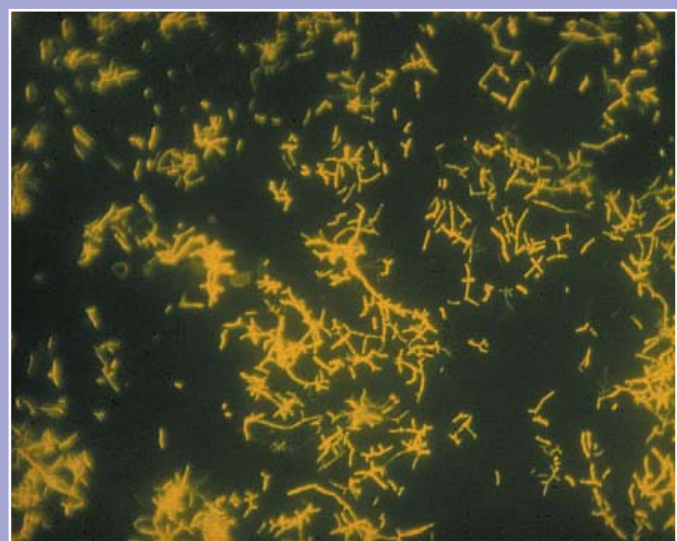
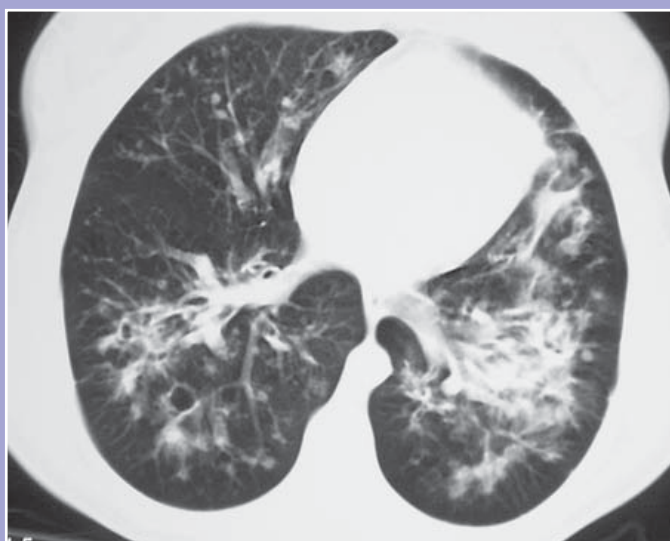


An Atlas of Investigation and Management

PAEDIATRIC RESPIRATORY DISEASE

Airways and Infection

A Bush • J Davies



CLINICAL PUBLISHING

An Atlas of Investigation and Management

PAEDIATRIC RESPIRATORY DISEASE

AIRWAYS AND INFECTION

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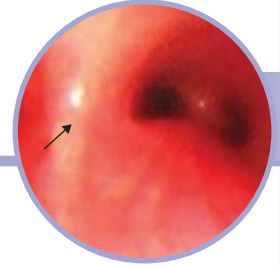
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Abbreviations

