Acute respiratory medicine

Melissa Heightman MB BChir MA MRCP, Specialist Registrar in Respiratory Medicine

Geoff Bellingan BSc MBBS PhD FRCP, Consultant in Respiratory Medicine and Critical Care

University College Hospital, London

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Respiratory disease accounts for a large part of acute medical presentations. Patients with acute respiratory problems are increasingly cared for on admissions units and can be discharged without respiratory physician input. Fortunately, the British Thoracic Society (BTS) and the National Institute for Health and Clinical Excellence (NICE) have produced excellent guidelines to assist in their management. Acute respiratory problems can be considered anatomically, separating into diseases of the airway, parenchyma, pleura and pulmonary vasculature, all of which can be complicated by respiratory failure.

Airways disease

Chronic obstructive pulmonary disease (COPD) and asthma can present similarly with wheeze and breathlessness but their distinction is important as management differs.

Chronic obstructive pulmonary disease

COPD prevalence is increasing and projected to be the third leading cause of death by 2020. The BTS[1] and NICE[2] issued guidelines in 1997 and 2004, respectively (Table 1). Significant developments have occurred in the use of non-invasive ventilation (NIV) for COPD patients with hypercapnic ventilatory failure (Table 1).[3] NIV helps by unloading fatigued respiratory muscles, keeping collapsed alveoli open, improving ventilation/perfusion (VQ) mismatching, reducing intubation, shortening hospital stay and lowering mortality. NIV is now available almost universally in UK hospitals, but it still cannot be used in nearly half of accident and emergency or medical assessment units. The need for short-term mechanical ventilation does not appear to predict short- or long-term mortality. Suitable patients should be identified early.[4]

Intravenous (iv) aminophylline is falling from favour following a Cochrane review demonstrating its failure to increase FEV_1 or shorten hospital admission, while at the same time increasing adverse effects.[5] Pulmonary rehabilitation is underutilised but beneficial, improving exercise capacity and quality of life (QoL).

Table 1. Chronic obstructive pulmonary disease (COPD).[1,2]

Investigations	• CXR, ECG, FBC, U&E • ABG if saturations <92% • theophylline level if on oral theophylline
Management	• oral prednisolone 30 mg for 7–14 days, then stop • triggers may be non-infective (humidity/pollution/smoke) and 1/3 may be viral. Antibiotics should be used only if increased sputum/change in colour or clinical/CXR evidence of pneumonia • if hypercapnia, ensure control of FiO_2 (aim saturation 90–92%) • NIV is the treatment of choice for hypercapnic ventilatory failure with acidosis (pH <7.36 >7.25); ensure safe environment and appropriate ceilings of treatment established • doxapram only if NIV is contraindicated or unavailable • assessment of suitability for intubation should include functional status/BMI/use of home oxygen/comorbidity and QoL – not just age and FEV_1
Discharge	• establish on long-term inhaled therapy, advice re smoking cessation, educate patients and carers • supported discharge by community nurses may be appropriate • assessment for LTOT should occur 6 weeks post-exacerbation (LTOT indicated if pO2 <7.3 on air, or <8 if evidence of pulmonary hypertension/polycythaemia) • influenza vaccination reduces exacerbation frequency • refer to pulmonary rehabilitation programmes if possible
NIV	• BIPAP used in hypercapnic ventilatory failure in COPD. NIV can also be used if ventilatory failure is due to chest wall deformities or in cases of obesity hypoventilation; specialist input is often helpful here. NOT recommended in asthma as intubation likely • CPAP used in hypoxic respiratory failure due to pulmonary oedema/pneumonia – high risk of failure, so best used in ICU • start promptly once indication confirmed • can use face or nasal masks • ensure appropriate environment/staff training • agree ceiling of therapy on starting treatment/liaise closely with ICU • contraindications include facial burns, haemodynamic instability, copious secretions, altered consciousness, undrained pneumothorax and bowel obstruction

ABG = arterial blood gas; BIPAP = biphasic positive airway pressure; BMI = body mass index; CPAP = continuous positive airway pressure; CXR = chest X-ray; FBC = full blood count; FEV_1 = forced expiratory volume in 1 sec; FiO_2 = fractional concentration of O_2 in inspired gas; ICU = intensive care unit; LTOT = long-term O_2 therapy: NIV = non-invasive ventilation; QoL =quality of life; pO2 = partial pressure of O_2; U&E = urea and electrolytes.

