Obstructive pulmonary disease

- A chronic inflammatory disease of the airways, the precise cause of which is incompletely understood.

- In susceptible individuals, inflammatory symptoms are usually associated with widespread, variable airflow obstruction and an increase in airways' response to a variety of stimuli.

- Obstruction is usually reversible, either spontaneously or with treatment'.

- Diagnosis depends on clinical judgement in addition to airflow measurement, provoking factors and reversibility on treatment.

- On average, each doctor in the UK will have about 125 asthma patients, and a community pharmacy can expect to see about twice this number.

- Up to 80% of children suffer episodic symptoms of wheezing, usually associated with respiratory infections, but most of these are not regarded as asthmatics.

The two clinical types of asthma

Feature	Episodic (extrinsic)	Chronic (intrinsic)
Proportion (%)[a]	20	50
Age of onset	Childhood	Usually adults
Atopic patient	Yes: family history common[b]	No
Known allergens or precipitating factors	Yes	None or URTI Often sensitive to aspirin
Skin tests	Positive	Negative
Severity	Usually episodic Often mild	Often chronic May be severe
Treatment	Effective	Moderately effective, oral corticosteroids may be required

Pathophysiology

- The underlying problem is intense airways inflammation, leading to bronchial hyperreactivity.

- Asthmatics may be up to 100 times more sensitive than normal subjects and atopic individuals suffering from hay fever but not asthma form an intermediate group.

- Also, remodelling over time causes changes in all the layers of the airway walls (e.g. goblet cell hyperplasia, shortening of smooth muscle cells and swelling of the adventitia), which contribute to hyper-reactivity, especially in chronic asthma.

- Inflammation is clearly the single most significant sign.

- In an acute attack, the epithelium is intensely infiltrated with eosinophils, causing the release of pro-inflammatory eosinophil products (e.g. proteins and neurotoxins), which damage the epithelium.

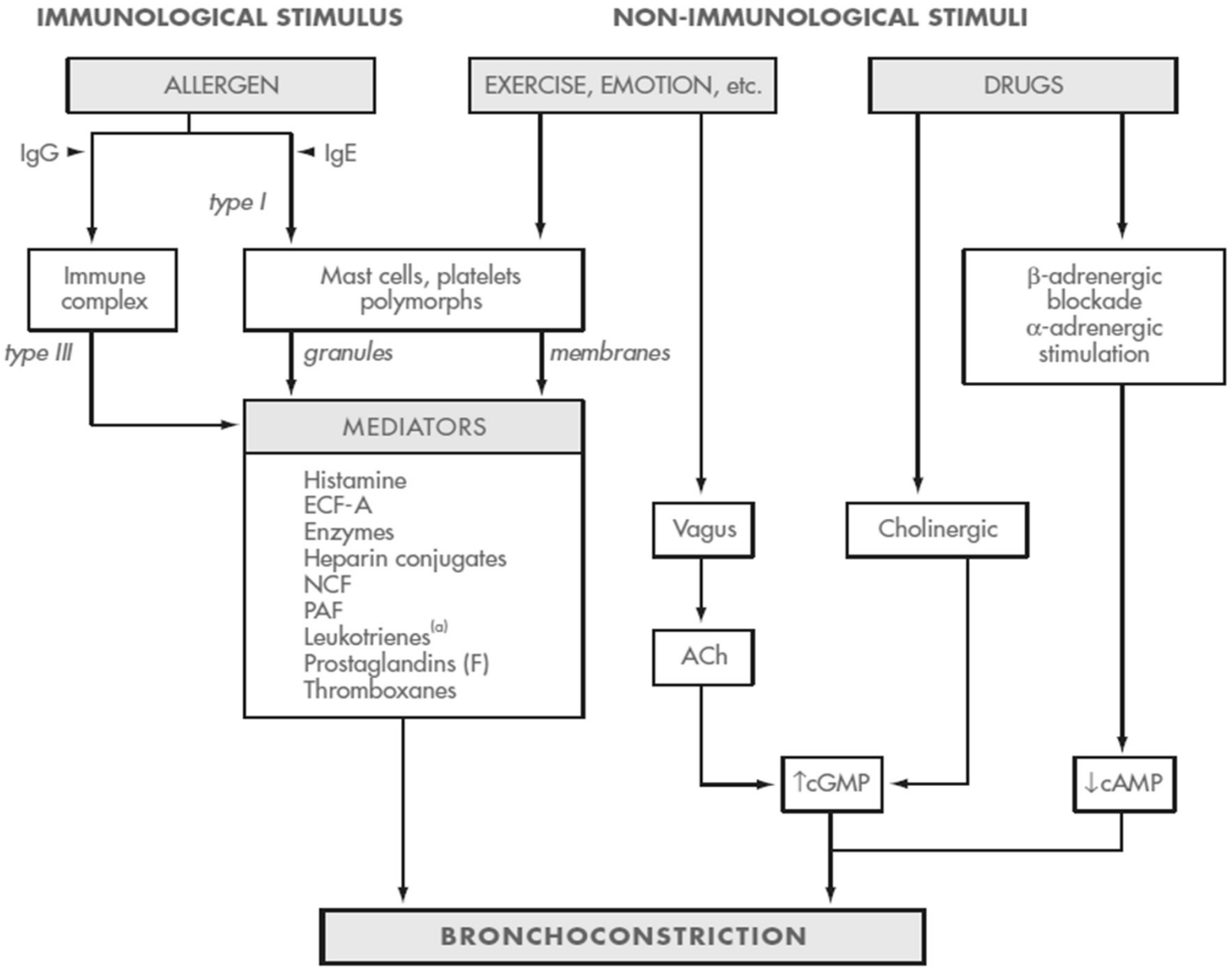
Some substances and conditions that may precipitate asthmatic attacks

