123 Doc EDUCATION

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Volume 5, Issue 9: **Respiratory**

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Volume 5, Issue 9

Foundation Years Journal

Foundation Years Journal is an international peer-viewed journal which seeks to be the pre-eminent journal in the field of patient safety and clinical practice for Foundation Years' doctors and educators. The Journal welcomes papers on any aspect of health care and medical education which will be of benefit to doctors in the Foundation training grade in the UK or international equivalents.

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Volume 5, Issue 9: Respiratory

Foundation Years Journal is the ONLY journal for Foundation Years, doctors and educators, specifically written according to the MMC curriculum. It focuses on one or two medical specialties per month and each issue delivers practical and informative articles tailored to the needs of junior doctors. The Journal closely follows the Foundation Years syllabus to provide the best educational value for junior doctors. In addition to good clinical and acute care articles, assessment questions give junior doctors the chance to gauge their learning. Each issue provides comprehensive clinical cases for trainees as well as practical teaching assessments for educators. Readers will benefit from:

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Editorial For Neurology Issue Of Foundation Years Journal 2011

Many persons like to hold a book or journal in the hand. The ability to browse by turning pages, for those to annotate, who are prepared to deface paper copies to read without needing to find electronic apparatus to enable viewing (whether by computer, by Kindle device or otherwise), all are powerful stimuli to keep to conventional hard copy, paper publications. The feel of a book, the smell of the paper (maybe the binding), the colourful printing, and the variations in font and style all contribute to this sensual experience. However, paper copies become dated and cannot easily be amended except in loose-leaf form where they lose much of their aesthetic appeal. They are more expensive to produce at the point of the user. They decay with use, whether aided by fingers, thumbs or by mice, and they are bulky for publishers and readers to transport.

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Hence, this trends towards electronic publishing. Electronic journals have many advantages and can be accessed from computers worldwide. This journal offers all of these advantages and on this occasion brings to readers aspects of important neurological topics relevant to Foundation Years practitioners.

The neurosciences, of which, everyday clinical neurology forms a part, have made amazing progress over the last couple of decades. The interactions between laboratory and clinical research, and with clinical medicine that deals with illness in patients at its most elementary level, have contributed to these advances. However, sometimes research and cutting edge thinking from the laboratory is difficult to apply to some of the immediate clinical problems exhibited by patients. Common sense (whatever that is) and thinking is needed with acute problems and so is rapid decision making. Some of the topics covered in this issue deal with acute medicine, and neurology is now very much part of this since nearly one fifth of those admitted acutely have neurological problems, and others with less acute matters still get admitted to hospital. Papers published here express some of the most important points that Foundation Years doctors experience during their everyday duties, lessons they wish to share with others in order to help prevent mishaps.

Indeed, such practitioners are encouraged to submit to this journal. There is so much to be learned from our everyday activities and our patients are in many ways our best teachers, using their symptoms and signs to make us think. It is in many ways a moral imperative to share this information with others and to publish for the widest circulation. Specific lessons that may be drawn from the papers in this issue of the Foundation Years Journal, include epilepsy and the causes of blackouts together with some useful tips on the use of the EEG in diagnosis, an important supportive test in some patients. Stroke is now an emergency in more ways than previously (since more can be done), a brain attack that needs handling acutely and which can result from venous sinus thrombosis, two more areas covered in this journal. The techniques of lumbar puncture are still important although much that was investigated previously by this technique now is revealed by the increasingly complicated imaging processes that have become available.

Acute neuromuscular weakness is a further presenting feature that has many causes and this condition may be quite puzzling in many patients. Increasingly complicated drugs and drug regimes may lead to toxicity, an important cause of disability that can easily be overlooked; baclofen is a useful drug for spasticity and intoxication is disabling. Trigeminal neuralgia can be treated in many ways; not all being effective and a paper on this topic should help guide those who deal with its early manifestations.

And what of that imperative to publish? Here we are guided in the values of clinic letters and of the role of the doctor as educator. All very important stuff, hopefully interesting, certainly enlightening, and without doubt we hope a stimulus for readers to provide further papers dealing with the many topics in neurology that may perplex all of us including those working in the Foundation Years.

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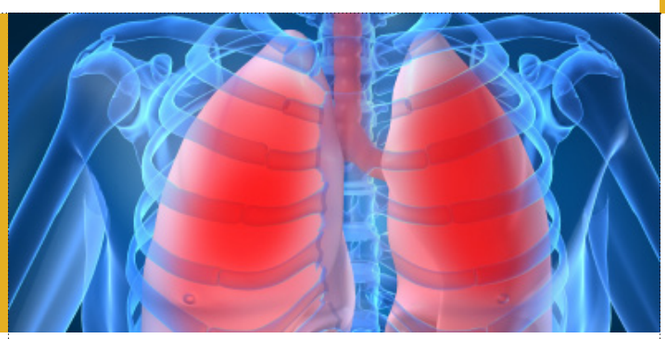
PALLIATIVE CARE IN END-STAGE CHRONIC LUNG DISEASE

Jennifer Scaife and Stephen Murphy

Palliative Care in End-stage Chronic Lung Disease. Good Clinical Care.



Abstract

The prognosis for severe COPD is comparable to inoperable lung cancer but few patients dying from COPD receive adequate palliative and end of life care. Early identification of patients with poor prognostic features and a multi-disciplinary approach to treatment are required to optimise symptom control, quality of life and end of life care.

Introduction

Chronic respiratory diseases are amongst the commonest causes of morbidity and mortality in the UK. There are estimated to be about 3,000,000 people in the UK with COPD and more than 30,000 COPD related deaths annually. More people in the UK die from COPD than many common cancers. [1]

Death from COPD is usually preceded by a progressive deterioration in lung function combined with a steady decline in general health status and quality of life over a period of years. Typically patients with severe COPD will experience several admissions to hospital due to acute exacerbations before eventually dying from the disease.

