Chapter 3
Respiratory system

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1 Asthma

Complete control of asthma is defined as no daytime symptoms, no night-time awakening due to asthma, no asthma attacks, no need for rescue medication, no limitations on activity including exercise, and normal lung function.

Pregnancy and breast-feeding
Severe acute attacks of asthma can have an adverse effect on pregnancy and should be treated promptly in hospital with conventional therapy, therefore women with asthma should be treated as normal and closely monitored during pregnancy.

1.1 Management of chronic asthma

Lifestyle changes
Weight loss in overweight patients; smoking cessation; breathing exercises

Exercise-induced Asthma
Usually indicates poorly controlled asthma, treatment may need stepping up

Stepping down
To avoid unwanted side effects and unnecessary costs, treatment is gradually stepped down every three months (25–50% each time) once control is achieved. Patients should be maintained at the lowest possible dose of inhaled corticosteroid.

1.1.1 Children under 5 years (BTS/SIGN Guidelines)

1. Mild intermittent asthma
   Inhaled short-acting beta2 agonist (such as salbutamol or terbutaline)
2. Regular preventer therapy
   a. Add inhaled corticosteroid (ICS), or
   b. Add leukotriene receptor antagonist (LTRA) if child unable to take ICS (not as effective)
3. Initial add-on therapy
   a. 2–5 years, add LTRA or ICS
   b. under 2 years, proceed to step 4
4. Persistent poor control
   refer to respiratory paediatrician

Steroid card should be issued for high doses, especially in children where high doses are associated with systemic side-effects, including growth failure, reduced bone mineral density, and adrenal suppression.

Monitor eyes for cataracts, and weight and height for growth.

1.1.2 Adult and child over 5 years (BTS/SIGN Guidelines)

1. Mild intermittent asthma
   Inhaled short-acting beta2 agonist
2. Regular preventer therapy
   a. Add inhaled corticosteroid (ICS), or
   b. Add LTRA or theophylline if child unable to take ICS (not as effective)
3. Initial add-on therapy
   a. Add regular inhaled long-acting beta2 agonist (LABA) (formoterol or salmeterol)
   b. No response to the LABA, discontinue and increase dose of inhaled corticosteroid,
   c. consider trial of a LTRA or m/r theophylline
4. Persistent poor control
   a. Increase ICS to max dose
   b. consider adding fourth drug LTRA, m/r theophylline, modified-release beta2 agonist
5. Continuous use of oral corticosteroids
   a. Refer to specialist care
   b. Initiated on regular oral corticosteroid

1.2 Management of acute asthma

Management
1. High flow oxygen (40-60%) to maintain a SpO2 level between 94–98%
2. beta2 agonist administered by an oxygen-driven nebuliser (to avoid pulmonary O_2 displacement)
3. oral prednisolone once daily for at least 5 days or until recovery
4. Can add the following if no improvement:
   a. nebulised ipratropium bromide
   b. intravenous dose of magnesium sulfate
   c. intravenous aminophylline (caution if patient already on theophylline)

Moderate acute asthma
- Increasing symptoms
- Peak flow > 50–75% best or predicted
- No features of acute severe asthma

Severe acute asthma
Any one of the following:
- Peak flow 33–50% best or predicted
- Respiratory rate ≥ 25/min
- Heart rate ≥ 110/min
- Inability to complete sentences in one breath

Life-threatening acute asthma

Any of the following, in a patient with severe asthma:

- Peak flow < 33% best or predicted
- Arterial oxygen saturation (Sp02) < 92%
- Partial arterial pressure of oxygen (PaO2) < 8 kPa
- Normal partial arterial pressure of carbon dioxide (PaCo2) (4.6–6.0 kPa)
- Silent chest
- Cyanosis (blue discoloration)
- Poor respiratory effort
- Arrhythmia
- Exhaustion
- Altered conscious level
- Hypotension

Near-fatal acute asthma

- Raised PaCO2, requiring mechanical ventilation with raised inflation pressures, or both

