Respiratory problems on the acute take: pleural disease and acute dyspnoea

Nicola J Stevenson and Jon Simpson

Nicola J Stevenson
MRCP MD, Consultant in Respiratory Medicine, Wirral University Teaching Hospital

Jon Simpson
FRCP MD AFOM, Consultant in Respiratory Medicine, Manchester Royal Infirmary

This article is based on a conference held at the Royal College of Physicians on 5 March 2007 organised jointly with the British Thoracic Society

Clin Med 2008;8:288–91

ABSTRACT – Respiratory disease contributes significantly to the workload of the acute medical take. This article, aimed at all physicians, reviews the evidence base for common respiratory conditions presenting as an acute emergency. There is particular emphasis on pleural disease and respiratory diagnoses likely to present with acute breathlessness.

KEY WORDS: asthma, dyspnoea, non-invasive ventilation, pleural disease, pulmonary embolus, respiratory infection

Introduction

Respiratory problems are the cause of up to one third of acute medical admissions. It is, therefore, important that all clinicians treating acute medical patients recognise common presentations of respiratory disease. This paper discusses evidence-based management of such respiratory conditions, with particular emphasis on pleural disease and causes of acute breathlessness.

Pleural disease

Pleural effusion

Pleural effusions are common and can cause diagnostic and treatment dilemmas. Aspiration of pleural fluid to establish if it is an exudate or transudate is usually the first step. For most patients the total protein level of the pleural fluid (as well as appearance of the fluid) will be sufficient to classify the effusion.[1] Where diagnostic uncertainty exists then Light's criteria can be used, pleural fluid/serum protein >0.5, pleural fluid lactate dehydrogenase (LDH)/serum LDH >0.6, and pleural fluid LDH >2/3 of normal serum level.[2] Exudates meet at least one criteria and transudates none.

The cause of a transudative pleural effusion is usually non pulmonary and treatment is aimed at the underlying cause. If the fluid is an exudate, malignancy is the most common cause (up to 75%). Malignant effusions can be diagnosed by pleural fluid cytology alone in 60% of cases; others will need some form of pleural biopsy. With the possible exception of areas with a high incidence of tuberculosis, a computed tomography (CT) guided or thoracoscopic biopsy is more likely to provide a diagnosis than a blind Abram's biopsy.[3]

The majority of large exudative pleural effusions will recur and will need pleurodesis. In centres where thoracoscopy (medical or surgical) is available, diagnosis, drainage, and pleurodesis can be achieved during a single intervention. Graded talc is the safest and most effective agent for pleurodesis and is more effective when introduced thoracoscopicaly than by a chest tube.

Pleural infection

Pleural infection (empyema) is associated with significant morbidity and mortality. It is twice as common in males and has peaks in childhood and fifth to seventh decade. There is a higher incidence in patients with diabetes, alcohol dependence and gastro-oesophageal reflux. Where an empyema is suspected and the pleural fluid is not obviously purulent the pH should be measured. The development of empyema is a progressive process that moves from a 'simple' effusion (pH >7.2), to a complicated effusion (pH <7.2), and finally to an empyema in which frank pus is present. If the measured pH of the pleural fluid is <7.2 or organisms are identified by microbiology then drainage is required.[4]

All patients should receive antibiotics based on bacterial culture results and local microbiological advice. Community- and hospital-acquired infections have different aetiology (streptococcal 50% and anaerobic bacteria 20% *v* methicillin-resistant *Staphylococcus aureus* 25%, enterobacteriaceae 18% and enterococci 12%) and survival (83% *v* 53%) respectively.

Small-bore intercostal drains are effective and are well tolerated with a low complication rate. However, they should be flushed regularly with saline to ensure patency. Currently there is no role for intrapleural streptokinase; the First Multicenter Intrapleural Sepsis Trial (MIST1) did not show a reduction in mortality, rate of surgery, or length of hospital stay.[5] The Second Multicenter Intrapleural Sepsis Trial (MIST2) group are investigating the role of other fibrinolytic agents.