Patients with COPD experience a wide range of symptoms, especially towards the end of life and it is important to recognise these in order to implement appropriate treatment and facilitate good palliation.

Case History

A 69 year old man with severe COPD is admitted with an acute exacerbation. He is more breathless than usual and has been coughing up increasing quantities of sputum. On examination he is conscious but has a coarse tremor. He is cachectic with evidence of a hyper-expanded chest. His respiratory rate is 36 per minute and he is using his accessory muscles of respiration. His chest is hyper-resonant and on auscultation there is very poor air entry and widespread wheeze.

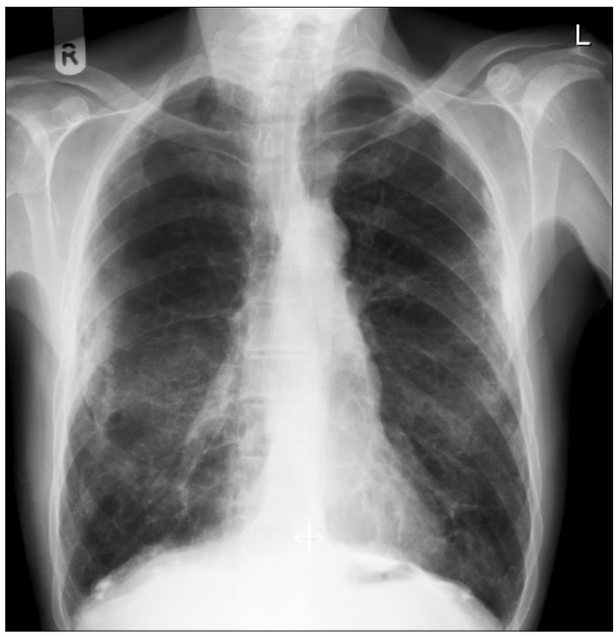


Figure 1
Case Report: Chest X-ray

His usual medication includes: fluticasone/salmeterol, tiotropium and salbutamol inhalers, nebulised salbutamol and modified release theophylline. He is on long-term oxygen (2L/min for 15 hours a day.) He is housebound and has increasing difficulty with the activities of daily living, becoming increasingly dependent on his family. He has had 2 previous admissions for COPD in the past year, the most recent of which required Non-Invasive ventilation (NIV).

A letter revealed that 9 months previously when reviewed in the chest clinic he was breathless on walking between rooms, had frequent panic attacks and complained of excessive fatigue. He had received multiple courses of steroids. Assessment included: FEV1 0.6 L (25% of predicted), body mass index 17 kg/m2; MRC dyspnoea score 5 (scale 1-5); and a 6 minute walking test distance of 50 metres. Oxygen saturations were 88% on air and arterial blood gas (ABGs) measurement pH 7.39, pO2 7.0 KPa, pCO2 5.5 KPa, HCO3 25. On the hospital anxiety and depression (HAD) score he scored high for anxiety and borderline for depression.

PALLIATIVE CARE IN END-STAGE CHRONIC LUNG DISEASE

Jennifer Scaife and Stephen Murphy

Discussion

Pathophysiology of COPD

Chronic inflammation triggered by cigarette smoking causes destruction of the lung parenchyma "emphysema" and airway narrowing due to chronic bronchitis (Figure 2.). Hyperinflation of the lungs and airflow obstruction result in inefficient respiration. During exercise "dynamic compression" of the airways worsens airflow obstruction causing air trapping "dynamic hyperinflation" (Figure 3). [2]

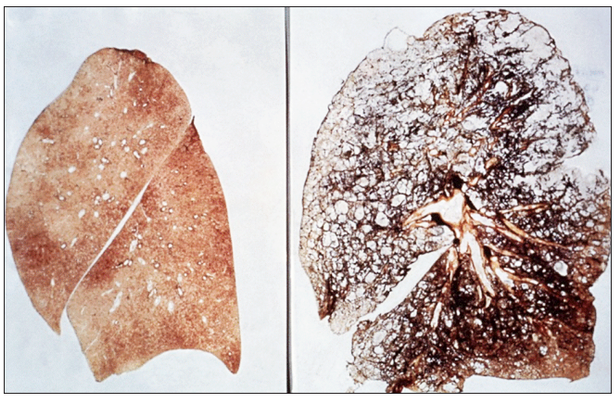


Figure 2
Pathology of COPD.
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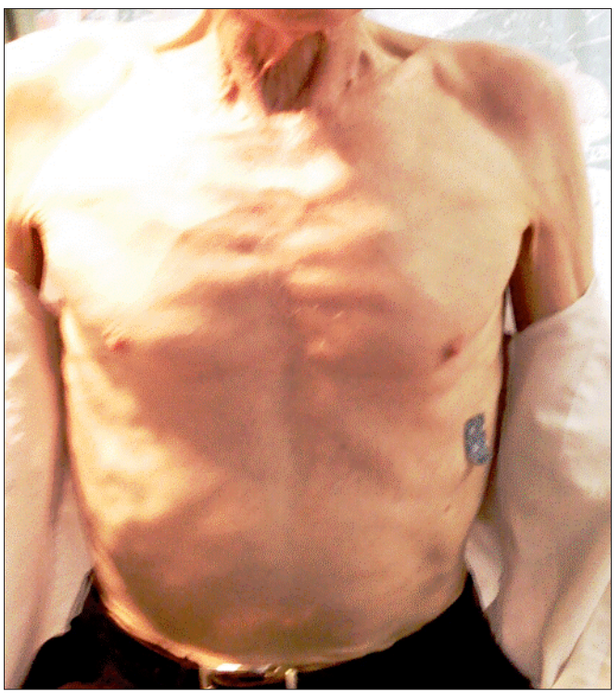

Figure 3
Hyperinflated chest

The patient is unable to increase tidal volume adequately and a combination of afferent signals from stretch-receptors throughout the lungs and chest wall, coupled with increased respiratory drive causes patients to experience tightness of the chest and unsatisfied inspiration. This may lead to anxiety and a sense of panic that increases respiratory drive further aggravating breathlessness.