2 Croup

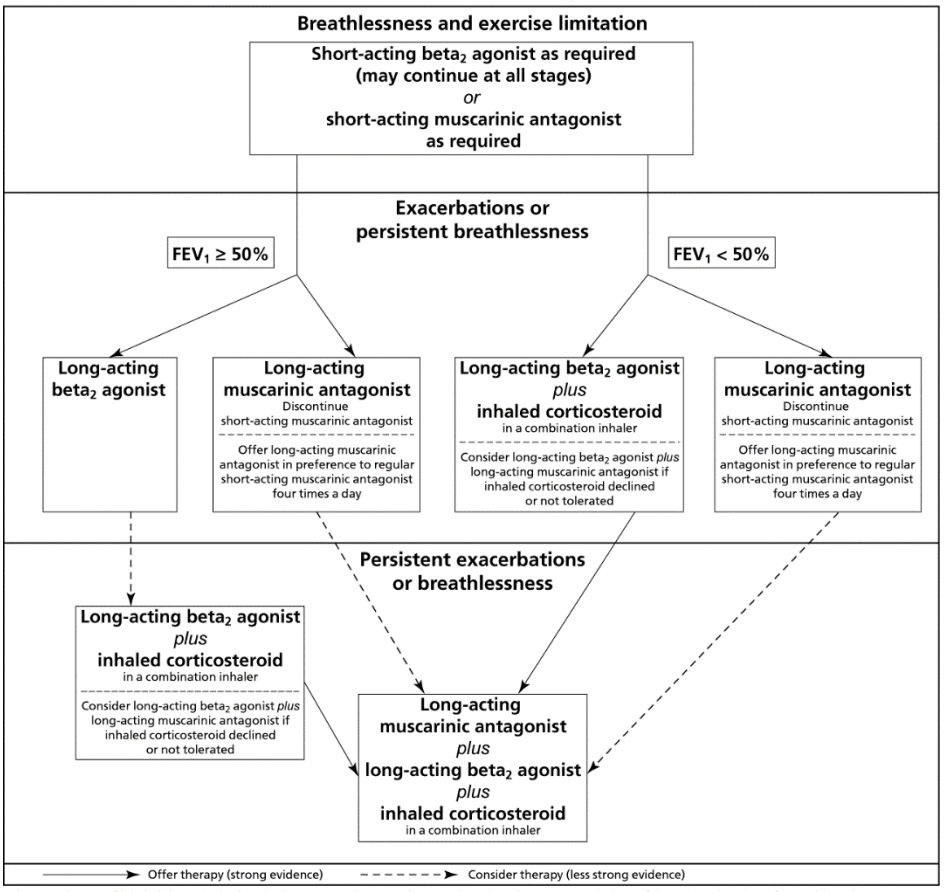
Mild croup is largely self-limiting; but treatment with a single dose of a corticosteroid e.g. dexamethasone is usually offered. More severe croup (or mild croup that might cause complications) calls for hospital admission, dexamethasone or budesonide (by nebulisation) will often reduce symptoms; the dose may need to be repeated after 12 hours if necessary. If still not controlled, nebulised adrenaline solution is given.

3 COPD

Smoking cessation greatly reduces mortality risk and increase prognosis. Cor pulmonale require referral to specialist, peripheral oedema can be treated with furosemide. Abnormal BMI requires referral to dietician; nutritional supplements is <18.5, and weight loss if >25. Mucolytic (carbocisteine) may provide relief of chronic productive cough.

Long-term oxygen therapy (15 hours a day) is needed in severe COPD and hypoxaemia. Exacerbations are treated with nebulised bronchodilators (salbutamol or ipratropium); antibiotics if infection is suspected, and 7 to 14-day course of corticosteroid is breathlessness interferes with daily activity.