Environmental and medical factors	Examples
Common allergens	Pollens, especially grasses; mould spores; animal fur and dander; house dust mite (*Dermatophagoides pteronyssimus*); proteolytic enzymes, e.g. biological detergents, some foods and food additives
Foods	Milk, eggs, nuts, alcoholic drinks, tartrazine colorant, sulphur dioxide preservative
Non-specific irritants	Dusts; cigarette smoke; atmospheric pollutants, especially sulphur dioxide
Exercise	
Medical conditions	Pregnancy; menstruation; respiratory infections, especially viruses; thyrotoxicosis; levothyroxine therapy; reflux oesophagitis

Some drugs and medicines that may provoke asthmatic attacks

General drugs
Antimicrobials: cefaloridine, erythromycin, griseofulvin, nitrofurantoin, penicillins, streptomycin, tetracyclines Aspirin, some non-steroidal anti-inflammatory drugs Beta-blockers, carbamazepine, sulfasalazine, iodine-based contrast media, dextrans, pituitary snuff, preservatives and dyes used in formulation
Drugs and devices used in asthma treatment
Ipratropium bromide, methylxanthines, hydrocortisone Dry powder inhalers, aerosol propellants, nebulized hypotonic solutions

Some factors involved in producing bronchoconstriction.



Clinical features

- The classic symptoms of asthma are attacks of breathlessness, wheezing, ‘chest tightness’ and cough that start within 15 min of exposure to a trigger factor.

- Depending on the severity of the attack, peak flow may fall to 25–75% of that recorded between attacks, and usually recovers over a period of 60–90 min without treatment.

- In a severe attack there will be hyperventilation and hyperinflation, to the extent that patients are incapable of speaking in complete sentences, with prolonged expiration and the use of the accessory muscles of respiration.