Quadriceps myopathy may be a particular feature of COPD exacerbations, causing anaerobic metabolism at low work rates, increasing CO_2 retention.

Many COPD patients benefit from being discharged on anticholinergic and beta-agonist bronchodilators. Interestingly, tiotropium has a 24-hour duration of action, dissociating 100 times more slowly from M1 and M3 receptors than ipratropium; it also reduces exacerbations and improves QoL. Long-acting beta-agonists achieve similar improvements to short-acting counterparts, although formoterol may be superior. Long-term inhaled glucocorticoids are indicated in severe COPD (FEV_1 <50% predicted or frequent exacerbations). They may slow decline in FEV_1 and reduce exacerbation frequency, but the clinical significance is uncertain.

Table 2. Asthma severity.

Near fatal asthma	• Raised pCO_2 or requiring mechanical ventilation
Life-threatening asthma	
Any one of:	• PEF <33% best or predicted • SpO_2 <92%/cyanosis • normal $PaCO_2$ (4.6–6.0 kPa) • silent chest • feeble respiratory effort • bradycardia • hypotension • exhaustion • confusion/coma
Acute severe asthma	
Any one of:	• PEF 33–50% best or predicted • respiratory rate >25/min • heart rate >110/min • inability to complete sentences in one breath
Moderate asthma exacerbation	• increasing symptoms • PEF >50–75% predicted • no features of acute severe asthma
Brittle asthma	• wide PEF variability (>40% diurnal variation for >50% of the time over >150 days despite intense treatment) • sudden severe attacks on background of well controlled asthma

$PaCO_2$ = partial pressure of CO_2 in alveolar gas; pCO_2 = partial pressure of CO_2; PEF = peak expiratory flow; SpO_2 = peripheral oxygen saturation.

Asthma

Acute asthma is common and potentially life-threatening. BTS guidelines were published in 1997[6] (updated 2004[7] and 2005[8]). Important considerations are:

- predicting when admission is required
- determining when intensive care unit (ICU) admission is necessary
- knowing the most effective treatment delivery, and
- ensuring appropriate discharge medication and follow-up.

Enquiries into asthma deaths suggest that most occur with severe chronic disease. Inadequate inhaled therapy, follow-up and psychosocial vulnerability often also play a part. Assessing the severity of an attack is multifactorial (Table 2).

Treatment is outlined in Table 3 and includes oxygen, beta-agonists and

Table 3. Treatment of asthma exacerbations.

- Oxygen to maintain saturation >92%
- Nebulisers or MDI with a spacer is equally suitable for mild and moderate asthma
- Severe asthmatics benefit from continuous nebulisation (5–10 mg salbutamol/hour)
- Higher doses of salbutamol offer no benefit over standard doses
- Anticholinergic agents (usually ipratropium bromide) are beneficial in moderate to severe acute asthma
- Evidence for iv beta-agonists is limited; they should be used only if inhaled therapy cannot be used reliably
- Early (90 min) corticosteroids (40–50 mg prednisolone or 200 mg hydrocortisone) significantly reduces admission; should be given to all acute asthmatics. No benefit of iv over oral demonstrated. Steroids should be continued for at least 5 days to reduce relapse; tapering dose is unnecessary
- Inhaled steroids can be continued whilst on oral treatment; pooled evidence suggests this is beneficial
- Addition of iv $MgSO_4$ to beta-agonists and corticosteroids is beneficial in all patients who have not had a good response to inhaled bronchodilators, with greatest effects in severe asthmatics. Recommended dose 2 g iv over 20 min (up to 10–20 g can be given in ICU over 12 hours with close monitoring of serum Mg^{++}).
- No added benefit demonstrated from iv aminophylline
- Routine antibiotics not appropriate – most triggering infections will be viral
- Insufficient evidence for use of LTRAs or long-acting beta-agonists in acute asthma (currently reserved as add-on therapy in outpatients)
- The use of heliox can not be recommended on current evidence