Use of inhaled therapies in chronic obstructive pulmonary disease



Advice on the use of inhaled therapies in chronic obstructive pulmonary disease is based on the recommendations of the National Institute for Health and Care Excellence (2010). Management of chronic obstructive pulmonary disease in adults in primary and secondary care. London: NICE. Available from www.nice.org.uk/CG101 Reproduced with permission

4 Bronchodilators

4.1 Selective beta$_2$ agonists

Selective beta2 agonists produce bronchodilation. A short-acting beta2 agonist is used for immediate relief of asthma symptoms while some long-acting beta2 agonists are added to an inhaled corticosteroid in patients requiring prophylactic treatment.

Hypokalaemia

Potentially serious hypokalaemia may result from beta$_2$ agonist therapy. Caution and monitoring is required in severe asthma, as risk is increased with concomitant theophylline, corticosteroid, and diuretic use, as well as with hypoxia.

4.1.1 Short-acting beta2 agonists

Salbutamol and terbutaline are the safest and most effective short-acting beta2 agonists for asthma. If a beta2 agonist is needed more than three times a week, or if night-time symptoms occur at least once a week, or if the patient has suffered an asthma attack in the last 2 years, then prophylactic treatment should be considered.

4.1.2 Long-acting beta2 agonists

Formoterol and salmeterol are longer-acting beta2 agonists, they have a role in long-term control of chronic asthma in patients who regularly use an inhaled corticosteroid. Salmeterol should NOT be used for acute relief of an asthma attack; it has a slower onset of action than salbutamol or terbutaline; however, Formoterol is licensed for short-term symptom relief.

CHM advice

CHM has advised that formoterol and salmeterol for chronic asthma, should:

- be added if control with regular ICS has failed
- not be initiated in patients with rapidly deteriorating asthma
- be introduced at a low dose and the effect properly monitored before considering dose increase
- be discontinued in the absence of benefit
- not be used for the relief of exercise-induced asthma symptoms unless regular inhaled corticosteroids are also used
- be reviewed as clinically appropriate: stepping down therapy should be considered when good long-term asthma control has been achieved

4.2 Antimuscarinics

Ipratropium can provide short-term relief in chronic asthma and COPD. Aclidinium, glycopyrronium, tiotropium, and umeclidinium are licensed for the maintenance treatment of patients with chronic obstructive pulmonary disease.

Tiotropium (via Respimat® device) is also licensed as an adjunct to inhaled corticosteroids and long-acting beta2 agonists for the maintenance treatment of patients with asthma who have suffered one or more severe exacerbations in the last year.

Cautions

prostatic hyperplasia, bladder outflow obstruction, and those susceptible to angle-closure glaucoma (see below); they may also be associated with paradoxical bronchospasm

4.2.1 Ipratropium bromide

Acute angle-closure glaucoma has been reported with nebulised ipratropium, particularly when given with nebulised salbutamol; care needed to protect patient's eyes from nebulised drug or from drug powder.

4.2.2 Theophylline (high risk)

Theophylline is a antimuscarinic used as a bronchodilator in asthma, and stable COPD. Aminophylline is rarely given as an infusion for severe acute asthma.

Therapeutic Range: 10 to 20mg/L (although a plasma theophylline concentration of 5 to 15mg/L may still be effective); loading doses may be required

4.2.3 Warning signs

(report immediately to a doctor)

- *Toxicity*
  (vomiting, agitation, restlessness, dilated pupils, sinus tachycardia, hyperglycaemia, severe hypokalaemia may develop rapidly, haematemesis, convulsions, cardiac arrhythmias)
- *Symptoms of uncontrolled asthma*
  (cough, wheeze, tight chest)

- *Frequent courses of antibiotics and/or oral corticosteroids*
  (poor asthma control)

4.2.4 Monitoring

Serum potassium; plasma theophylline concentration

4.2.5 Interactions

- *Potentially serious hypokalaemia may result from beta agonist therapy. Caution required in severe asthma, because this effect may be potentiated by concomitant use of theophylline, corticosteroids, and diuretics as well as hypoxia. Plasma potassium should be monitored in severe asthma*
- *Increased plasma concentration with diltiazem, cimetidine, ciprofloxacin, erythromycin, oestrogens, fluvoxamine, verapamil*
- *The plasma-theophylline concentration is increased in heart failure, hepatic impairment, viral infections, in the elderly*
- *Possible increased risk of convulsions when theophylline given with quinolones*
- *Reduced plasma concentrations with alcohol, carbamazepine, primidone, phenobarbital and phenytoin, ritonavir*
- *The plasma-theophylline concentration is decreased in smokers, dose adjustment may be necessary; inform GP before stopping or starting smoking*

