An Atlas of Investigation and Management

PAEDIATRIC RESPIRATORY DISEASE

AIRWAYS AND INFECTION

Edited by

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## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>ADA</td>
<td>adenosine deaminase</td>
</tr>
<tr>
<td>AHI</td>
<td>apnoea hypopnoea index</td>
</tr>
<tr>
<td>AI</td>
<td>apnoea index</td>
</tr>
<tr>
<td>AR</td>
<td>autosomal recessive</td>
</tr>
<tr>
<td>ASL</td>
<td>airway surface liquid</td>
</tr>
<tr>
<td>ATP</td>
<td>adenosine triphosphate</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacillus Calmette-Guérin</td>
</tr>
<tr>
<td>BiPAP</td>
<td>bi-level positive airway pressure</td>
</tr>
<tr>
<td>BTS</td>
<td>British Thoracic Society</td>
</tr>
<tr>
<td>CaCC</td>
<td>calcium-activated chloride channel</td>
</tr>
<tr>
<td>CF</td>
<td>cystic fibrosis</td>
</tr>
<tr>
<td>CFTR</td>
<td>cystic fibrosis transmembrane conductance regulator</td>
</tr>
<tr>
<td>CgC</td>
<td>common interleukin g chain</td>
</tr>
<tr>
<td>CHARGE</td>
<td>Coloboma of the iris and retina, Heart disease, Atresia of choanae, Retarded growth, Genital hyperplasia, Ear defects</td>
</tr>
<tr>
<td>COPD</td>
<td>chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>CPAP</td>
<td>continuous positive airway pressure</td>
</tr>
<tr>
<td>CSA</td>
<td>central sleep apnoea</td>
</tr>
<tr>
<td>DIOS</td>
<td>distal intestinal obstruction syndrome</td>
</tr>
<tr>
<td>ENaC</td>
<td>epithelial sodium channel</td>
</tr>
<tr>
<td>ENT</td>
<td>ear, nose and throat</td>
</tr>
<tr>
<td>FBC</td>
<td>full blood count</td>
</tr>
<tr>
<td>FEV₁</td>
<td>forced expiratory volume in one second</td>
</tr>
<tr>
<td>FiO₂</td>
<td>fraction of inspired oxygen</td>
</tr>
<tr>
<td>FVC</td>
<td>forced vital capacity</td>
</tr>
<tr>
<td>GOR</td>
<td>gastro-oesophageal reflux</td>
</tr>
<tr>
<td>GP</td>
<td>general practitioner</td>
</tr>
<tr>
<td>HDU</td>
<td>high dependency unit</td>
</tr>
<tr>
<td>HiB</td>
<td>Haemophilus influenzae type B</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>hMPV</td>
<td>human metapneumovirus</td>
</tr>
<tr>
<td>HRCT</td>
<td>high-resolution computed tomography</td>
</tr>
<tr>
<td>IF</td>
<td>immunofluorescence</td>
</tr>
<tr>
<td>Ig</td>
<td>immunoglobulin</td>
</tr>
<tr>
<td>IL-7Ra</td>
<td>interleukin 7 receptor a</td>
</tr>
<tr>
<td>JAK-3</td>
<td>janus-associated kinase 3</td>
</tr>
<tr>
<td>MBL</td>
<td>mannose-binding lectin</td>
</tr>
<tr>
<td>MCC</td>
<td>mucociliary clearance</td>
</tr>
<tr>
<td>MDR TB</td>
<td>multidrug-resistant tuberculosis</td>
</tr>
<tr>
<td>MRSA</td>
<td>Methicillin-resistant <em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Clinical Excellence</td>
</tr>
<tr>
<td>NO</td>
<td>nitric oxide</td>
</tr>
<tr>
<td>OAI</td>
<td>obstructive apnoea index</td>
</tr>
<tr>
<td>OME</td>
<td>otitis media with effusion</td>
</tr>
<tr>
<td>ORCC</td>
<td>outwardly rectifying Cl⁻ channel</td>
</tr>
<tr>
<td>OSAS</td>
<td>obstructive sleep apnoea syndrome</td>
</tr>
<tr>
<td>PaCO₂</td>
<td>arterial carbon dioxide tension</td>
</tr>
<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
</tr>
<tr>
<td>PEFR</td>
<td>peak expiratory flow rate</td>
</tr>
<tr>
<td>PICU</td>
<td>paediatric intensive care unit</td>
</tr>
<tr>
<td>PJP</td>
<td><em>Pneumocystis jiroveci</em> pneumonia</td>
</tr>
<tr>
<td>PPI</td>
<td>proton pump inhibitors</td>
</tr>
<tr>
<td>PSG</td>
<td>polysomnography</td>
</tr>
<tr>
<td>RAG</td>
<td>recombination activating genes</td>
</tr>
<tr>
<td>RAST</td>
<td>radioallergosorbent test</td>
</tr>
<tr>
<td>RSV</td>
<td>respiratory syncytial virus</td>
</tr>
<tr>
<td>SaO₂</td>
<td>arterial oxygen saturation</td>
</tr>
<tr>
<td>SCID</td>
<td>severe combined immunodeficiency</td>
</tr>
<tr>
<td>TB</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>URTI</td>
<td>upper respiratory tract infection</td>
</tr>
<tr>
<td>WCC</td>
<td>white cell count</td>
</tr>
<tr>
<td>XL</td>
<td>X-linked</td>
</tr>
<tr>
<td>ZAP-70</td>
<td>zeta-associated kinase-70</td>
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Asthma: diagnosis and assessment