ICU = intensive care unit; iv = intravenous; LTRA = leukotriene receptor antagonist; MDI = metered dose inhaler; $MgSO_4$ = magnesium sulphate.

corticosteroids as the mainstay. Addition of iv $MgSO_4$ to beta-agonists and corticosteroids is beneficial in all patients who have not responded well to inhaled bronchodilators, particularly severe asthmatics.[9] Those failing to respond, evidenced by worsening hypoxia, hypercapnia, acidosis, exhaustion or drowsiness, require ICU referral. In general NIV is not suitable and should never be given outside ICU. Intubation and mechanical ventilation are often difficult and should be performed by an experienced intensivist.

Discharge should occur when stable on inhaled therapy, ideally with peak expiratory flow rate above 75% predicted with less than 20% diurnal variability. An acute admission is a good opportunity to optimise long-term treatment, especially as many of those admitted have the poorest disease control and a social situation making them vulnerable to poor compliance: 15% reattend within two weeks. Guidelines stress asthma education; self-management programmes, written action plans and regular medical follow-up have evidence supporting their efficacy.

Parenchymal disease

The most common parenchymal acute respiratory disease is community-acquired pneumonia (CAP). Patients with interstitial lung disease can present acutely with superadded infections, exacerbations of underlying disease or occasionally with new presentations such as cryptogenic organising pneumonia or pulmonary haemorrhage. Such patients should be urgently referred to respiratory physicians.

Community-acquired pneumonia

The BTS produced guidelines for CAP in 2001[10] (updated 2004).[11] An important part of management is identifying those who are likely to need admission to ICU. The CURB-65 score (Table 4) is well established for assessing severity and predicting prognosis. Investigations and antibiotics are reviewed in Table 4. Hypoxaemic patients who are resistant to

Key Points

Excellent up-to-date British Thoracic Society or National Institute for Health and Clinical Excellence guidelines are available for all common acute respiratory problems

Patient education is vital in asthma, with best outcomes relating to self-management programmes, a clear written action plan for the patient and regular medical follow-up

Non-invasive ventilation is beneficial in chronic obstructive pulmonary disease patients with hypercapnic ventilatory failure; it should be established promptly

CURB-65 criteria are useful indicators of severity, outcome and for referral to critical care

KEY WORDS: asthma, chronic obstructive pulmonary disease, community-acquired pneumonia, non-invasive ventilation, pleural effusion, pneumothorax, pulmonary embolus

Table 4. Community-acquired pneumonia (CAP).

CAP and CURB-65	1 point for each of: • confusion (MMT </= 8 or new disorientation) • Urea >7 mmol/l • RR >30 bpm • BP systolic <90 mmHg or diastolic <60mmHg • age >65 Score 0 or 1: may not require admission Score 2: consider inpatient care Score ≥3: manage as severe pneumonia
CAP Investigations (from BTS 2004 guidelines)	• CXR, FBC, U&Es • Severe: – blood and sputum cultures – legionella/pneumococcal antigens – paired serological tests • Non-severe: – blood and sputum cultures (pre-antibiotics if possible) • consider mycobacterium TB if history/CXR suggestive • consider underlying malignancy – follow-up CXR if smoker/slow response to treatment
If poor response to treatment consider alternative diagnosis (PE/bronchiectasis/bronchial carcinoma/foreign body/COP/pulmonary eosinophilia) or unusual pathogen	
Antibiotic guidelines for CAP:	
• Hospitalised patients with non-severe pneumonia	7 days oral amoxicillin plus macrolide or fluoroquinolone with enhanced pneumococcal activity (levofloxacin or moxifloxacin)
• Severe pneumonia	10 days iv co-amoxiclav, cefuroxime or cefotaxime plus iv macrolide/or iv levofloxacin plus iv benzylpenicillin (eg if penicillin allergy or local concern regarding *Clostridium difficile* diarrhoea with beta-lactam use)
Antibiotic treatment should be rationalised according to positive microbiology and iv treatment changed to oral as soon as clinically appropriate and the temperature has been normal for 24 hours	