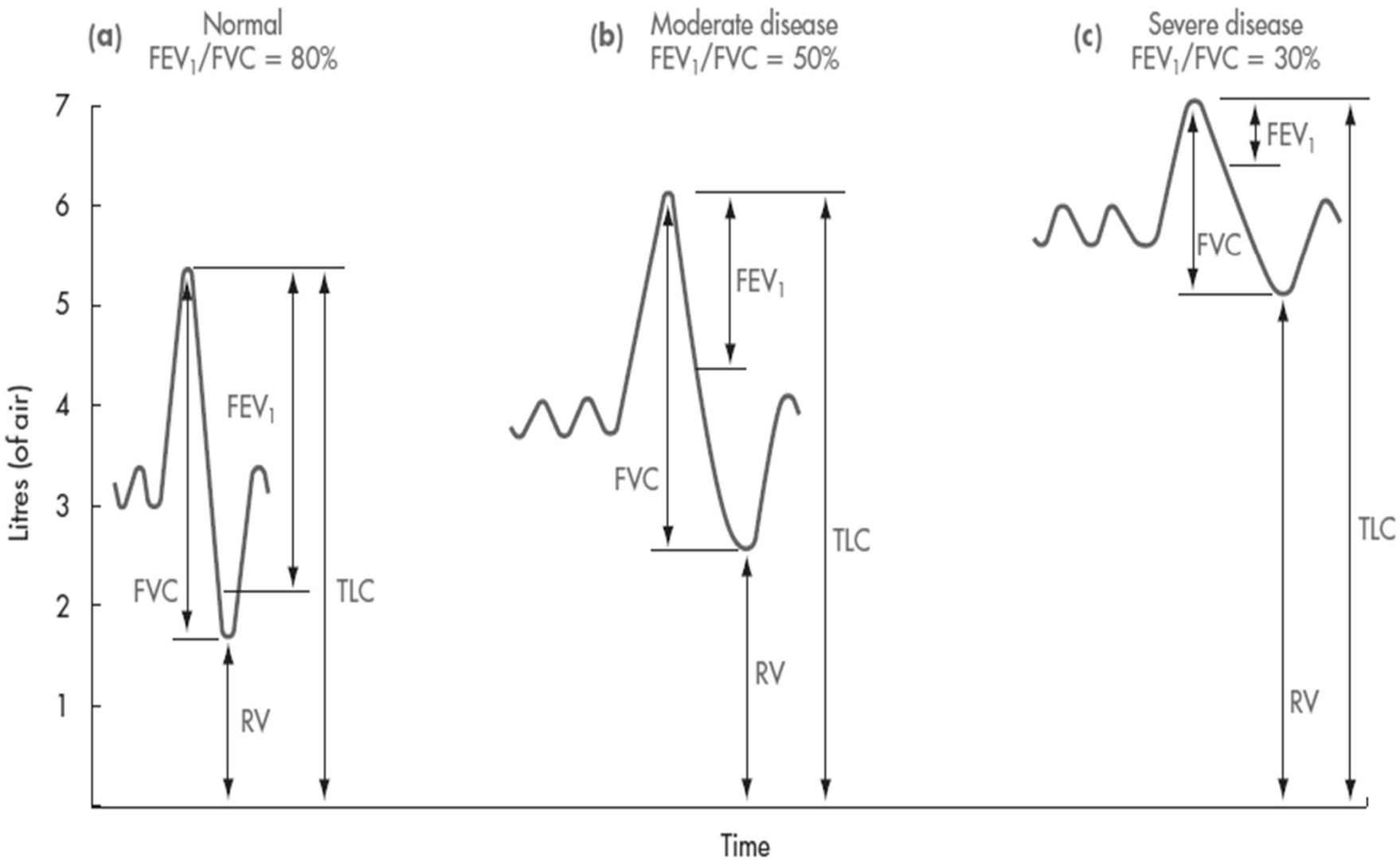
Indicators of asthma severity

Indicator	Adults	Children over 2 years[a]	Children under 2 years[a]
Moderate exacerbation: No features of acute severe asthma			
Symptoms	Increasing[b]	Cough and/or wheeze	Cough and/or wheeze
PEF	50–75% of best or predicted (mild airflow obstruction)	Attack exercise-induced <50% of best or predicted	Attack exercise-induced N/A
Acute severe asthma			
	Any of the following:	**Any** of the following:	**Any** of the following:
Breathlessness	Cannot complete sentences in one breath	Cannot complete sentences in one breath **or** too breathless to talk or feed Rhonchi	Too breathless to talk or feed Rhonchi
Respiratory rate	≥25/min	>30/min (>5 years) >50/min (2–5 years) Use of accessory muscles of respiration	>50/min Use of accessory muscles of respiration
PEF	30–49% of best or predicted (moderate air flow airways obstruction)	≤50% of best or predicted	N/A
Heart rate	≥110/min	>120/min (>5 years) >130/min (2–5 years)	>130/min

Indicators of asthma severity

Life-threatening asthma	Adults	Children over 2 years[l]	Children under 2 years[l]
	Any of the following:	**Any** of the following:	**Any** of the following:
Breathlessness and central nervous signs	Feeble respiratory effort, silent chest Exhaustion, confusion, coma	Silent chest or poor respiratory effort Exhaustion, confusion, agitation, reduced consciousness or coma	Silent chest or poor respiratory effort Exhaustion, confusion agitation, reduced consciousness or com
PEF	<30% of best or predicted (severe air flow obstruction)	<33% of best or predicted	N/A
Oxygenation	Cyanosis SpO_2 <92%[c] P_aO_2 <8 kPa	Cyanosis	Cyanosis
Carbon dioxide	P_aCO_2 normal[d]		
Heart signs	Bradycardia (<60/min) **or** other dysrhythmia		
Blood pressure	Hypotension		
Near fatal asthma; always requires hospital admission			
	Any of the symptoms/signs of life-threatening asthma **and/or** raised P_aCO_2 **and/or** requiring mechanical ventilation with raised inflation pressures	Any of the symptoms/signs of life-threatening asthma	