Ian M. Balfour-Lynn

Introduction

Childhood asthma and recurrent viral wheezing are two of the most common conditions that general practitioners (GPs) and paediatricians assess and treat. Despite concerns that asthma has been becoming more common worldwide, it seems that visits to GPs and hospital admissions for asthma have been reducing over the last decade in children aged less than 14 years (1.1). Nevertheless, prevalence is approximately 10% and over half of all cases of asthma begin in childhood. This chapter covers diagnosis and assessment (1.2) but treatment has not been included (the

2 Asthma: diagnosis and assessment

Presenting features
- Wheeze
- Dry cough
- Breathlessness
- Noisy breathing

Detailed history and physical examination
- Pattern of illness
- Severity/control
- Differential clues

Is it asthma?
- Probably
- Possibly
- (or comorbidity)

Investigate or question to seek:
- Causal factors
- Exacerbating factors
- Complications
- Comorbidity

Asthma Action Plan
- Follow relevant course of action
- Seek specialist assistance

Poor response Good response

Asthma likely Asthma unlikely

1.2 Diagnosis of asthma in children (from: BTS/SIGN guideline on the management of asthma. Thorax 2003; 58(Suppl 1): i1–i94).

1.3 Hypothetical yearly peak prevalence of wheezing for three different wheezing phenotypes in childhood. The dashed lines suggest wheezing can present different curve shapes due to many different factors, including overlap of the groups. Reproduced with permission from Stein RT, Holberg CJ, Morgan WJ, et al. Peak flow variability, methacholine responsiveness and atopy as markers for detecting different wheezing phenotypes in childhood. Thorax 1997; 52: 946–52.
Recurrent wheezing in infancy is nearly always associated with viral upper respiratory tract infections. There is a reluctance to give an infant under 2 years of age the label of ‘asthma’; however, features suggesting the child has genuine infantile asthma include personal and family history of atopy and a pattern of cough/wheeze whereby symptoms are more chronic than episodic. The diagnosis of asthma becomes more obvious as the child gets older and continues to have recurrent cough and wheeze.

Three different wheezing phenotypes have been identified in the first 11 years of life (1.3). The group of ‘transient early wheezers’ tends to have reduced lung function that persists through childhood. The ‘non-atopic wheezers’ of infants, toddlers and early school years are mostly associated with increased peak flow variability, which may persist long after the wheezing itself ceases. The third group is IgE-associated wheeze/asthma, which may occur at any stage during childhood and is related to a combination of atopy, increased bronchial responsiveness and increased peak flow variability.

### History

The history is critical in making the diagnosis and is often the only factor that can be relied upon. It is important to realize there is confusion among parents as to what is meant by wheeze, and the harsh sounds made by upper airway secretions are often mistaken for wheeze. Specific pointers to asthma are outlined in Table 1.1.