Spontaneous pneumothorax

Primary pneumothoraces occur in otherwise normal lungs and are usually self-limiting; secondary pneumothoraces arise in patients with underlying lung disease and can be life threatening. Pneumothorax should be considered in any patient presenting with dyspnoea. Routine expiratory chest radiographs are not required. CT scanning is sometimes indicated, for example, if extensive subcutaneous emphysema or a small loculated pneumothorax is present.

Primary spontaneous pneumothorax typically occurs in young tall thin male smokers. The risk of recurrence is 15% within the first year. Smoking increases the risk in a dose-dependant manner; all smokers should be advised to stop. Small asymptomatic primary pneumothoraces (<2 cm rim between the lung margin and chest wall) should be observed. Patients with symptomatic or large pneumothoraces should have simple aspiration as first line treatment.[6] Re-expansion fails to occur in 20–40% and further aspiration or intercostal tube drainage is therefore needed.

Secondary spontaneous pneumothoraces are often symptomatic. There is a high recurrence rate (40–80%), with risk factors including age, pulmonary fibrosis and emphysema. Patients should be admitted to hospital. Observation is only recommended if the pneumothorax is small and the patient has minimal symptoms. Prompt treatment is needed, usually with intercostal drain insertion. The threshold for definitive measures to prevent recurrence, eg pleurodesis, should be low.

Indications for surgical referral include second ipsilateral pneumothorax, first contralateral pneumothorax, bilateral spontaneous pneumothorax, persistent air leak, spontaneous haemothorax, and professions at risk, for example, pilots and divers.[6]

Acute dyspnoea

The wheezy patient

In asthma, the importance of high concentration oxygen (usually called high-flow oxygen) should be stressed. The commonly available devices for delivering high-flow oxygen (eg non re-breathing bag or Venturi system) may not be sufficient in patients with a high inspiratory flow rate. These patients may require oxygen delivered by warmed, humidified, high-flow systems. Such systems are usually only available in critical care areas.

A single dose (1.2–2 g) of intravenous magnesium sulphate is recommended in patients with acute severe asthma who have not had a good initial response to treatment. Meta-analysis in children supports its use by demonstrating improvement in peak expiratory flow and reduction in need for hospitalisation.[7]

Intravenous aminophylline is safe in recommended dosage supervised by experienced staff and may provide additional bronchodilatation in patients with near fatal or life-threatening asthma.[8] Concerns over its safety are due to the toxic effects and narrow therapeutic window. Reported deaths from aminophylline were due to extremely high doses not used in everyday clinical practice.[9]

Conference programme

PLEURAL DISEASE FOR THE ACUTE AND GENERAL PHYSICIAN

- **The diagnosis and management of pleural effusion**
  Dr Robert Davies *(co-organiser)*
- **The diagnosis and management of pleural infection**
  Dr Nick Maskell, Southmead Hospital, Bristol
- **The diagnosis and management of pneumothorax**
  Dr Gary Lee, Oxford Radcliffe Hospitals NHS Trust

LUMLEIAN LECTURE

- **Asbestos and the mesothelioma epidemic**
  Professor Julian Peto, London School of Hygiene and Tropical Medicine

DYSPNOEA ON ACUTE TAKE

- **The wheezy patient**
  Dr Robert Niven, Wythenshawe Hospital, Manchester
- **Pulmonary embolism**
  Dr Tony Fennerty, Harrogate District Foundation Trust
- **Pulmonary infection**
  Dr Mark Woodhead, Manchester Royal Infirmary
- **Non-invasive ventilation – who is it good for?**
  Dr Paul Plant, St James's University Hospital, Leeds
- **Would you invasively ventilate this patient?**
  Dr Andrew Bentley, Wythenshawe Hospital, Manchester
- **Closing remarks**
  Dr Jon Simpson *(co-organiser)*

A meta-analysis of 14 randomised trials of helium–oxygen mixture (heliox) showed that the work of breathing was reduced in intubated patients but this did not translate into improved recovery.[10] On current evidence, heliox is therefore not recommended in acute asthma.[8]

There are other conditions which present with wheeze and breathlessness in the acute setting including vocal cord dysfunction and disordered breathing patterns. Diagnosis is often difficult and patients should therefore be treated as acute asthma and be referred for a detailed assessment in a specialist centre once stable. If patients are intubated, a peak inflation pressure <20 cm H_20 suggests that acute severe asthma is unlikely and an alternative diagnosis should be considered.