As the disease progresses, repeated exacerbations accelerate the decline in lung function but the impact of the disease is not limited to respiratory symptoms. Severe COPD is a systemic illness and affects the health and well-being of patients in a number of ways (Table 1).

Symptom	Mechanism
Breathlessness	Hyperinflation of the chest, increased work of breathing, hypoxic drive, anxiety, impaired mechanics
Pain; back & chest	Osteoporosis and hyperinflation of the chest.
Poor mobility	Dyspnoea, disuse atrophy of skeletal muscles & steroid induced myopathy, poor nutrition & deconditioning due to inactivity.
Poor sleep quality	Orthopnoea, cough, anxiety, pain
Cachexia	Too breathless to eat/prepare food, catabolic effect of exacerbations & systemic steroids, increased metabolic rate because of work of breathing
Depression & anxiety	Breathlessness and physical incapacity, fear of death and social isolation

Table 1
Symptoms of Severe COPD

Assessing COPD Severity

The monitoring and treatment of patients with COPD has been standardised through the use of internationally accepted guidelines: Global Initiative on Obstructive Lung Disease[3]. Integral to this is assessment of severity or stage of the disease which is determined by comparing the measured FEV1 with the predicted FEV1, see table 2.

Global Initiative on Obstructive Lung Disease GOLD Classification FEV1/FVC < 0.7 at all stages		
Stage		FEV1 % Predicted
1	Mild	> 80%
2	Moderate	>50% <80%
3	Severe	>30% <50%
4	Very Severe	<30% or <50% and chronic respiratory failure

Table 2
Classification of COPD Severity

Most patients dying from COPD have very severe (GOLD stage 4) disease. However measurement of lung function alone provides a very limited assessment of the impact of the disease. Several clinical variables, in addition to lung function, are of prognostic importance in COPD. These variables have been combined in a composite score which may help with predicting long-term prognosis and facilitate management decisions including discussions about end of life care.

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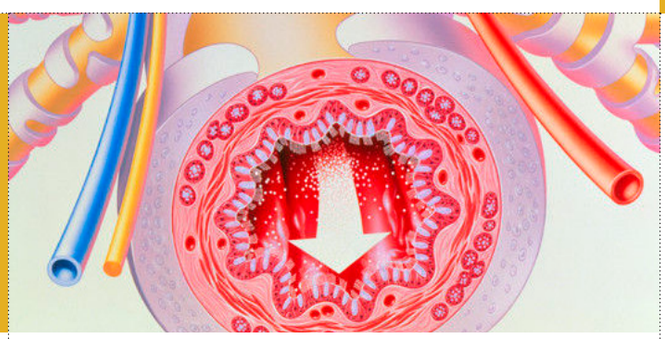

The BODE score (BMI, Obstruction, Dyspnoea score, Exercise capacity) is a better predictor of long-term prognosis than FEV1 and is increasingly used in routine practice for assessing disease progression, see table 3 [4].

SCORE	0	1	2	3
Body Mass (Kg/m2)	>21	<21		
Obstruction (FEV1 % of predicted)	> 65 %	50-64 %	36-49 %	< 35 %
Dyspnoea (MRC score)	1-2	3	4	5
Exercise :6 minute walk distance (m)	>350	250-349	150-249	<149

Table 3
BODE (Body mass, Obstruction, Dyspnoea, Exercise) Index.
Maximum score is 10.

Management of End-stage COPD

The management of end-stage COPD is tailored according to the needs of the patient and requires a multidisciplinary approach.

Treatment of Breathlessness

Breathlessness is the dominant symptom of severe COPD. Treatment includes the following:

1. Optimising bronchodilator therapy

Bronchodilators are the mainstay of treatment for all stages of COPD. They improve breathlessness in COPD by reducing hyperinflation. Patients with severe COPD benefit from a combination of long-acting bronchodilators. All patients with severe COPD should receive a long acting beta agonist (LABA) plus a long acting antimuscarinic (LAMA). LABAs include salmeterol or formoterol and may be prescribed alone or in combination with an inhaled corticosteroid. Tiotropium is currently the only available LAMA.

Nebulisers In patients with stable COPD nebulised bronchodilators have no clear therapeutic advantage. However near the end of life and during acute exacerbations, patients with advanced disease may be too weak to use an MDI effectively, in which case nebulised bronchodilators may be preferable.

Theophylline is a weak bronchodilator but has been shown to produce a significant improvement in dyspnoea in patients with severe COPD. Low dose theophylline may be as effective as high doses but with fewer adverse effects. If used, it should be prescribed once or twice daily to achieve trough levels of 10 to 12 µg/mL.

Roflumilast a Phosphodiesterase 4 Inhibitor (PD4 inhibitor) is a new class of anti-inflammatory drug specifically developed for COPD. It is effective in reducing frequency of exacerbations in patients with severe COPD with symptoms of chronic bronchitis and frequent exacerbations.

2. Mucolytic Therapy

Mucolytic drugs are used increasingly in COPD for palliation of cough and breathless in patients with excessive mucous production. They may be used acutely during an exacerbation and also long-term in patients with chronic bronchitis or concurrent bronchiectasis.