The differential diagnosis of recurrent wheeze is quite large (Table 1.2). Points suggesting alternative diagnoses are shown in Table 1.3 and, in particular, symptoms that started in the first weeks of life, and particularly on the first day of life, need careful diagnostic evaluation.

### Examination

Examination of the child is often unremarkable. Attention needs to be paid to growth, chest shape and auscultation. Chest shape may reveal bilateral Harrison sulci or an increased anterior–posterior diameter, which can indicate frequent or chronic airways obstruction (1.4). Auscultation may well be normal at the time in a clinic setting; however, asthma should be suspected if wheeze is heard by a health professional and distinguished from upper airway noises. If the child is acutely unwell, there may be wheeze, tachypnoea, recession and even cyanosis. Beware the silent chest with inadequate air entry, which indicates severe bronchospasm and is an emergency. Part of the examination must include watching how the child takes their inhaled medication. This is often done poorly and it is critical to ensure the child has an age-appropriate device, which is undamaged and being used correctly.
Table 1.2 Non-asthmatic causes of wheeze (or noises that may be mistaken for wheeze)

<table>
<thead>
<tr>
<th>Category</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper airway disease</td>
<td>Adenotonsillar hypertrophy, rhinosinusitis, postnasal drip</td>
</tr>
<tr>
<td>Congenital structural airway disease</td>
<td>Complete cartilage rings, cysts, webs</td>
</tr>
<tr>
<td>Bronchial/tracheal compression</td>
<td>Vascular rings and sling, enlarged cardiac chamber, lymph nodes enlarged by tuberculosis or lymphoma, congenital thoracic malformations</td>
</tr>
<tr>
<td>Endobronchial disease</td>
<td>Foreign body, tumour</td>
</tr>
<tr>
<td>Oesophageal/swallowing problems</td>
<td>Gastro-oesophageal reflux, incoordinate swallow, laryngeal cleft or H-type tracheo-oesophageal fistula</td>
</tr>
<tr>
<td>Chronic pulmonary suppuration</td>
<td>Cystic fibrosis, primary ciliary dyskinesia, immunodeficiency, bronchiectasis of unknown aetiology</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Obliterative bronchiolitis, bronchopulmonary dysplasia, congenital or acquired tracheo/bronchomalacia, pulmonary oedema</td>
</tr>
</tbody>
</table>

Table 1.3 Points in the history suggesting alternative diagnosis

- What the child/family are describing is not really wheeze
- Upper airway symptoms: snoring, constant rhinitis, sinusitis
- Symptoms from the first days of life
- Very sudden onset of symptoms
- Chronic moist cough or sputum production
- Wheeze associated with feeding, irritable after feed, worse lying down, vomiting
- Choking on feeds
- Any feature of a systemic immunodeficiency
- Chronic diarrhoea, poor growth
- Disappearance of symptoms when asleep

Table 1.4 Points in the examination suggesting alternative diagnosis

- Digital clubbing
- Signs of weight loss, failure to thrive
- Upper airway disease: enlarged tonsils and adenoids, prominent rhinitis, nasal polyps
- Severe chest deformity out of proportion to symptoms
- Fixed monophonic wheeze
- Stridor (monophasic or biphasic)
- Asymmetric wheeze (louder or restricted to one side)
- Signs of cardiac or systemic disease

1.4 Marked chest deformity with Harrison sulci in a 12-year-old steroid-dependent asthmatic boy.
Certain features are strongly suggestive of an alternative diagnosis to asthma (Table 1.4).

**Investigation to confirm diagnosis**

No single investigation can give 100% confirmation of asthma, which is essentially a clinical diagnosis. However, some simple tests will strengthen the likelihood of the diagnosis, such as measurement of peak expiratory flow rate. Measurement of flow volume loops with spirometry can give even more information than simple peak flow rates. Spirometry may show an obstructive pattern on the flow-volume loop, with greater reduction in forced expiratory volume in 1 second than forced vital capacity (1.5). If a bronchodilator is then given, repeat spirometry may indicate the degree of bronchodilator responsiveness (1.6). Spirometry before and after exercise may also reveal exercise-induced bronchospasm. Skin-prick testing for common aeroallergens (e.g. grass and tree pollens, house dust mite, aspergillus mould, cat and dog) will indicate atopic status (1.7). A chest radiograph may exclude several diagnoses and may show hyperinflation in more severe cases (1.8). Response to anti-asthma therapy can be very useful for confirming the diagnosis.
Further investigations may be required to exclude alternative and concomitant diagnoses (Table 1.5), most of which are covered in detail in other chapters of this atlas.