Spirograms in normal subjects and in obstructive lung disease



Management:

The aims of management are to:

- control symptoms, minimize anxiety and permit as normal a life as possible, including participation in sports;
- minimize the need for reliever medication and eliminate exacerbations;
- educate the patient about the disease and its treatment;
- identify and eliminate triggers, thus minimizing morbidity and preventing death.

- Drug treatment is often thought of in terms of either prophylaxis or the relief of symptoms.

- In asthma, both approaches are commonly used concurrently, and combination therapy is normal.

- However, effective prophylaxis should minimize exacerbations and avoid the need for rescue therapy.

General approach to the treatment of target feautures in asthma

Target feature	Therapeutic aim	Drugs used	
		Class	Examples[a]
Inflammation and and bronchial hyper-reactivity	Reduce • eosinophil recruitment and activation • lymphocyte activity • toxicity to epithelial cells	Corticosteroids	Inhaled: beclometasone, budesonide, ciclesonide, fluticasone, mometasone Oral: prednisolone
	• mast cell etc. degranulation	Inhibitors of mediator release	Sodium cromoglicate?[b] Nedocromil sodium? Theophylline?
	• cytokine activity	Leukotriene receptor antagonists	Selective beta$_2$-agonists Montelukast, zafirlukast
Bronchoconstriction	Bronchodilatation: • increase sympathomimetic activity	Selective beta$_2$-agonist	Inhaled: salbutamol, terbutaline, fenoterol, reproterol, tulobuterol Long-acting Inhaled: formoterol, salmeterol Oral: bambuterol
	• block parasympathetic activity • increase cAMP levels in bronchiolar muscle cells?	Antimuscarinic Phosphodiesterase inhibitors Inhibitors of mediator release	Ipratropium Aminophylline? Theophylline? Sodium cromoglicate?[b] Nedocromil sodium?

Treatment in an acute attack:

- This is designed to promote recovery and prevent deterioration to the point when hospital treatment becomes necessary.

- Occasional attacks in an adult can be treated with an inhaled selective SABA bronchodilator.

- If there are more frequent or more severe episodes, routine prophylactic treatment is added.

- This usually starts with an inhaled regular standard-dose corticosteroid, plus an inhaled SABA bronchodilator when required.

Step 1: Mild intermittent asthma: occasional relief bronchodilators

Inhaled short-acting beta$_2$-agonist as required (up to once daily)[b]
Note: Move up to Step 2 if needed twice weekly or more, if there are night-time symptoms more than once a week, or if there has been an exacerbation in the last 2 years requiring systemic corticosteroid or a nebulized bronchodilator.
Check adherence and inhaler technique[c]

Step 2: Regular preventer therapy: regular inhaled prophylactic therapy

Inhaled short-acting beta$_2$-agonist as required ***plus***
regular standard-dose inhaled corticosteroid[d] (alternatives are considerably less effective)

Step 3: Add-on therapy: inhaled corticosteroids plus long-acting inhaled beta$_2$-agonist

Inhaled short-acting beta$_2$-agonist as required ***plus***
Regular standard-dose inhaled corticosteroid[d] ***plus***
Long-acting inhaled beta$_2$-agonist[f]
If asthma not controlled
Increase dose of inhaled corticosteroid up to maximum standard dose
If asthma still not controlled add **one** of: leukotriene receptor antagonist **or** modified-release oral theophylline **or** modified-release oral beta$_2$-agonist[e]

Step 4: Persistent poor control: high-dose inhaled corticosteroids plus regular bronchodilators

Inhaled short-acting beta$_2$-agonist as required ***plus***
Regular high-dose inhaled corticosteroid[e] ***plus***
Long-acting inhaled beta$_2$-agonist[f] ***plus***
In adults a 6-week sequential trial adding one or more of: leukotriene receptor antagonist or modified-release oral theophylline or modified-release oral beta$_2$-agonist
In adults and teenagers >12 years: if still not controlled and high IgE levels consider a 12- to 16-week trial of omalizumab[g]