Pulmonary embolus

The presentation of pulmonary embolism (PE) is non-specific, and therefore a large number of acute medical patients undergo investigations for suspected PE. The combination of clinical assessment and the D-dimer test can reduce the number of requests for diagnostic imaging by 25–40%. There are various assessment tools (eg Wells,[11] Geneva,[12] British Thoracic Society[13]) to help clinicians stratify patients into clinical low, intermediate, or high risk.

The D-dimer has a high false positive rate and is only helpful when negative. It is most effective when used in combination with a clinical risk score. It should not be used a screening test, for hospital inpatients, patients with comorbidity, or in those with a high probability of PE. A persistently elevated D-dimer after six weeks may indicate a higher risk of developing further PE, but more research is needed.

If the combination of clinical risk and D-dimer cannot exclude a PE then CT pulmonary angiography (CTPA) should be performed. If the CTPA does not reveal PE, the risk of developing a clinically significant PE over the following three months, if untreated, is <2%.

Pulmonary embolism should be treated initially with low molecular weight heparin and then warfarin for three to six months (provoked event), six months (idiopathic event) and lifelong (second event or life-threatening first event). Thrombolysis (alteplase 100 mg over 2 hours) should be used to treat acute massive PE with associated cardiogenic shock.

Respiratory infection

Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) and community-acquired pneumonia (CAP) are the most common respiratory infections presenting on the acute take. AECOPD are usually caused by viral rather than bacterial infections. Viral infections are associated with a longer recovery time and higher levels of airway inflammatory markers.[14] The presence of purulent sputum during AECOPD helps predict the presence of bacterial infection. Antibiotics have been shown to be beneficial in the presence of increased sputum volume or purulence and increased breathlessness.[15] Not all AECOPD therefore need antibiotics; if they are used, first line treatment should be amoxicillin or a tetracycline, alternatives include a macrolide, co-amoxiclavulonic acid and fluoroquinolones. By contrast, all patients with CAP should receive antibiotics as this is usually a bacterial infection (with *Streptococcus* pneumonia being the most common).

The validated CURB 65 score (confusion, urea >7 mmol/l, respiratory rate ≥30 min, systolic blood pressure <90 mmHg or diastolic blood pressure <60 mmHg, age ≥65 years) is a useful tool to predict severity and guide management.[16] The mortality with a CURB 65 score of 0 or 1 is 1%, a score of 2 is up to 10% and a score of ≥3 is 20% or greater. Antibiotics should be given as soon as possible; administration within four hours of arrival at hospital is associated with reduced in-hospital mortality.[17] The choice of antibiotic(s) depends on the severity of the pneumonia and local hospital guidelines.

Non-invasive ventilation

Ventilatory support is now widely used on acute medical admissions in non-critical care areas. The acute/general physician needs to be familiar with the indications for its use. The two techniques commonly used are continuous positive airway pressure (CPAP) and bi-level positive pressure ventilation, now commonly called non-invasive ventilation (NIV) (also known as bi-level positive airway pressure (BiPAP), non-invasive positive pressure ventilation (NIPPV) or variable positive airway pressure (VPAP)).

In acute exacerbations of COPD, NIV should be considered in the presence of respiratory acidosis (pH <7.35 and hypercapnia) despite maximal medical therapy including controlled oxygen. It has been demonstrated to reduce mortality (number needed to treat = 10), the need for intubation and length of hospital stay.[18,19] There are few absolute contraindications. Despite earlier concerns, patients with hypercapnic coma can be treated successfully.[20]

Most NIV machines can provide only a medium concentration of oxygen (40–50%). Because of this NIV should only be used to treat pneumonia or acute asthma in the critical care setting where more sophisticated NIV equipment (delivering a high concentration of oxygen) and facilities for immediate intubation are available. Non-invasive ventilation may be preferable to CPAP in patients with pneumonia.