ADA	adenosine deaminase	HRCT	high-resolution computed tomography
AHI	apnoea hypopnoea index	IF	immunofluorescence
AI	apnoea index	Ig	immunoglobulin
AR	autosomal recessive	IL-7Ra	interleukin 7 receptor α
ASL	airway surface liquid	JAK-3	janus-associated kinase 3
ATP	adenosine triphosphate	MBL	mannose-binding lectin
BCG	Bacillus Calmette-Guérin	MCC	mucociliary clearance
BiPAP	bi-level positive airway pressure	MDR TB	multidrug-resistant tuberculosis
BTS	British Thoracic Society	MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
CaCC	calcium-activated chloride channel	NICE	National Institute for Health and Clinical Excellence
CF	cystic fibrosis	NO	nitric oxide
CFTR	cystic fibrosis transmembrane conductance regulator	OAI	obstructive apnoea index
CgC	common interleukin γ chain	OME	otitis media with effusion
CHARGE	Coloboma of the iris and retina, Heart disease, Atresia of choanae, Retarded growth, Genital hyperplasia, Ear defects	ORCC	outwardly rectifying Cl^- channel
COPD	chronic obstructive pulmonary disease	OSAS	obstructive sleep apnoea syndrome
CPAP	continuous positive airway pressure	PaCO_2	arterial carbon dioxide tension
CSA	central sleep apnoea	PCR	polymerase chain reaction
DIOS	distal intestinal obstruction syndrome	PEFR	peak expiratory flow rate
ENaC	epithelial sodium channel	PICU	paediatric intensive care unit
ENT	ear, nose and throat	PJP	<i>Pneumocystis jiroveci</i> pneumonia
FBC	full blood count	PPI	proton pump inhibitors
FEV_1	forced expiratory volume in one second	PSG	polysomnography
FiO_2	fraction of inspired oxygen	RAG	recombination activating genes
FVC	forced vital capacity	RAST	radioallergosorbent test
GOR	gastro-oesophageal reflux	RSV	respiratory syncytial virus
GP	general practitioner	SaO_2	arterial oxygen saturation
HDU	high dependency unit	SCID	severe combined immunodeficiency
HiB	<i>Haemophilus influenzae</i> type B	TB	tuberculosis
HIV	human immunodeficiency virus	URTI	upper respiratory tract infection
hMPV	human metapneumovirus	WCC	white cell count
		XL	X-linked
		ZAP-70	zeta-associated kinase-70