Step 5: Continuous or frequent use of corticosteroid tablets

Inhaled short-acting beta$_2$-agonist as required ***with***
Regular high-dose inhaled corticosteroid[e] ***and***
Regular long-acting inhaled beta$_2$-agonist[f] ***plus***
Regular prednisolone tablets (as a single morning dose)
Consider **oral** long-acting beta$_2$-agonist[h]
Note: In addition to regular prednisolone continue high-dose inhaled corticosteroids[c] to spare the prednisolone dose: **these patients should be referred to an asthma clinic**

Management of chronic asthma in children under 5 years

Step 1: Occasional relief bronchodilators

Short-acting beta$_2$-agonist as required (not more than once daily)
Move to Step 2 if needed twice a week or more, if night-time symptoms occur more than once a week or if there has been an exacerbation in the last 2 years
Use a short '**rescue course**' of *prednisolone* at **any time** or **any step**[c]

Step 2: Regular inhaled prophylactic therapy

Inhaled short-acting beta$_2$-agonist as required
plus regular inhaled standard paediatric dose corticosteroid[d], by pMDI or DPI via a large-volume spacer. If inhaled corticosteroid cannot be used a leukotriene receptor antagonist may be added, but is less effective
Consider (to stabilize patient) a 3- to 5-day course of soluble prednisolone tablets[c] or temporary doubling of inhaled corticosteroid dose

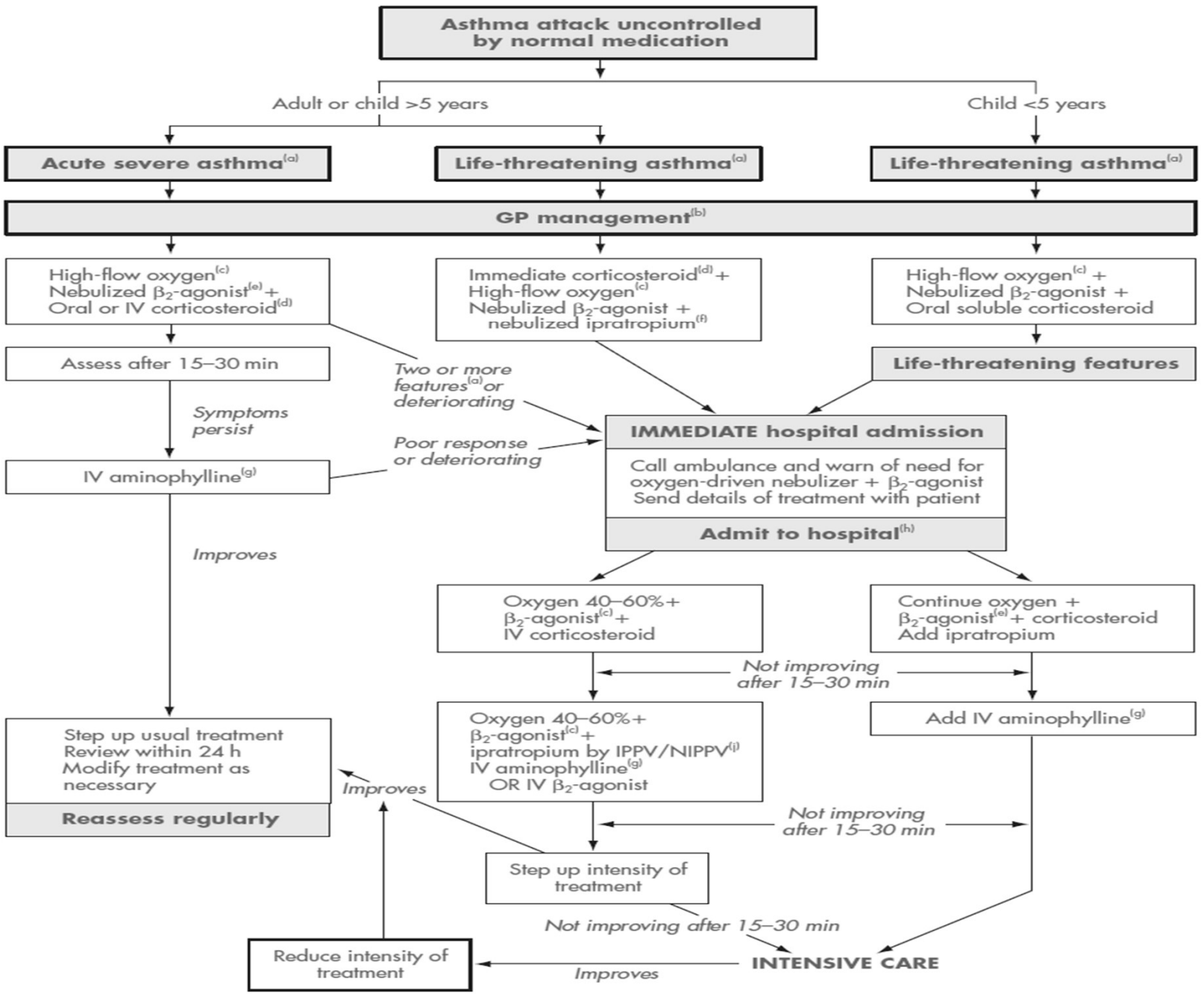
Step 3: Increased-dose inhaled corticosteroids