CPAP has been shown to be effective in patients with cardiogenic pulmonary oedema who remain hypoxic despite maximal medical treatment. A recent meta-analysis showed no difference in intubation rates or mortality between CPAP and NIV.[21] Because high concentrations of oxygen are delivered with CPAP, this is preferable for treating pulmonary oedema.

Further information

The British Thoracic Society website (www.brit-thoracic.org.uk) has evidence-based guidelines for most of the topics covered in this paper.

References

1 Maskell NA, Butland RJ. BTS guidelines for the investigation of a unilateral pleural effusion in adults. *Thorax* 2003;58(Suppl 2):ii8–17.
2 Light RW, Macgregor MI, Luchsinger PC, Ball WC, Jr. Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med* 1972;77:507–13.
3 Antunes G, Neville E, Duffy J, Ali N. BTS guidelines for the management of malignant pleural effusions. *Thorax* 2003; 58(Suppl 2):ii29–38.
4 Davies CW, Gleeson FV, Davies RJ. BTS guidelines for the management of pleural infection. *Thorax* 2003;58(Suppl 2):ii18–28.
5 Maskell NA, Davies CW, Nunn AJ *et al.* U.K. Controlled trial of intrapleural streptokinase for pleural infection. *N Engl J Med* 2005; 352:865–74.
6 Henry M, Arnold T, Harvey J. BTS guidelines for the management of spontaneous pneumothorax. *Thorax* 2003;58(Suppl 2):ii39–52.
7 Cheuk DK, Chau TC, Lee SL. A meta-analysis on intravenous magnesium sulphate for treating acute asthma. *Arch Dis Child* 2005; 90:74–7.
8 British Thoracic Society, Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. *Thorax* 2003; 58(Suppl 1):i1–94.
9 Eason J, Markowe HL. Aminophylline toxicity—how many hospital asthma deaths does it cause? *Respir Med* 1989;83:219–26.
10 Colebourn CL, Barber V, Young JD. Use of helium-oxygen mixture in adult patients presenting with exacerbations of asthma and chronic obstructive pulmonary disease: a systematic review. *Anaesthesia* 2007;62:34–42.
11 Wells PS, Anderson DR, Rodger M *et al.* Derivation of a simple clinical model to categorize patients probability of pulmonary

embolism: increasing the models utility with the SimpliRED D-dimer. *Thromb Haemost* 2000;83:416–20.
12 Le Gal G, Righini M, Roy PM *et al.* Prediction of pulmonary embolism in the emergency department: the revised Geneva score. *Ann Intern Med* 2006;144:165–71.
13 Campbell IA, Fennerty A, Miller AC. British Thoracic Society guidelines for the management of suspected acute pulmonary embolism. *Thorax* 2003;58:470–83.
14 Seemungal TA, Harper-Owen R, Bhowmik A *et al.* Respiratory viruses, symptoms, and inflammatory markers in acute exacerbations and stable chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;164:1618–23.
15 Anthonisen NR, Manfreda J, Warren CP *et al.* Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 1987;106:196–204.
16 Lim WS, van der Eerden MM, Laing R *et al.* Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003;58:377–82.
17 Houck PM, Bratzler DW, Nsa W *et al.* Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. *Arch Intern Med* 2004;164:637–44.
18 Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *Lancet* 2000;355:1931–5.
19 Chakrabarti B, Angus RM. Ventilatory failure on acute take. *Clin Med* 2005;5:630–4.
20 Diaz GG, Alcaraz AC, Talavera JC *et al.* Noninvasive positive-pressure ventilation to treat hypercapnic coma secondary to respiratory failure. *Chest* 2005;127:952–60.
21 Peter JV, Moran JL, Phillips-Hughes J *et al.* Effect of non-invasive positive pressure ventilation (NIPPV) on mortality in patients with acute cardiogenic pulmonary oedema: a meta-analysis. *Lancet* 2006;367:1155–63.