BP = blood pressure; bpm = breaths per minute; BTS = British Thoracic Society; CAP = community-acquired pneumonia; COP = cryptogenic organising pneumonia; iv = intravenous; CXR = chest X-ray; FBC = full blood count; MMT = Mini-Mental Test; PE = pulmonary embolism; RR = respiratory rate; TB = tuberculosis; U&Es = urea and electrolytes.
CURB = **C**onfusion: new mental confusion defined as an Abbreviated **M**ental Test score ≤8; **U**rea: raised >7 mmol/l; **R**espiratory rate: raised ≥30/min; **B**lood pressure: low BP (systolic <90 mmHg and/or diastolic ≤60 mmHg).

high-flow oxygen may benefit from continuous positive airway pressure (CPAP). They commonly proceed to intubation, so CPAP should ideally only be used in ICU. Caution with high-flow oxygen is necessary in COPD patients with hypercapnia, especially if the respiratory rate is already low.

Patients should not be discharged if they have a fever above 37.8°C, heart rate above 100/min, respiratory rate below 24/min, systolic blood pressure (BP) below 90, oxygen saturations below 90%, inability to maintain oral intake or abnormal mental status. These features are all associated with a high readmission rate and mortality. All patients should be reviewed six weeks after discharge. In smokers, those over 50 or those with persistent symptoms, a follow-up chest X-ray (CXR) to check for resolution should be arranged, with bronchoscopy considered for persisting changes or symptoms such as haemoptysis.

Pleural disease

Pleural effusions

The BTS released guidelines for pleural fluid analysis in 2003 (Table 5).[12] The key is to distinguish whether the effusion is an exudate or transudate. Accurate history and examination are essential, and a diagnostic tap performed unless the effusions are bilateral and the clinical setting strongly suggestive of a transudate.

Drainage is urgently required only if an empyema is diagnosed (frank pus, Gram stain, or pleural pH <7.2). Otherwise it is usually best to establish the cause prior to drainage, although a therapeutic tap can be performed to relieve symptoms if necessary. Tuberculous effusions typically resolve with tuberculosis (TB) treatment without requiring drainage. Cytology is positive in 40–87% of malignant effusions and should always be repeated if negative. Blind pleural biopsy slightly increases diagnostic yield above cytology but has a much higher yield when looking for TB, although pleural adenosine deaminase may supersede this. Parapneumonic effusions are common, occurring in 20–40% of patients hospitalised with pneumonia. In an undiagnosed exudative effusion (25% of cases) a thoracoscopic biopsy is the gold standard. Computed tomography (CT) can be useful to look for parenchymal, mediastinal or pleural disease to direct biopsy, particularly in those unsuitable for thoracoscopy. If no clear diagnosis is established, TB, pulmonary embolism (PE) and malignancy should be reconsidered and a watch and wait policy adopted.

Table 5. Pleural fluid analysis.

- Note colour
  - if milky, check TG/cholesterol to look for chylothorax
  - if bloodstained, suggestive of malignancy, PE or benign asbestos effusions
  - check haematocrit (if >50% peripheral blood, suggests haemothorax)
  - pus: empyema and drainage required
- Send for protein/LDH/glucose/Gram stain/AFB/culture (in sterile tube and blood culture bottles)/cytology (20 ml adequate)/pH if parapneumonic effusion suspected
- Exudate if protein >30 g/dl
- Light's criteria useful if protein 25–35 g/dl (likely exudate if LDH >2/3 upper normal serum level or pleural to serum LDH >0.6, pleural to serum protein >0.5. If still equivocal, if the difference between pleural and serum protein levels is >3.1 g/dl, a transudate is likely)
- Differential cell counts sometimes useful: >50% pleural lymphocytosis common in malignancy, TB and post-CABG; presence of neutrophils suggests an acute process
- Pleural fluid ADA/TB PCR can be useful if tuberculous effusion suspected
- Request pleural amylase level if pancreatitis or oesophageal rupture is suspected. A pleural:serum amylase >1.0 indicates a raised level

AFB = acid fast bacilli; ADA = adenosine deaminase; CABG = coronary artery bypass grafting; LDH = low-density lipoprotein; PCR = polymerase chain reaction; PE = pulmonary embolus; TB = tuberculosis; TG = triglyceride.