3. Pulmonary Rehabilitation

Patients with severe COPD stop exercising because of breathlessness or muscle fatigue. Reduced physical activity leads to further deconditioning which is compounded by poor nutrition, steroid use and systemic inflammation. Pulmonary rehabilitation is a structured programme that includes a programme of physical training, education about the disease, nutritional, psychological, social, and behavioural intervention. [5]

4. Oxygen Therapy

There are three circumstances in which oxygen is given in stable severe COPD:

· Long-term oxygen therapy (LTOT) Oxygen for 15 or more hours per day has been shown to prolong life in patients with severe COPD and hypoxia. LTOT should be prescribed if pO2 < 7.3 KPa or if pO2 < 8.0 KPa and there is evidence of cor pulmonale or secondary polycythaemia.

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· Ambulatory oxygen may be offered to patients on LTOT who are often outside the home. Lightweight ambulatory oxygen should also be considered in patients with exercise induced desaturation and PaO2 < 7.3 KPa after formal assessment to demonstrate improvement in exercise capacity and/or breathlessness with supplemental oxygen.

· Short Burst Oxygen Therapy (SBOT) is for palliation of breathless at rest or before and after exercise. There is little evidence that oxygen improves dyspnoea at rest in COPD but it does reduce dyspnoea and accelerates recovery from exercise.

5. Non-invasive ventilation (NIV)

NIV is life saving in acute hypercapnic respiratory failure due to COPD. The criteria for initiating NIV are: a confirmed diagnosis of COPD and arterial blood gases as follows: pH < 7.35 and pCO2 > 6.0 KPa (on controlled O2).

NIV may not be appropriate for patients in the terminal stages of the disease. Predictors of mortality for patients treated with NIV include: Poor performance status (bed/chair bound due to dyspnoea), severe acidosis (pH <7.26), co-morbidity, anaemia, diastolic hypotension.

Response to treatment is assessed after one hour, again at 4 hours and thereafter according to clinical condition. A lack of improvement in respiratory rate or pH < 7.26 after 4 hours is predictive of treatment failure.

6. Opiates

Opiates may be used effectively and safely to alleviate dyspnoea in patients with end-stage COPD. Dyspnoea is reduced by 15-20% and there may be an increase in exercise tolerance. Several studies found no increased respiratory depression or mortality. Morphine should be started at a dose of 5mg 4 hourly and up titrated slowly.

7. Benzodiazepines

Limited evidence base but anecdotally helpful, especially when dyspnoea associated with anxiety. Diazepam is prescribed at a dose of 2mg TDS, alternatively the shorter acting Lorazepam 0.5 1mg as required up to three times daily.

8. Fan/open windows

There is evidence that stimulation of nasal or mucosal receptors or facial receptors in region of trigeminal nerve can affect the afferent pathway to the sensory cortex and alter the perception of dyspnoea. Cheap, and easy to use, with less social stigma. It doesn't draw attention to the user in the way oxygen does.

9. Energy conserving measures

Such as walking aids reduce demand for ventilation. Occupational therapy assessment is often helpful.

10. Breathing techniques

For patients that hyperventilate, breathing control exercises improve the mechanical efficiency of breathing and lower the demand for ventilation. Aims to reduce ventilation rate and prolong expiration. These techniques are difficult to learn at end of life so they need to be started early.

11. Relaxation techniques

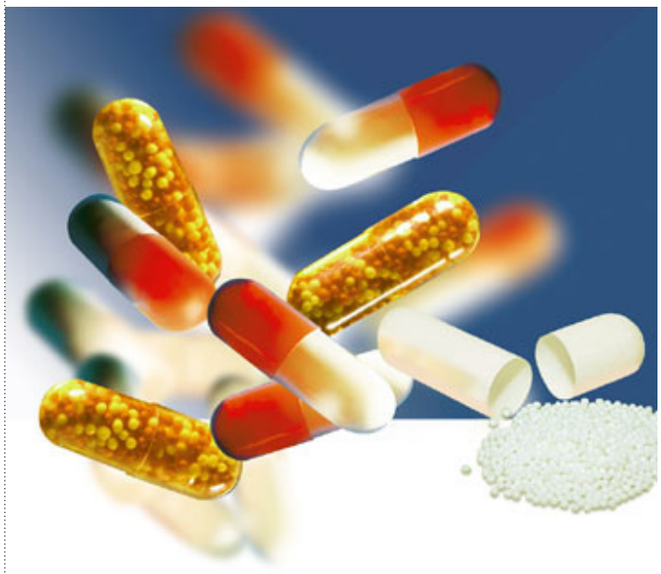
Anxiety and breathlessness is a vicious cycle. Patients benefit from education about the panic cycle and how to break it.

Anxiety Depression

Anxiety and depression are common in COPD and associated with increased morbidity including more frequent hospital admissions and poor quality of life. Anti-depressants (TCAs/SSRIs) have been shown to give benefit in COPD. Benzodiazepines are effective in alleviating anxiety and panic in COPD. Cognitive behavioural therapy (CBT) may help by addressing misconceptions patients have about their condition such as the need for oxygen when breathless (but not hypoxic) and maladaptive behaviour like overuse of bronchodilators. The specialist palliative care team should be able to advise on this.

Cachexia

Cachexia (BMI < 21kg/m2) is common and a poor prognostic factor in severe COPD (Figure 4.). Patients with severe COPD have an increased metabolic rate due to inefficient respiration and chronic inflammation. Nutritional intake is poor because they are "too breathless to eat" and have difficulty preparing meals. This is compounded by exacerbations and frequent courses of prednisolone that lead to muscle wasting. Nutritional support, including nasogastric feeding should be considered in severely cachectic patients.