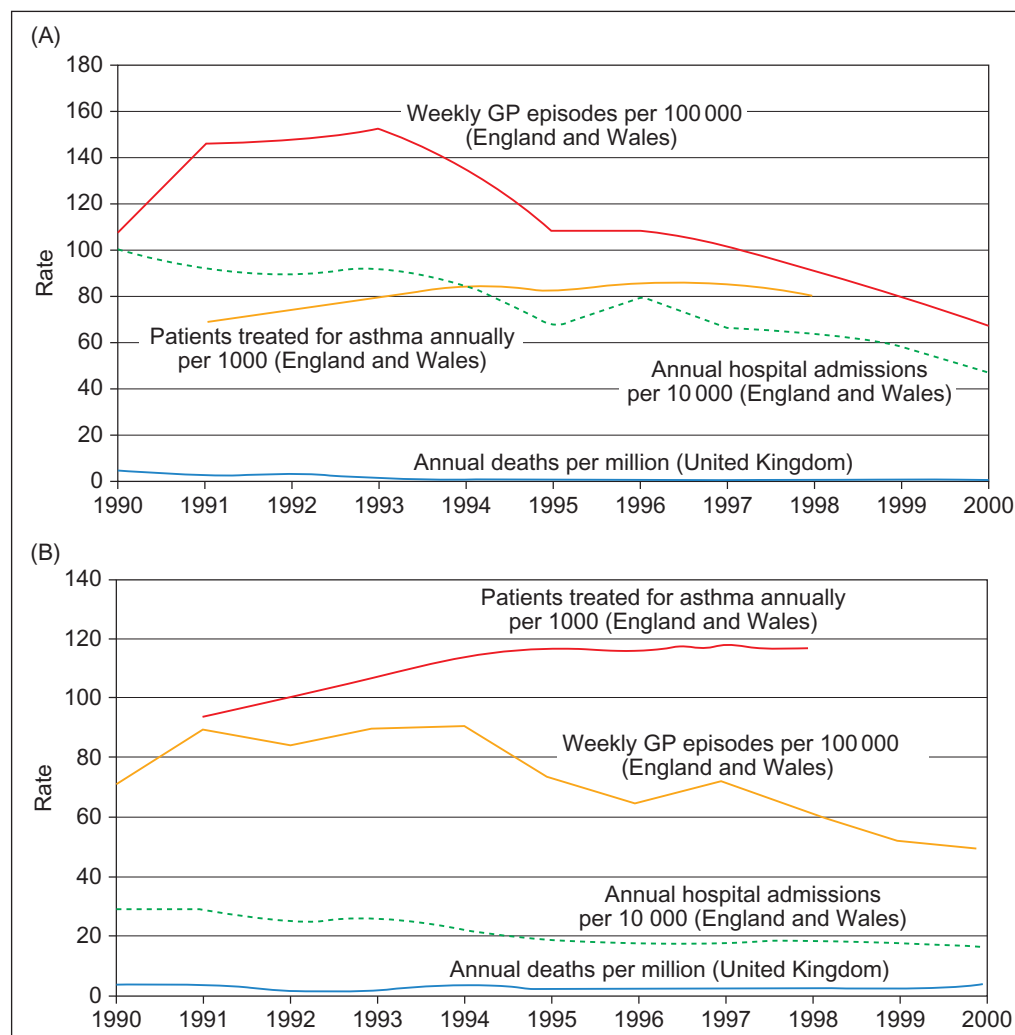
Asthma: diagnosis and assessment

Ian M. Balfour-Lynn

Introduction

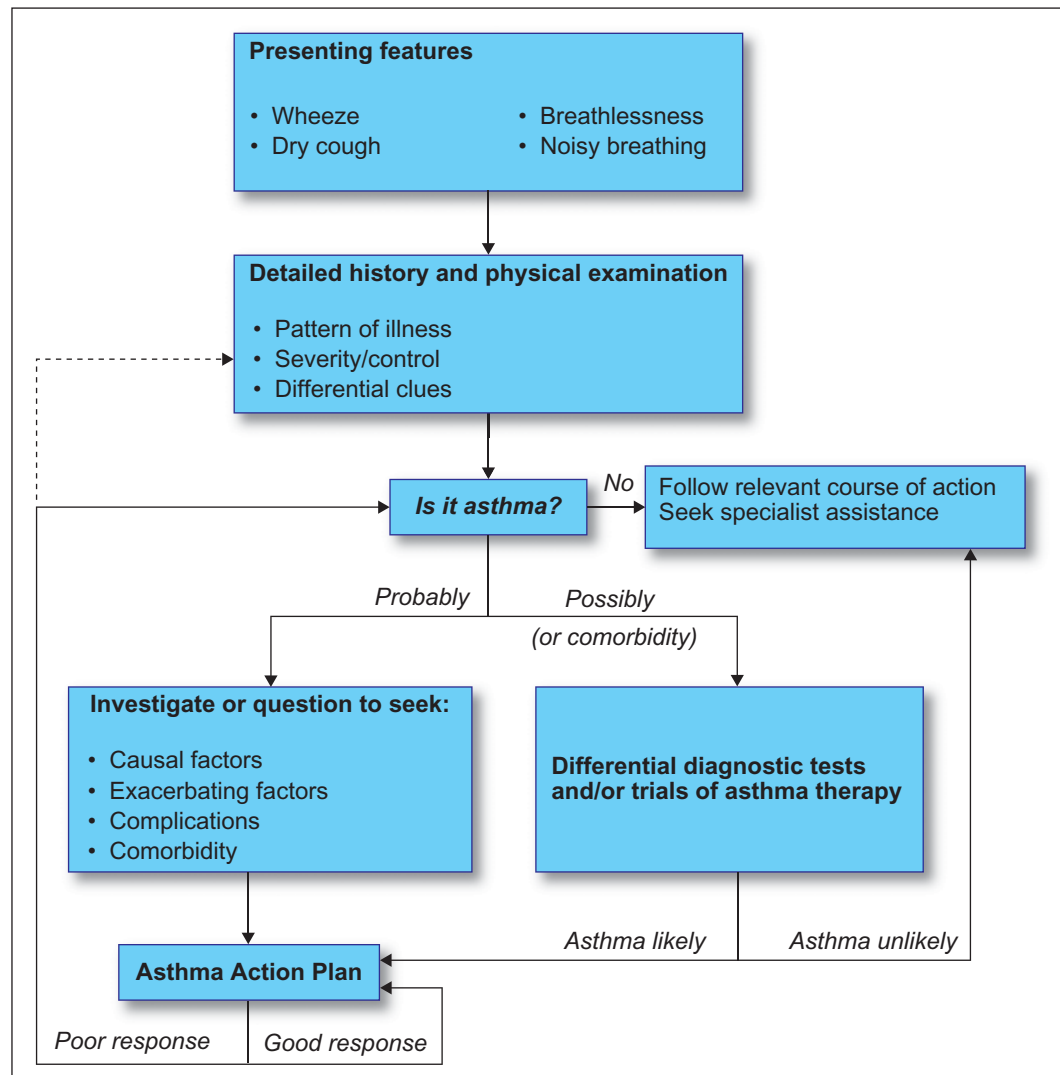
Childhood asthma and recurrent viral wheezing are two of the most common conditions that general practitioners (GPs) and paediatricians assess and treat. Despite concerns that asthma has been becoming more common worldwide,