4.2.6 Pregnancy and breastfeeding

Risk of asthma exacerbations outweighs risk of treatment; continue taking as normal with monitoring

4.2.7 Maintaining the same brand

The rate of absorption from modified-release preparations can vary between brands. If a prescription for a modified-release oral theophylline preparation does not specify a brand name, the pharmacist should contact the prescriber and agree the brand to be dispensed. Additionally, it is essential that a patient discharged from hospital should be maintained on the brand on which that patient was stabilised as an in-patient.

5 LEUKOTRIENE RECEPTOR ANTAGONISTS

Montelukast and zafirlukast, block the effects of leukotrienes (inflammatory mediators) in the airways. They are effective in asthma when used alone or with an inhaled corticosteroid.

Hepatic disorders

Increased risk with Zafirlukast; seek medical attention if symptoms or signs such as persistent nausea, vomiting, malaise, jaundice, or dark urine develop

Churg-Strauss syndrome

Rare risk reported following the reduction or withdrawal of oral corticosteroid therapy. Symptoms include eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, or peripheral neuropathy.

6 CORTICOSTEROIDS

6.1 ASTHMA

Corticosteroids are effective in asthma; they reduce airway inflammation (and hence reduce oedema and secretion of mucus into the airway). Corticosteroid inhalers must be used regularly for maximum benefit; alleviation of symptoms usually occurs 3 to 7 days after initiation. Beclometasone, budesonide, fluticasone, and mometasone appear to be equally effective.

6.2 COPD

Inhaled corticosteroid therapy may reduce exacerbations when given in combination with an inhaled long-acting beta2 agonist.

6.3 CAUTIONS

Paradoxical bronchospasm

Discontinue treatment and offer alternative therapy if bronchospasm occurs; may be prevented by inhalation of a short-acting beta2 agonist beforehand (or by using dry powder inhalation instead of aerosol inhalation).

Candidiasis

The risk of oral candidiasis can be reduced by using a spacer device; rinsing the mouth with water after

inhalation of a dose may also be helpful. Antifungal oral suspension or oral gel can be used to treat oral candidiasis without discontinuing therapy.

6.4 Side effects

Steroid card should be issued for high doses, especially in children where high doses are associated with systemic side-effects, including growth failure, reduced bone mineral density, and adrenal suppression.

Small risk of glaucoma; monitor eyes for cataracts, and weight and height for growth.

6.5 Beclometasone diproprionate

Brands are not interchangeable

Beclometasone inhalers (Qvar® and Clenil Modulite®) are not interchangeable and should be prescribed by brand name; Qvar® has extra-fine particles, and is twice as potent as Clenil Modulite®.

Fostair® is a combination beclometasone and formoterol inhaler; Fostair® has extra-fine particles and is more potent than traditional beclometasone dipropionate CFC-free inhalers.

Unlicensed use

Easyhaler beclometasone is not licensed for children under 18 years; Qvar, Clenil 200 and 250 are not licensed for children under 12.

7 Allergic conditions

7.1 Antihistamines

All antihistamines are valuable in the treatment of nasal allergies, particularly hay fever; they reduce rhinorrhoea (runny nose) and sneezing. Oral antihistamines are used to prevent urticaria and are used to treat urticarial rashes, pruritus, and insect bites and stings; they are also used in drug allergies.

Some antihistamines are used in nausea and vomiting e.g. including cinnarizine, cyclizine, and promethazine. Buclizine is included as an anti-emetic in Migraleve tablets. Promethazine is also used for occasional insomnia.