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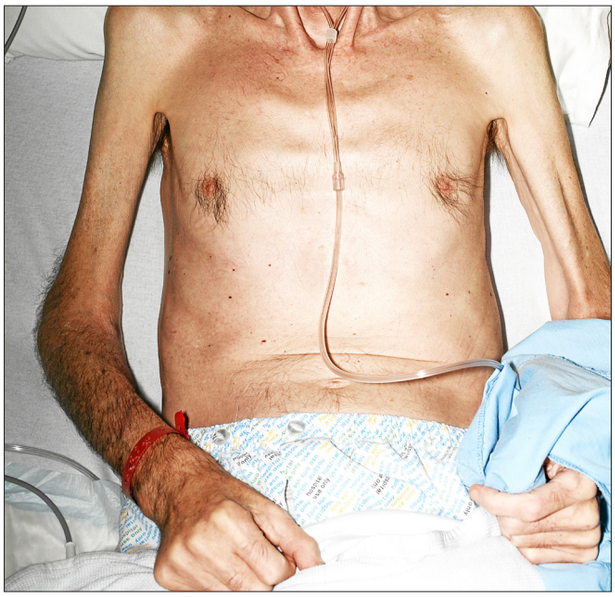

Figure 4
Cachexia of COPD

Palliative and end-of life care

Palliative and end-of life care of people with end-stage respiratory disease has historically been done quite badly. Patients are often unaware that they have a life-threatening condition and may see their symptoms as a normal part of aging. The prognosis for end-stage COPD is comparable to that of inoperable non-small cell lung cancer (NSCLC) but COPD patients receive substantially less palliative and end of life care. [6]

Studies show that clinicians often shy away from difficult conversations about end of life preferences.

Due to the usual disease course of slow decline punctuated by dramatic exacerbations, identification of the terminal phase of the disease is difficult (Figure 5) [7]. Unlike in "cancer" there is often no defined point in which treatment switches from 'active' to purely palliative.

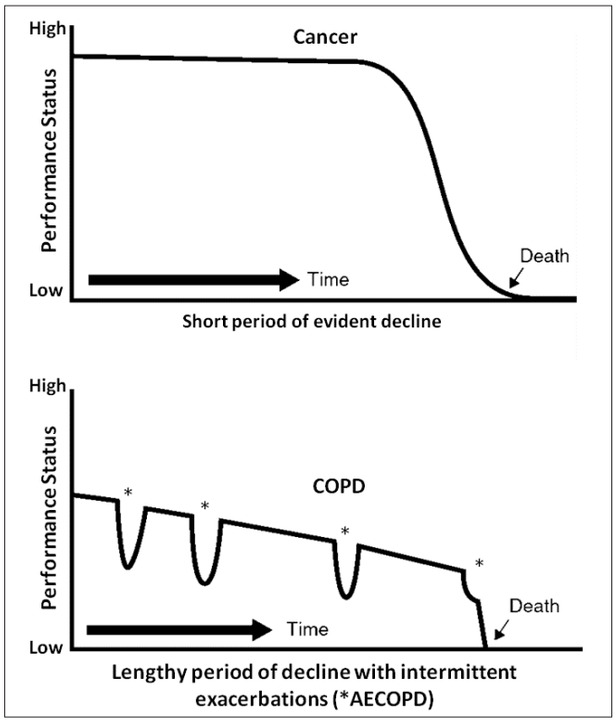

Figure 5
Disease Trajectories in Cancer and COPD
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For many patients with COPD and their families the end of life is all too often unanticipated and a chaotic experience[8]. As such the palliative care needs of patients with COPD should be assessed throughout the "patient journey" and end of life care is best considered and planned from an early stage when the patient is well enough to make informed decisions about their treatment. The timing of this conversation could be linked to suitable milestones such as an admission to hospital with AECOPD, starting long term oxygen therapy, or a BODE score of 10.

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Palliative Care in End-stage Chronic Lung Disease. Good Clinical Care.

The patient should be informed about possible scenarios including the need for mechanical ventilation. Advanced care directives take account of patients' needs and wishes and are increasingly used to plan end of life care but need to be discussed well in advance of the terminal admission.

Community based services have a particularly important role to play in the management of end-stage COPD. The patient's community matron or district nurse should be included in discussions about end of life care at the earliest opportunity. For patients with end-stage disease and intractable symptoms specialist palliative care advice should be sought.

Questions

Question 1: What interventions may have been offered when he was reviewed in clinic and what issues may have been discussed?

Investigations on admission to hospital included: ABGs on 28% oxygen via a Venturi mask as follows: pH 7.19, pCO2 11.5, pO2 8.0 KPa, HCO3 28.0 mmol/l; Chest x-ray (Figure 1).

Question 2: What do the ABGs and CXR show?

He is started on regular nebulised salbutamol and ipratroprium and prednisolone 30mg daily. His sputum is purulent so IV co-amoxyclav is added. You speak to the consultant respiratory physician on call and ask for advice.

Question 3: What points may have been discussed and what decisions made?

The patient is started on NIV and you reassess him after 1 hour. He is tolerating NIV and his respiratory rate has decreased to 32/min, but he remains acidotic: pH 7.20, pCO2 10.6 KPa pO2 9.0 KPa. NIV is continued and ABGs repeated 4 hours after admission: pH 7.21, pCO2 10.0, pO2 8.9.

NIV is continued overnight but 12 hours after starting the patient is increasingly distressed and wants the mask removed. He refuses further ABGs and tells you that he has had 'enough'. NIV is discontinued and replaced with nasal oxygen to maintain saturations at around 90%. He is reviewed 1 hour later and asked if he would reconsider NIV. However he makes it clear that he does not wish to do so.

Question 4: What factors do you consider in deciding whether to continue with NIV?

The decision to stop NIV is discussed with his family who say that his quality of life is poor and they are supportive of the decision to stop NIV.

He remains severely dyspnoeic and also complains of pain in his back and chest, particularly when being moved.

Question 5: What treatment options would you consider?