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

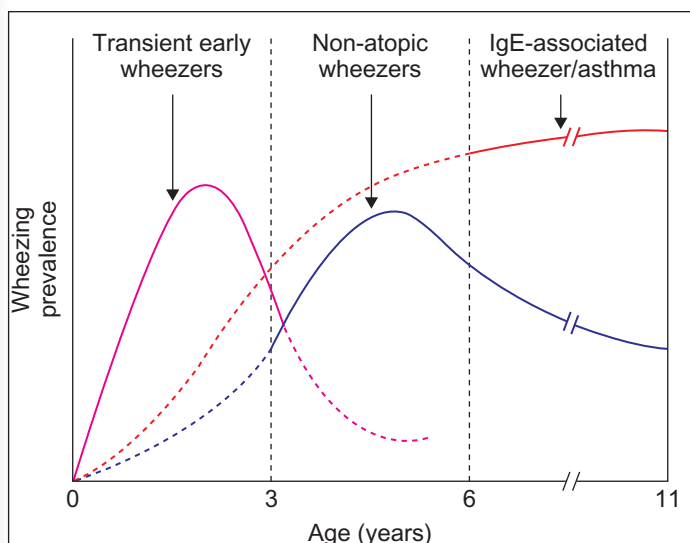


1.1 Trends in annual rates for primary care consultations, hospital admissions and mortality for asthma among children aged <5 years (A) and aged 5–14 years (B). Taken from Gupta R, Strachan D. Asthma and allergic diseases. In: *The Health of Children and Young People*. Office for National Statistics, March 2004. Available from: www.statistics.gov.uk/children/.

2 Asthma: diagnosis and assessment



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.

UK guidelines can be consulted for details of the stepwise approach to treatment).

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

Table 1.1 Symptoms and other points in history suggestive of asthma

Cough	Recurrent Dry, tight Non-productive Night-time Exercise-induced Not always/only with viral URTIs Onset usually after 3–4 months of age
Wheeze (assuming there really is a wheeze)	Recurrent Exercise-related Associated with furry household pets Induced by viral URTIs
Breathlessness or difficulty breathing	Particularly shortly after onset of exercise and relieved by rest
Other symptoms	Otherwise well child, i.e. no other symptoms, normal growth
Risk factors	Past history, e.g. premature birth, mechanical ventilation, bronchiolitis requiring hospitalization. Signs of atopy, e.g. atopic eczema, hay fever, genuine food allergy, particularly to egg
Family history	Parents or siblings with asthma, eczema, hay fever Smoking parents

URTI, upper respiratory tract infection.

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.