Sedating antihistamine:

Promethazine; alimemazine; chlorphenamine; hydroxyzine

Non-sedating antihistamines

Acrivastine; cetirizine; desloratidine; fexofenadine; levocetirizine; loratadine; mizolastine

Side effects

Sedating antihistamines have significant antimuscarinic activity and they should therefore be used with caution in prostatic hypertrophy, urinary retention, susceptibility to angle-closure glaucoma

Rare side-effects of antihistamines include hypotension, palpitation, arrhythmias, extrapyramidal effects, dizziness, confusion

7.1.1 Hydroxyzine: risk of QT-interval prolongation and Torsade de Pointes

Hydroxyzine is associated with a small risk of QT-interval prolongation and Torsade de Pointes; these events are most likely to occur in patients who have risk factors for QT prolongation, e.g. concomitant use of drugs that prolong the QT interval, cardiovascular disease, family history of sudden cardiac death, significant electrolyte imbalance (low plasma-potassium or plasma-magnesium concentrations), or significant bradycardia.

To minimise the risk of such adverse effects, the following dose restrictions have been made and new cautions and contra-indications added:

- Hydroxyzine is contra-indicated in patients with prolonged QT-interval or who have risk factors for QT-interval prolongation;
- Avoid use in the elderly due to increased susceptibility to the side-effects of hydroxyzine;
- Consider the risks of QT-interval prolongation and Torsade de Pointes before prescribing to patients taking drugs that lower heart rate or plasma-potassium concentration;
- In adults, the maximum daily dose is 100 mg;
- In the elderly, the maximum daily dose is 50 mg (if use of hydroxyzine cannot be avoided);
- In children with body-weight up to 40 kg, the maximum daily dose is 2 mg/kg;
- The lowest effective dose for the shortest period of time should be prescribed

7.2 Allergen immunotherapy

7.2.1 Desensitising vaccines

Due to concerns of safety, desensitising vaccines are recommended for the following indications:

- seasonal allergic hay fever (caused by pollen) that has not responded to anti-allergic drugs;
- hypersensitivity to wasp and bee venoms.

Desensitising vaccines should generally be avoided or used with particular care in patients with asthma. They should also be avoided in pregnant women, in children under five years old, and in those taking beta-blockers, or ACE inhibitors.

8 Cough and congestion

8.1 Aromatic inhalations

Volatile substances such as menthol and eucalyptus oil encourages deliberate inspiration of warm moist air which is often comforting in bronchitis; inhalations are also used for the relief of nasal obstruction in acute rhinitis or sinusitis.

Aromatic decongestants are not advised for infants under the age of 3 months. Sodium chloride 0.9% nasal drops is preferred, but suction aspiration can also be conducted.

8.2 Cough preparations

Cough may be a symptom of an underlying disorder, such as asthma, GORD, or rhinitis, which should be addressed before prescribing cough suppressants. Cough may be a side-effect of another drug, such as an ACE inhibitor, or it can be associated with smoking or environmental pollutants.

Suppressants

Codeine may be effective but it is constipating and can cause dependence; dextromethorphan and pholcodine have fewer side-effects.

Demulcent

Contain soothing substances such as syrup or glycerol and some patients believe that such preparations relieve a dry irritating cough. Preparations such as simple linctus have the advantage of being harmless and inexpensive.

Expectorants

Guaifenesin or ipecacuanha; claim to promote expulsion of bronchial secretions, but there is no evidence that any drug can specifically facilitate expectoration.

8.3 OTC Cough preparations

Children under 6 years should not be given OTC cough and cold medicines containing the following ingredients:

- antihistamines
- cough suppressants
- expectorants
- decongestants

OTC cough and cold medicines can be considered for children aged 6–12 years, but treatment should be restricted to 5 days or less.

Codeine for cough and cold: restricted use in children

Codeine is contra-indicated in:

- children younger than 12 years old
- patients of any age known to be CYP2D6 ultra-rapid metabolisers
- breastfeeding mothers
- all children under 18 who undergo surgery of tonsils or adenoids for sleep apnoea
- all children under 18 with respiratory problems