He is started on a small dose of Oramorph (5mg) every 4 hours and finds this beneficial.

He is given 5 dose of Oramorph (5mg) for dysnoea and pain over 24 hours. He continues to deteriorate and is now unable to take any medicines orally. He is spending most of his time asleep. The multidisciplinary team agree that he is entering the last days of life.

Question 6: What care pathway would you considered?

His dyspnoea and pain remain well controlled on the Diamorphine and he is nursed by an open window. He dies a peaceful pain-free death with his family present.

PALLIATIVE CARE IN END-STAGE CHRONIC LUNG DISEASE

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Answers

When assessed in clinic he had evidence of very severe COPD complicated by respiratory failure, cachexia, anxiety and depression. Interventions that would have been considered include:

- Inhaled corticosteroids/long-acting beta agonist (LABA) combination inhaler and a long acting antimuscarinic (LAMA).
- Mucolytic therapy to help sputum clearance
- Azithromycin (250 mg Mon, Wed, Frid) reduces exacerbation frequency in selected patients
- PD4 Inhibitor (Roflumilast) to reduce exacerbation frequency in patients with chronic bronchitis
- Long-term oxygen therapy
- Pulmonary rehabilitation
- Consider walking aid
- Relaxation/breathing techniques
- Treatment of anxiety/depression
- Nutritional assessment/ supplemental feeding
- Annual influenza vaccination, and pneumococcal vaccination
- Referral to a community matron for monitoring and advice on symptom control and treatment of exacerbations including patient initiated steroids and antibiotics.

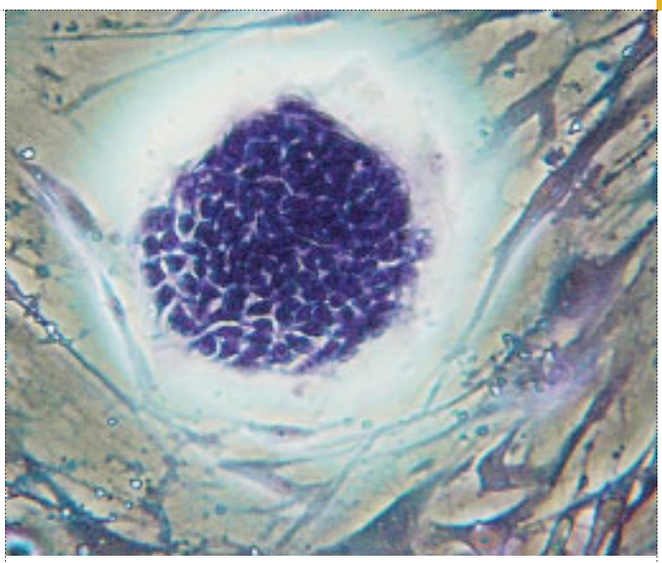
Given the poor prognostic factors including a maximum BODE score a discussion about end of life issues should have been initiated and the patient and family provided with information on possible scenarios and advance care planning.

- He has acute hypercapnic respiratory failure (pH < 7.35 and pCO2 > 6.0). The chest x-ray shows hyperinflated lungs and pleural plaques.

- Appropriateness of NIV. He satisfies criteria for NIV but has poor prognostic features including very poor performance status.

The ceiling of care and resuscitation status should be discussed when starting NIV because the mortality rate for patients with AHRF is about 25-30%. His family should be informed of the prognosis.

- The respiratory consultant is of the view that he has capacity and in accordance with GMC guidelines his wishes are paramount. He has a number of poor prognostic factors. Furthermore he has failed to improve with NIV after 4 hours indicating that survival is unlikely.



- In the terminal stages of COPD palliation of dyspnoea may benefit from opiates or benzodiazepines or a combination of both. The benefit of oxygen may be outweighed by the inconvenience of wearing a mask. The cooling effect of high flow oxygen may be helpful but also consider other measures such as an electric fan or an open window.

- Initiation of the Liverpool Care Pathway (LCP) for the dying. Convert Oramorph ® to equivalent dose of diamorphine via syringe driver. 25mg of Oramorph is equivalent to 6.25mg diamorphine. Prescribe other anticipatory medications as per the LCP document.

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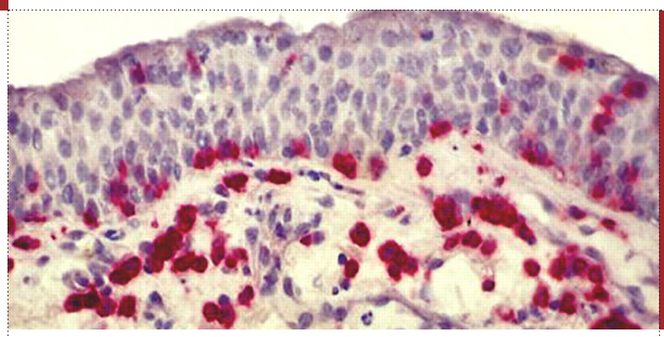
CHRONIC OBSTRUCTIVE PULMONARY DISEASE: AIMING FOR A GOOD OUTCOME

G Haji & G Wilson



Chronic Obstructive Pulmonary Disease: Aiming for a good outcome.
Patient Management.

Introduction

Respiratory medicine offers the trainee doctor an interesting and varied career. The trainee can build relationships with patients through the management of their chronic diseases. There is wide scope for both diagnostic and therapeutic interventions. It allows you to see and have the capability to treat critically-ill patients due to the nature of the conditions respiratory physicians treat and the close interaction with high dependency and critical care.

The acute nature of the speciality will place you at the forefront of delivering care to a group of patients who are clinically unwell. Acute exacerbations of chronic obstructive pulmonary disease (COPD) are common, particularly in the winter months. NICE has produced guidelines on COPD management. Foundation programme training should expose the trainee to patients with acute exacerbations of COPD. Through the application of good medical practice the aim is to ensure a good outcome for the individual patient, including ensuring adequate treatment of the end of a patient's life. A basic understanding of the chronic management of COPD is required.