4 Asthma: diagnosis and assessment

Table 1.2 Non-asthmatic causes of wheeze (or noises that may be mistaken for wheeze)

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

Table 1.3 Points in the history suggesting alternative diagnosis

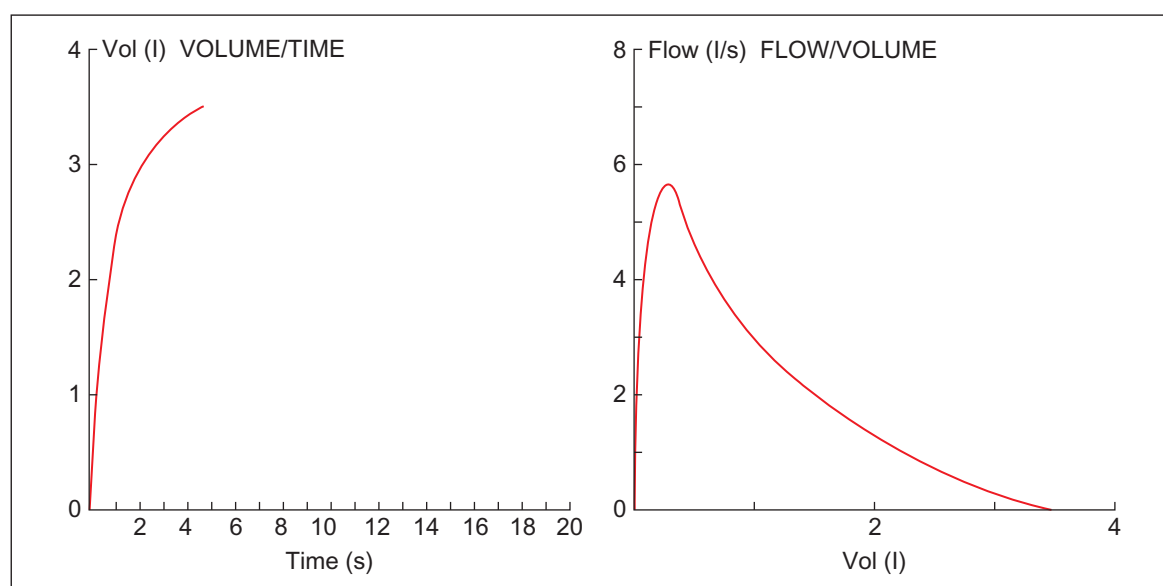
- What the child/family are describing is not really wheeze
- Upper airway symptoms: snoring, constant rhinitis, sinusitis
- Symptoms from the first days of life
- Very sudden onset of symptoms
- Chronic moist cough or sputum production
- Wheeze associated with feeding, irritable after feed, worse lying 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.

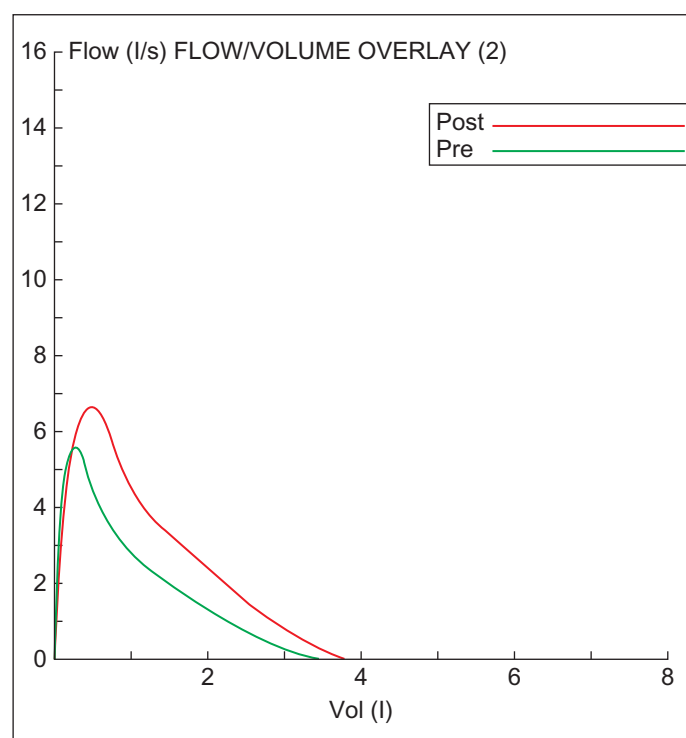


1.5 Spirometric flow volume loop in a 16-year-old asthmatic girl, indicating mild obstructive airways disease likely to be due to asthma. The forced expiratory volume in 1 second was 67% and forced vital capacity 103% predicted.