### Assessment of asthma severity

History should include the impact on school attendance, disturbed sleep, hospital admissions, courses of oral corticosteroids, and the dose of inhaled corticosteroids required to stay symptom-free. Examination may reveal Harrison’s sulci and hyperinflation. Lung function may be surprisingly normal, even in those with severe chronic asthma. A peak flow meter can also be used at home, and if measured once or twice daily over a period of a week or so, marked peak flow variability can indicate poor control.

### Assessment of difficult asthma

Referral of a child with apparently severe asthma to a tertiary unit requires a complete and systematic re-evaluation of the situation. The commonest reasons for failure to respond to asthma treatment are that the treatment is not being taken
Asthma: diagnosis and assessment

Table 1.5 Investigations specific for alternative diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro-oesophageal reflux</td>
<td>pH study, isotope milk scan</td>
</tr>
<tr>
<td>Vascular ring</td>
<td>Chest radiograph, spirometry, flexible bronchoscopy, echocardiography, barium swallow, HRCT angiography</td>
</tr>
<tr>
<td>Vocal cord dysfunction</td>
<td>Spirometry, laryngoscopy</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Sweat test, stool elastase, DNA analysis</td>
</tr>
<tr>
<td>Inhaled foreign body</td>
<td>Expiratory chest radiograph, rigid bronchoscopy</td>
</tr>
<tr>
<td>Obliterative bronchiolitis</td>
<td>HRCT chest scan, adenovirus titres in serum</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>HRCT chest scan</td>
</tr>
<tr>
<td>Primary ciliary dyskinesia</td>
<td>Nasal ciliary brushings, nasal nitric oxide</td>
</tr>
<tr>
<td>Tracheo/bronchomalacia</td>
<td>Flexible bronchoscopy, bronchography</td>
</tr>
<tr>
<td>Recurrent aspiration</td>
<td>Bronchoalveolar lavage for lipid-laden macrophages, chest X-ray, HRCT chest scan, video fluoroscopy</td>
</tr>
<tr>
<td>Immune deficiency</td>
<td>Immune function testing</td>
</tr>
</tbody>
</table>

HRCT, high-resolution computed tomography.

Step 1

- Allergy testing
- Spirometry and reversibility
- Chest radiograph
- Sweat test
- Salivary cotinine
- Exhaled nitric oxide (NO)
- ± Prednisolone, cortisol, theophylline blood levels

- Respiratory nurse specialist home visit
- Detailed history including psychosocial, environmental exposure
- Assess inhaler technique
- Contact local hospital regarding accident and emergency visits and admissions
- Contact GP, chemist regarding prescription usage
- Contact school regarding medication policy, absence

1.8 Chest radiograph of an 8-year-old asthmatic boy, showing hyperinflation.

1.9 Step 1 of the Royal Brompton Hospital protocol for assessment of children with difficult asthma.
or that the child does not have asthma. The diagnostic approach undertaken at the Royal Brompton Hospital for children with difficult asthma is outlined in 1.9 and 1.10. The inflammatory cell profile from an endobronchial biopsy or induced sputum may help direct further treatment (1.11–1.13).

1.10 Steps 2 and 3 of the Royal Brompton Hospital protocol for assessment of children with difficult asthma. During step 2 assessment, intramuscular triamcinolone is given at the time of the bronchoscopy and step 3 takes place 2 weeks later.

1.11 Flexible bronchoscopy at the level of the carina (arrow) showing macroscopic severe inflammation in a 5-year-old with difficult asthma.

1.12 Endobronchial biopsy in a child with difficult asthma showing inflammation and a thickened reticular basement membrane (arrow).

1.13 Induced sputum from an asthmatic patient showing predominance of eosinophils (arrows). Stained with diffquik, 40× magnification (courtesy of G. Nicholson).
Further reading