Abstract

The aim of this case history is to highlight some of the current issues around assessing and treating a patient with an acute exacerbation of COPD. It details the presentation to hospital of a 78 year-old woman with severe COPD during her final acute exacerbation. She had once again presented to the accident and emergency department significantly short of breath despite the use of her home oxygen. In spite of thorough assessment, investigation and appropriate management, she did not survive.

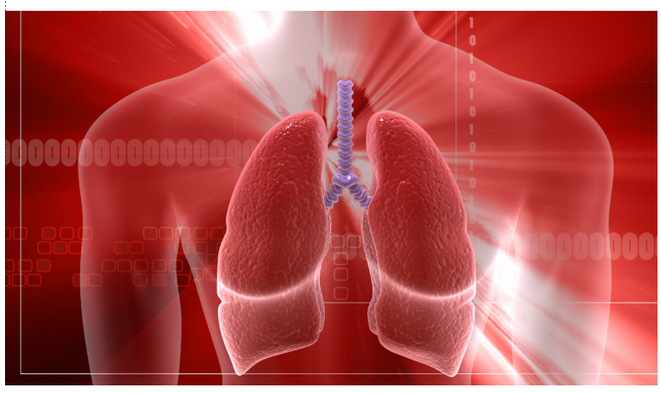
Treatment was rapidly administered and NIV was used in an attempt to correct an acute respiratory acidosis which had developed on a background of chronic respiratory failure secondary to COPD, with ensuing cor pulmonale. Appropriate decisions were made early about the ceiling of care and despite maximal therapy the patient deteriorated. Once a diagnosis of dying was made the patient was managed accordingly to ensure that her death was not distressing. As a foundation year doctor when faced with complex cases such as this, with clinically very unwell patients who may not survive it is very important to seek help early.

Case History

A 78 year-old woman with a 65 pack-year history of smoking presented, to hospital, acutely short of breath. She was housebound, lived alone and around her house she was independent in carrying out her daily activities. She had no official care package. Her exercise tolerance on a good day was less than 10 yards. She received long-term oxygen therapy (LTOT) and managed to leave this by her armchair and take the few steps into the kitchen for the occasional cigarette. Aside from recurring acute exacerbations of COPD requiring hospitalisation and non invasive ventilation (NIV) over the past few years there was relatively little contact with healthcare professionals and no other significant diagnosis. Drug history included a combination long-acting beta agonist with inhaled steroid and a long-acting inhaled anticholinergic.

In the emergency department a good history was given despite her hypoxia. She had worsening shortness of breath, a diminished exercise tolerance and a productive cough over the preceding week. There was no chest pain or haemoptysis. Of note since her most recent admission her ankles had become progressively more swollen and she now slept with four pillows instead of three.

Initial assessment revealed that she had a patent airway and was able to talk; oxygen saturations were poor, around 80% despite varying concentrations of inspired oxygen. Auscultation of the chest revealed wheeze with extremely limited airflow and clinical signs of hyperinflation. Circulation was adequate with a sinus tachycardia and generation of a good blood pressure to enable adequate tissue perfusion albeit with significantly hypoxic blood. There was peripheral, pitting oedema, an elevated JVP and loud second heart sound. GCS was initially 15/15. She had received NIV on the medical high dependency unit (MHDU) twice in the previous four months.



CHRONIC OBSTRUCTIVE PULMONARY DISEASE: AIMING FOR A GOOD OUTCOME

G Haji & G Wilson

Initial investigations showed a respiratory acidosis with a pH of 7.21, acute with chronic hyper-capnic respiratory failure underlying this. A chest X ray (CXR) revealed hyper-expanded lungs, right lower lobe consolidation and generalised fluid overload. The patient had made it very clear both in the past and during this admission that she did not want to be intubated and this was agreed with her medical staff. A Do Not Attempt Resuscitation order was completed. This was felt to be appropriate based on functional status, a recent FEV1 of 0.6L and the patient's wishes.

Despite maximal medical therapy and the use of NIV the patient deteriorated over the next 48 hours and so the NIV was removed and appropriate sedation was administered. This active management of treatment withdrawal and sedation prior to death prevented her from dying in an uncomfortable agitated state with a tight fitting NIV mask on.

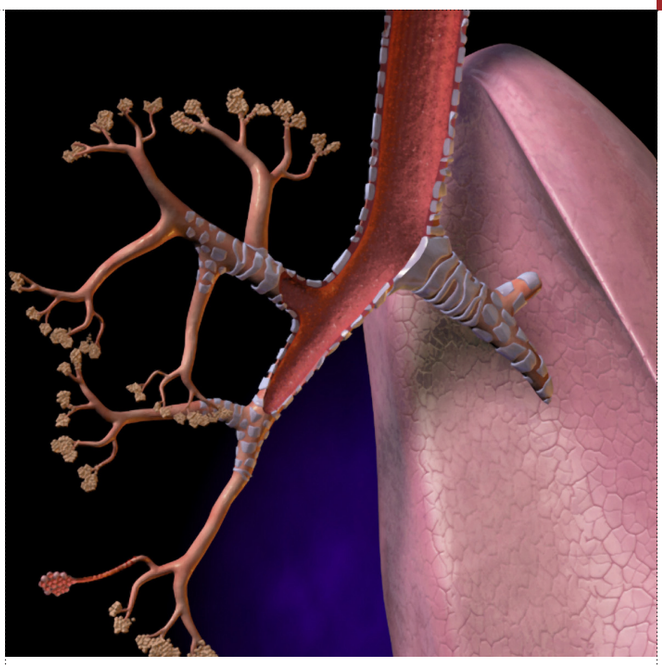
Discussion

COPD is still a major cause of illness and death worldwide. Ongoing patient care and hospitalisation uses significant healthcare resources.[1] For a long time, treatment has been preventative with smoking cessation, LTOT has been used for hypoxemic patients in selected groups. Home non-invasive ventilation is being used in patients with chronic hypercapnic respiratory failure. In terms of pharmacological treatment of disease long-term; tiotropium and combination long acting beta agonist with steroid (salmeterol and fluticasone), have been shown to be beneficial. Two landmark trials, UPLIFT and TORCH, have demonstrated slower decline in lung function, improved health status/quality of life and fewer exacerbations in patients using these inhaled therapies.[2,3]