Certain features are strongly suggestive of an alternative diagnosis to asthma (*Table 1.4*).

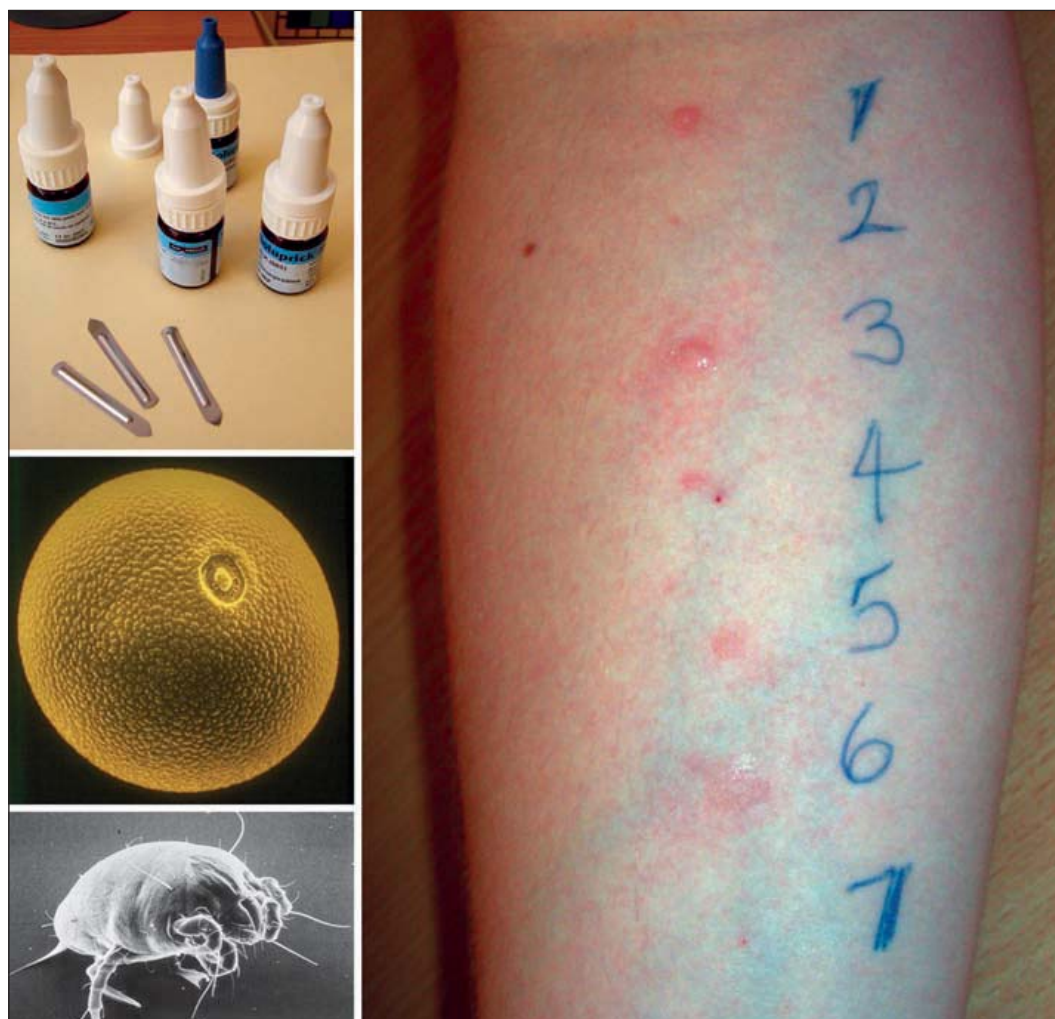
Investigation to confirm diagnosis

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.



1.6 Spirometric flow volume loop pre-bronchodilator (green) and post-bronchodilator (red) in a 16-year-old asthmatic girl, showing a 19% absolute rise in percentage predicted forced expiratory volume in 1 second, i.e. a moderate degree of bronchodilator responsiveness.