Spontaneous pneumothoraces

Non-trauma related spontaneous pneumothoraces are either primary (in absence of lung disease) or secondary (underlying lung disease), but most patients with presumed primary pneumothoraces have subpleural bullae at thoracoscopy, commonly smoking related. The BTS guidelines (2003) have a limited evidence base.[13] An inspiratory CXR is adequate initial imaging, although CT of the thorax may be required to differentiate pneumothorax from complex bullous lung disease, when aberrant tube position is suspected or surgical emphysema obscures the CXR.

Primary pneumothoraces

No intervention is necessary in primary pneumothorax if the rim of air is less than 2 cm and the patient is not breathless. For larger pneumothoraces, aspiration and repeat CXR should be tried initially and hospitalisation may be unnecessary. If this fails, it can be repeated or an intercostal tube inserted, to be removed 24 hours after full re-expansion/cessation of air leak. Small 10–14F tubes are adequate except for large leaks. For leaks persisting for more than 48 hours referral to the respiratory team for high volume, low pressure suction is mandatory. Referral may be made to thoracic surgeons for surgical pleurodesis.

Secondary pneumothoraces

Persistent leaks are common with secondary pneumothoraces and the lung may be harder to expand – hence guidelines suggest admission and aspiration of even small pneumothoraces. Patients with larger pneumothoraces, aged over 50 or who are breathless should proceed directly to drainage. Administration of oxygen can speed up spontaneous reabsorption of air by four times above baseline (approximately 1.25% of volume of hemithorax per day).

Table 6. Diagnosis of pulmonary embolus (PE).

Pulmonary embolus	
Excluded by:	• Normal D-dimer level and low clinical probability (for some assays an intermediate clinical probability) • Normal perfusion scan • Normal multislice CTPA
Confirmed by:	• Positive CTPA • High probability VQ scan and high clinical likelihood • Evidence of acute DVT with non-diagnostic CTPA/VQ scan
DVT is found in 70% of patients who present with PE; 50% of patients with proximal DVT develop a PE. Therefore, if DVT is suspected on clinical grounds, a positive leg ultrasound is often sufficient to confirm venous thromboembolism (if normal, a follow-up scan should be arranged to confirm)	

CTPA = computed tomographic pulmonary angiography; DVT = deep vein thrombosis; PE = pulmonary embolism; VQ = ventilation/perfusion.

Pulmonary embolism

Diagnosis of PE is important but notoriously difficult. The BTS issued guidelines in 2003.[14] The clinical presentation is varied and often non-specific. Further investigation is essential but hampered by the imperfect sensitivity of diagnostic techniques. Initial standardised assessment of clinical probability is fundamental and determines subsequent investigations and the interpretation of results. Assessment involves consideration of major risk factors, presentation (sudden dyspnoea, tachypnoea or chest pain in the absence of another explanation) and basic investigations (ECG and CXR). A negative D-dimer test is a useful negative predictor if coupled with effective pretest probability scoring; however, different D-dimer tests have different performances (Table 6).

Low molecular weight heparin (LMWH) should be given before imaging when clinical probability is intermediate or high; imaging should be performed within 24 hours of presentation or within one hour if massive PE is suspected. CT pulmonary angiography is the imaging modality of choice. Isotope scanning should be considered only if CXR is normal and there is no cardiopulmonary disease. A non-diagnostic result should always be followed by further imaging.

Thrombolysis is first line treatment for massive PE and can be instituted on clinical grounds if cardiac arrest is imminent. A 50 mg bolus of alteplase via a peripheral vein is recommended. The value of thrombolysis is otherwise not clear. Generally LMWH is preferable to unfractionated heparin, having equal efficacy and safety while easier to use. Oral anticoagulation should be started once PE is confirmed; it should be given for three months for a first idiopathic PE but for at least six months otherwise. Recent evidence suggests D-dimers are useful to determine duration of therapy.[15] Testing for thrombophilia should be performed in patients over 50 years, with recurrent PE or a strong family history. Investigation for occult malignancy should be triggered only if CXR/routine blood tests are abnormal or if suspected from the history.

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