a few years.[21]

Does cough variant asthma exist?

Large epidemiological studies show that in a community setting, where by definition the vast majority of children are well, isolated cough is rarely due to asthma and rarely responds to asthma medications.[22,23] There is no doubt that isolated cough may frequently be over-diagnosed as asthma.[24] Chronic non-specific cough often improves with time and without treatment.[25,26] However, in a specialist clinic, where a selected group of children are seen, children who cough in response to typical asthma triggers, and improve with asthma medications are not uncommonly seen.[27]

My diagnostic criteria are:

- Abnormally increased cough, with no evidence of any non-asthma diagnosis
- Clear-cut response to a therapeutic trial of asthma medications (see below)
- Relapse on stopping medications with second response to recommencing them.

Many children with chronic cough have only a non-specific problem, and have been shown on bronchoscopic and blind lavage studies to have no evidence of eosinophilic airway inflammation.[19,28] Follow-up studies show that most will get better over one or two years, however, others will show evidence of deterioration of BHR and develop the picture of classical asthma.[29] The only danger of a brief therapeutic trial, if the precautions above are adhered to, is that ineffectual and potentially harmful medication may be continued longterm unless a trial off therapy is rigorous. In older children who can perform lung function, there is no justification for a trial without documenting variable airflow obstruction.

THERAPEUTIC TRIALS

Ultimately, after a detailed evaluation, diagnostic doubt may remain and the question of a therapeutic trial is raised. If the main problem is cough and wheeze at the time of viral colds, and the GP is satisfied that the symptoms are sufficiently outside the normal range such that treatment is indicated, then intermittent bronchodilator therapy with

Table 3: Disease which present as recurrent cough and wheeze

- Upper airway disease – adenotonsillar hypertrophy, rhinosinusitis, postnasal drip
- Congenital structural bronchial disease – complete cartilage rings, cysts, webs
- Bronchial / tracheal compression – vascular rings and sling, enlarged cardiac chamber, lymph nodes enlarged by tuberculosis or lymphoma
- Endobronchial disease – foreign body, tumour
- Oesophageal / swallowing problems – reflux, incoordinate swallow, laryngeal cleft or tracheo-oesophageal fistula
- Causes of pulmonary suppuration – cystic fibrosis, primary ciliary dyskinesia, any systemic immunodeficiency including agamma-globulinaemia, severe combined immunodeficiency
- Miscellaneous – bronchopulmonary dysplasia, congenital or acquired tracheomalacia, pulmonary oedema

Table 4: Investigations to be considered in the child with recurrent cough and wheeze

- Suspected oesophageal disease – pH probe, barium swallow, tube oesophagram, oesophagoscopy
- Suspected upper airway disease – polysomnography, RAST tests (radiograph of postnasal space is rarely useful)
- Suspected cystic fibrosis – sweat test, nasal potentials, genotype, stool elastase, faecal fat
- Suspected primary ciliary dyskinesia – saccharine test, nasal ciliary motility, electron microscopy including orientation studies, nasal and exhaled nitric oxide
- Suspected systemic immunodeficiency – immunoglobulins and subclasses; vaccine antibodies; lymphocyte subsets; lymphocyte and neutrophil function tests; HIV test
- Suspected structural airway disease – fibreoptic bronchoscopy
- Suspected tuberculosis – Heaf test, fibreoptic bronchoscopy and / or gastric lavage, combined with culture and PCR
- Suspected cardiovascular disease – echocardiogram, barium swallow to exclude a vascular ring or pulmonary artery sling, angiography
- Suspected bronchiectasis – high resolution CT scan, investigations for local or systemic immunodeficiency

either an anticholinergic or β_2-agonist is suggested. Both medications may be tried; despite popular belief that there are no β_2 receptors in the airway under one year of age, there is evidence that some children respond to inhaled β_2-agonists.[30] The drug delivery device should be a mask and spacer, with appropriate instruction in use. If intermittent therapy is unavailing, a trial with an anti-inflammatory medication should be considered. It may seem illogical to use an inhaled steroid in VAW, but occasionally a trial of inhaled steroids may be merited under carefully circumscribed conditions. Occasionally, there is a dramatically beneficial effect, and the family realize that in fact the child had interval symptoms that were not appreciated until they were treated.

The other circumstance under which I would consider a therapeutic trial is in the child with non-specific chronic symptoms, especially if atopic. The choices would appear to be either inhaled bronchodilators, inhaled cortico-steroids, or oral steroid. There are no evidence-based data to guide the clinician in this dilemma; my own practice is to use moderately high dose inhaled steroids (budesonide 800 mcg/day) via a spacer, with a mask if age-appropriate. If the child shows no response, then asthma is a highly unlikely diagnosis. The alternative choices for a therapeutic trial would be high-dose β_2-agonists, cromoglycate, or oral prednisolone. Asthmatics should show some response to bronchodilators, but if they fail, a trial of a more potent medication is likely to be performed to ensure that asthma can be ruled out, so the β_2-agonist trial only delays matters. Cromoglycate has been shown to be largely ineffective in children of this age.[31] Oral steroids are effective in asthmatics, but also treat allergic rhinitis and temporarily reduce the size of the adenoids, and so are not specific for lower airway inflammation, as well as having a greater potential for side-effects.

If the symptoms disappear after three months on inhaled steroids, the treatment must be stopped to ensure that the child has not improved coincidentally. Only if symptoms recur on stopping inhaled steroids can the diagnosis of asthma be said to be established, and longterm treatment instituted. If there is no response to a therapeutic trial, then referral to a paediatrician with special expertise in respiratory medicine should be considered.

CONCLUSIONS

A careful history and physical examination, with judicious use of therapeutic trials, will enable most children with cough and wheeze under five years to be managed successfully. There is still a clear cut need for research to help us identify which children with early onset wheeze have airway inflammation which requires treatment to prevent an adverse outcome. Currently there are three indications for referral and observance of these rules should allow one to avoid most diagnostic blunders.

- If the diagnosis is in doubt
- If the treatment is not working
- If any party (GP or family) is not happy. ■

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