6 Asthma: diagnosis and assessment



1.7 Skin-prick testing in an asthmatic child who was mildly positive to dog (no. 5), more positive to grass pollen (no. 3) and strongly positive to house dust mite (no. 6). He was not allergic to cat (no. 4) or aspergillus mould (no. 7). Positive histamine control (no. 1) and negative control (no. 2) are also done. Also shown are some of the allergen solutions and lancets used for the test; grass pollen and a house dust mite – *Dermatophagoides pteronyssinus* (not to scale).

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.

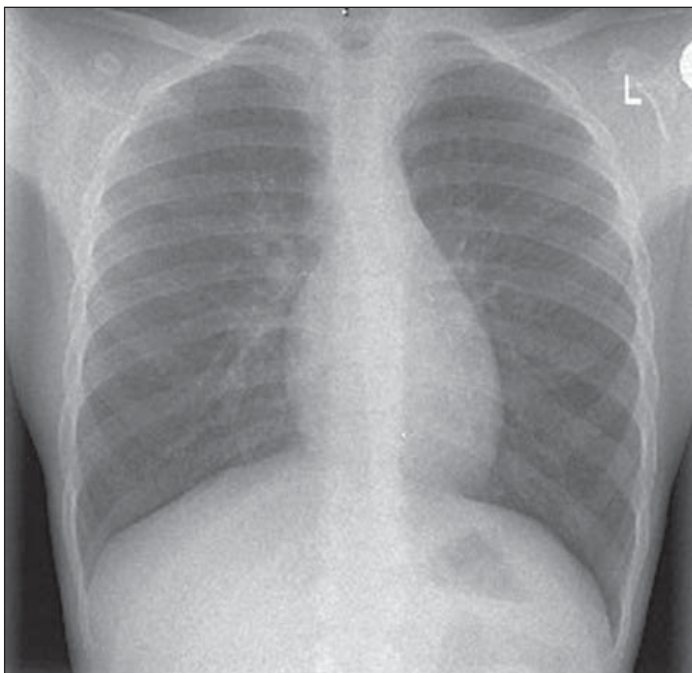
Assessment of difficult asthma

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

Table 1.5 Investigations specific for alternative diagnoses

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

HRCT, high-resolution computed tomography.