Inhaled short-acting beta$_2$-agonist as required
plus regular inhaled standard paediatric dose corticosteroid[c]
plus leukotriene receptor antagonist
Consider: Short course of soluble prednisolone tablets[c]
Regular inhaled salmeterol (long-acting beta$_2$-agonist[e] not in children <4y) **or** regular modified-release oral theophylline/aminophylline

Note: Modified-release oral theophylline/aminophylline may be helpful (particularly for nocturnal symptoms) but has appreciable side-effects in up to one-third of children (plasma- or salivary-concentration monitoring recommended). The manufacturer's literature should be consulted about suitable dosage and ages.

Step 4: Persistent poor control

Refer child to respiratory paediatrician


Asthma attack uncontrolled by normal medication
Adult or child >5 years
Child <5 years
Acute severe asthma[a]
Life-threatening asthma[a]
Life-threatening asthma[a]
GP management[b]
High-flow oxygen[c] Nebulized β2-agonist[e] + Oral or IV corticosteroid[d]
Immediate corticosteroid[d] + High-flow oxygen[c] Nebulized β2-agonist + nebulized ipratropium[f]
High-flow oxygen[c] + Nebulized β2-agonist + Oral soluble corticosteroid
Assess after 15–30 min
Life-threatening features
Symptoms persist
Two or more features[a] or deteriorating
Poor response or deteriorating
IV aminophylline[g]
IMMEDIATE hospital admission
Call ambulance and warn of need for oxygen-driven nebulizer + β2-agonist
Send details of treatment with patient
Admit to hospital[h]
Improves
Oxygen 40–60% + β2-agonist[c] + IV corticosteroid
Continue oxygen + β2-agonist[e] + corticosteroid
Add ipratropium
Not improving after 15–30 min
Step up usual treatment
Review within 24 h
Modify treatment as necessary
Reassess regularly
Oxygen 40–60% + β2-agonist[c] + ipratropium by IPPV/NIPPV[i] IV aminophylline[g] OR IV β2-agonist
Add IV aminophylline[g]
Improves
Not improving after 15–30 min
Step up intensity of treatment
Not improving after 15–30 min
Reduce intensity of treatment
Improves
INTENSIVE CARE

Beta-adrenergic receptor subtypes and some effects of their stimulation in certain tissues

Receptor type	Tissue in which present	Effect of stimulation
β_1	Heart	Increased rate, force, conduction velocity, automaticity
	Kidney	Renin secretion
	Fat tissue	Lipolysis
β_2	Smooth muscle	
	• bronchial	Bronchodilatation
	• vascular	Vasodilatation
	• intestinal • bladder	Reduced motility and tone
	Skeletal muscle	Increased contractility, glycogenolysis, potassium uptake; tremor (overdose)
	Pancreas	Increased insulin secretion
	Liver	Glycogenolysis, gluconeogenesis
	Central nervous system	Nervous tension, headache, insomnia

The approximate relative potencies[a] of corticosteroids used for the treatment of respiratory diseases

Systemic use		By inhalation	
Hydrocortisone	0.2	**Beclometasone**	**1** (2 in Qvar inhaler)
Deflazacort	0.8	Budesonide	1
Prednisolone	**1**	Ciclesonide	2.5
Methylprednisolone	1.3	Fluticasone	2
Triamcinolone	1.3	Mometasone	1.5
Dexamethasone	7		
Betamethasone	7		

Chronic obstructive pulmonary disease:

- is the collective term for a number of chronic, slowly progressive conditions, most of which are either caused by tobacco smoking or are exacerbated by it.

- The conditions produce widespread, persistent airways obstruction that is largely irreversible.

- The underlying condition in all of these is usually COPD or emphysema (or a combination of these).

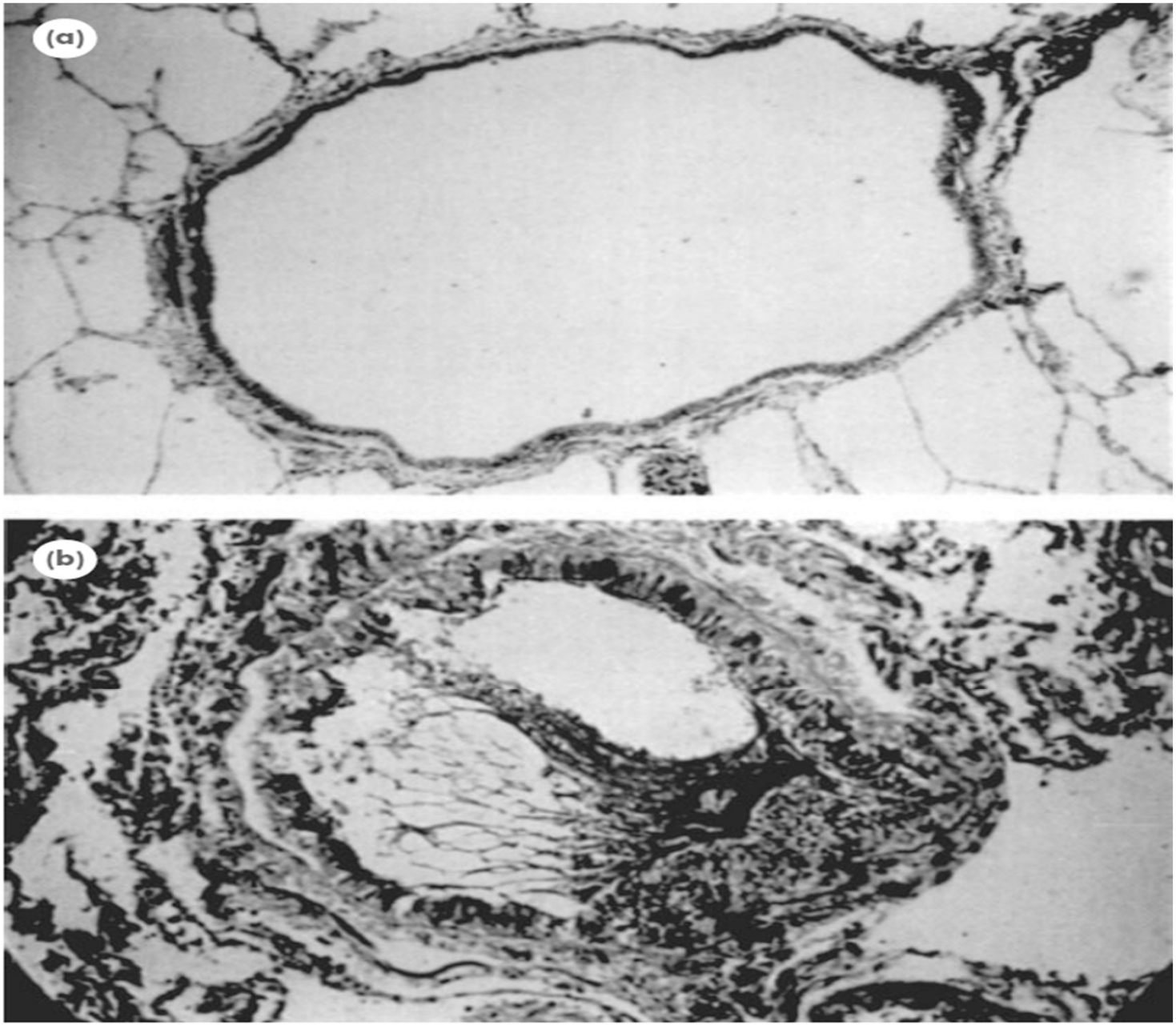
- The airway obstruction is due to a combination of inflammation, mucus secretion and parenchymal damage.

- The damage is the result of chronic inflammation that differs from that seen in asthma and which is usually the result of inhaling tobacco smoke.

- The term ‘bronchitis’ describes inflammation of the larger airways and should now be restricted to the acute condition.