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

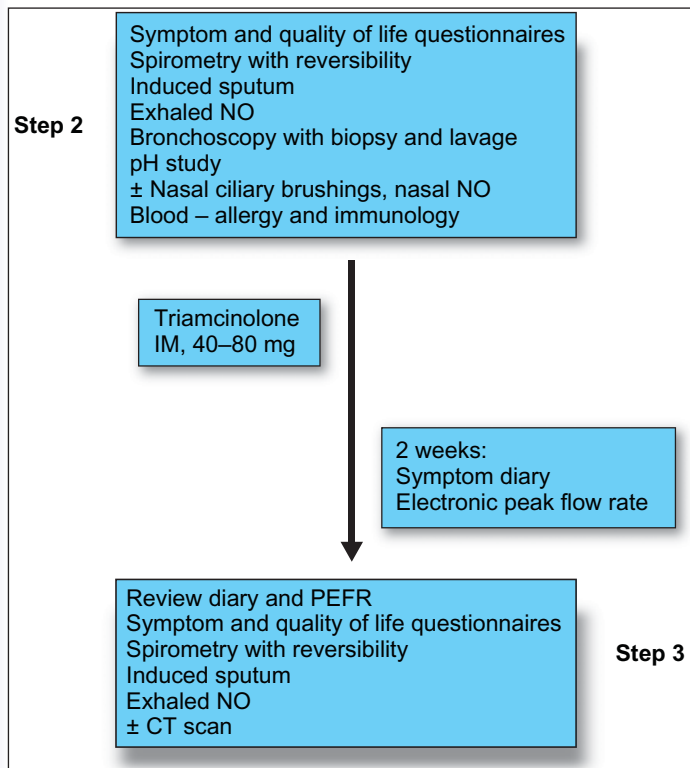
Step 1

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

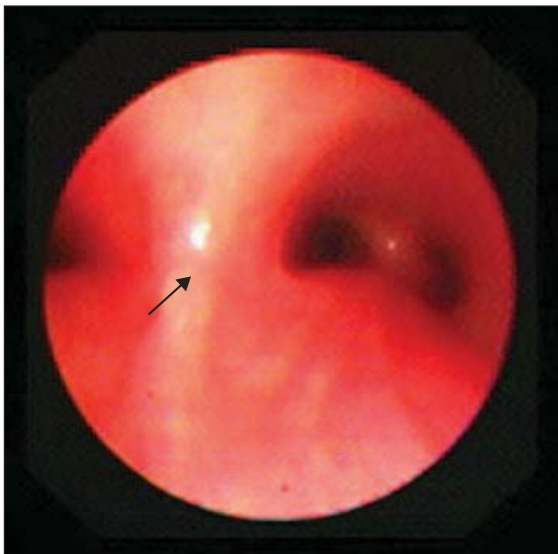
- Respiratory nurse specialist home visit
- Detailed history including psychosocial, environmental exposure
- Assess inhaler technique
- Contact local hospital regarding accident and emergency visits and admissions
- Contact GP, chemist regarding prescription usage
- Contact school regarding medication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

1.9 Step 1 of the Royal Brompton Hospital protocol for assessment of children with difficult asthma.

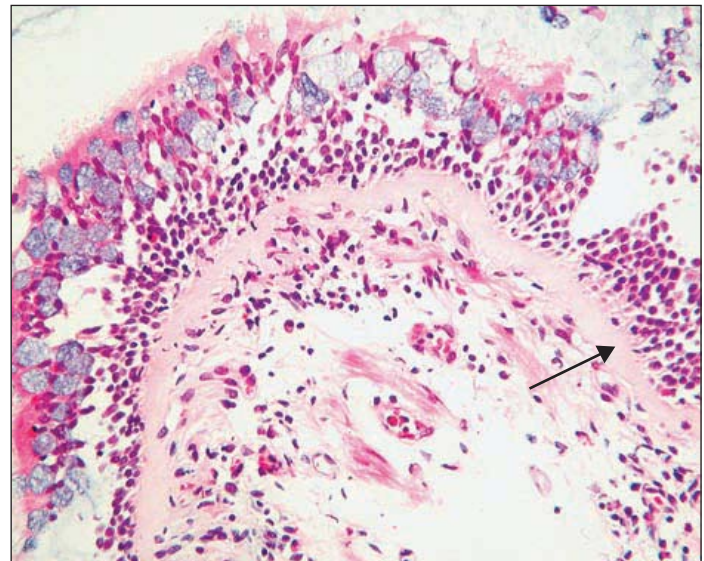
8 Asthma: diagnosis and assessment



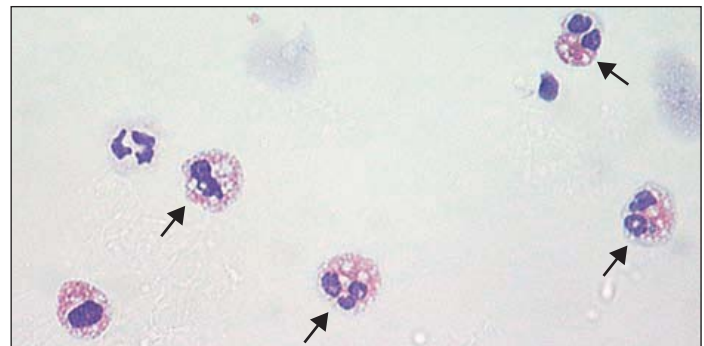
1.10 Steps 2 and 3 of the Royal Brompton Hospital protocol for assessment of children with difficult asthma. During step 2 assessment, intramuscular triamcinolone is given at the time of the bronchoscopy and step 3 takes place 2 weeks later.



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).

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**).

Further reading

British Thoracic Society, Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. *Thorax* 2008; 63(Suppl iv): iv1–iv121.

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