Differentiation between asthma and chronic obstructive pulmonary disease

Feature	Asthma	COPD
Symptoms under age 35 years	Common	Uncommon
Smoker or ex-smoker	Uncommon	Almost all
Chronic productive cough	Uncommon	Almost all, progressive
Breathlessness	Episodic, variable	Persistent and progressive
Night-time breathlessness and/or wheeze	Common	Uncommon
Significant diurnal or day-to-day variability of symptoms	Common	Uncommon
Reversibility with $beta_2$-agonists	>15%, except in remission	<15%


(a)
(b)

Clinical features:

- The cardinal early symptoms are as follows:
- ‘Smoker’s cough’: initially present on winter mornings, but later throughout the year.

- Sputum: usually copious and tenacious (mucoid). It may be yellow, green or khakicoloured (mucopurulent) during infective exacerbations.

- Dyspnoea: as with all obstructive airways diseases expiration is the difficult phase.

- Fever and the usual signs of infection during exacerbations.

- Cyanosis: if the respiratory deficit is severe; frank central cyanosis is discernible when there is about 5 g/dL of deoxygenated Hb in the blood.

- Hyperinflation: a consequence of air trapping.

- Plethoric complexion: patients may have a high facial colour due to secondary poly-cythaemia (erythrocytosis, a raised red cell count), a normal physiological response to hypoxaemia.

Management of COPD:

- Because most patients have a combination of inflammation and Alpha1-antitrypsin AAT deficiency, their treatment is based on similar principles. There is unlikely to be a significant reversible element.

- The aims of management of COPD are to:
- educate the patient about their disease and prognosis;
- prevent deterioration;
- minimize the frequency and severity of exacerbations and complications;
- give the best possible symptomatic relief;
- achieve a reasonable quality of life.

General approach to the management of target features in chronic obstructive pulmonary disease

Aim	Target feature	Management mode
Prevent deterioration	Bronchiolar irritation and inflammation	Stop smoking Avoid irritant and dusty environments Corticosteroids?[a]
Improve respiratory function	Poor ventilation Bronchoconstriction?	Physiotherapy $Beta_2$-agonist or antimuscarinic bronchodilators?[a] Theophylline?[a]
Symptomatic relief	Dyspnoea Excessive sputum Troublesome night cough	Oxygen Physiotherapy, inhalations Expectorants/mucolytics? Antitussives?
Treat exacerbations and complications	Infections	Prompt antibiotics, influenza vaccination
		Reduce weight if obese
		Diuretics or vasodilators
	Heart failure	Digoxin if fibrillating
		Venesection
Improve quality of life	Poor mobility	Oxygen
		Occupational therapy
		Home improvements, social support

Management of chronic obstructive pulmonary disease

Disease level	Symptoms and signs	Pharmacotherapy	Other considerations
Mild (FEV_1 60–80%)[a]	Currently asymptomatic	Nil	Stop smoking
	'Smoker's cough'	Bupropion, varenicline or nicotine replacement therapy	Optimize inhaler technique All treatments subject to objective ± subjective benefit as guide
	Little or no breathlessness	$Beta_2$-agonist as required **or** antimuscarinic **or** both (depends on response)	
	Infective exacerbations	Influenza + pneumonococcal immunization Antibiotics	
Moderate (FEV_1 40–59%)	Exercise limitation: breathless on moderate exertion Wheeze Cough ± sputum Abnormal breath sounds	$Beta_2$-agonist as required (if responsive) **or** add, or change to, antimuscarinic bronchodilator if poor response	As above plus: Use large-volume spacer Long-acting $beta_2$-agonist only if clearly beneficial (but see p. 294)
	Infective exacerbations	Antibiotics	Review medication
	FEV_1 ≤50%[a] or two or more exacerbations/year	Trial of corticosteroid[b] Influenza and pneumococcal vaccination	
	Anxiety ± depression	Anxiolytic ± antidepressant (see Chapter 6)	
Severe (FEV_1 <40%)	Breathless at rest or any exertion	$Beta_2$-agonist + antimuscarinic Assess for home nebulizer	Oral theophylline if tolerated and other bronchodilators not beneficial
	Prominent wheeze and cough	Trial of corticosteroid[b]	
	Infective exacerbations	Antibiotics	
	FEV_1 ≤50%[a] or two or more exacerbations/year	Trial of corticosteroid[b] Influenza and pneumococcal vaccination	
	Cyanosis	Oxygen (if beneficial)	Objective proof of benefit
	Peripheral oedema and polycythaemia	Treat for heart failure: diuretics, etc. (Chapter 3) Treat for respiratory failure: venesection?	
	Infective exacerbations	Antibiotics	