With regard to acute care, as demonstrated in this case, all junior doctors should be aware of the current, most appropriate treatment. Medical therapy with high-dose, short acting beta 2 agonists and anticholinergics should be instigated early; as should delivery of corticosteroid and antibiotics. Many patients will show improvement with simple measures and importantly appropriate oxygen therapy titrated according to saturations and arterial blood gas analysis. Be aware of patients with severe COPD who may go onto develop pulmonary hypertension and subsequent cardiac failure, appropriate use of diuretics may be very helpful in such situations.

In circumstances where NIV is to be used the decision should be made by a doctor with appropriate training and competence. Therefore if as a foundation doctor you are assessing such patients then escalate the matter early. Adequate facilities must also be available and NIV should be applied in appropriate environments. The British Thoracic Society (BTS) has set this out in its guidelines and familiarity with them is useful. These guidelines suggest there to be indications, as well as absolute and relative contraindications to the use of NIV. For example it is most useful between a pH of 7.25-7.35 and it should not be used with impaired conscious level.[4]

Documentation as to the ceiling of care is vital, as some patients will benefit from intubation early. If NIV is the ceiling of care; as determined by a doctor of appropriate clinical capability then NIV may be used outside of the guidelines.



It is always very important to recognise when interventions are futile and acknowledge a deteriorating condition in the context of severe underlying disease. A recognition that a patient is dying can be difficult but the inability to do so can lead to ongoing invasive procedures and treatments. This can ultimately lead to an undignified and uncomfortable death which is distressing for all involved. However the skilled management of a patient's last hours is an important part of the treatment delivered by the medical and nursing teams involved in their care.[5]

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INTERSTITIAL LUNG DISEASES

I Aslam, SP Hart, JA Kastelik

Interstitial Lung Diseases.
Patient Management.

Abstract

Interstitial lung diseases (ILD) describes a large group of disorders of lung interstitium. Whilst the majority of patients with ILD present with breathlessness and cough, these disorders may have multi-system involvement. Patients with ILD can be seen on acute medical take or on medical or surgical wards, and therefore understanding of ILD is of importance to junior doctors. The terminology, investigations and treatment of ILD can be perceived as somewhat complicated.

This article will provide a simple approach on how to assess, investigate and manage patients with ILD. More importantly, the requirements of careful diagnosis will be highlighted as this may affect not only the management options but also has important role in establishing the long term prognosis. The diagnosis of ILD frequently requires a multi-disciplinary approach, which involves a close communication between respiratory physicians, radiologists, histopathologists and thoracic surgeons. Some of the ILD can be confidently diagnosed based on clinical history, examination and radiological appearances of high resolution computed tomography of the thorax. However, in many cases further investigations including surgical lung biopsy may be required. The management usually depends on the type or severity of ILD.

Case report

A 72 year old man with no significant past medical history presented with a 2 months history of dyspnoea on exertion and dry cough. He denied any symptoms of muscle or joint aches and did not notice any skin rashes. He was not taking any regular or over the counter medications. He never smoked and did not have any occupational exposure to asbestos. He was a retired office worker, lived with his wife and did not have any pets. Clinical examination revealed that he was tachypnoeic at rest with respiratory rate of 20 breaths per minute and oxygen saturations of 88% on room air.

There was evidence of finger clubbing. Chest auscultation revealed bibasal fine inspiratory crackles. Spirometry revealed a restrictive lung defect. The chest radiograph showed small volume lungs and evidence of bibasal reticulo-nodular interstitial shadowing. Further investigations were requested including a full blood count, a biochemical profile including urea and electrolytes and liver function tests, ESR and CRP and autoimmune profile. High resolution computed tomography of the thorax was requested and revealed the evidence of bilateral peripheral sub-pleural fibrosis with areas of honeycombing and traction bronchiectasis.

All the blood tests were normal and full pulmonary function tests revealed reduced Forced Vital Capacity (FVC), reduced total lung capacity (TLC) and reduced diffusion capacity of carbon monoxide (DLCO). A diagnosis of idiopathic pulmonary fibrosis was made based on clinical and radiological evidence. The management was based on best supportive care strategy.

Introduction

Interstitial Lung Diseases (ILD) also known as Diffuse Parenchymal Lung Diseases (DPLDs) consist of disorders of known (collagen vascular disease, environmental or drug related) and unknown causes (Figures 1a and b, Table 1). The latter include idiopathic interstitial pneumonias (IIPs), granulomatous lung disorders (e.g. sarcoidosis), and other very rare conditions such as Lymphangioleiomyomatosis (LAM), pulmonary Langerhans'cell histiocytosis/ histiocytosis X (HX), and eosinophilic pneumonia. This review article aims to give an overview of the diagnosis and management of some of the more common ILD. The 2008 British Thoracic Society (BTS) guidelines and the 2001 American Thoracic Society (ATS) and the European respiratory society (ERS) statement give currently accepted advice on classification and management of ILD[1,2]. The most important distinction among the IIPs due to different prognostic outcomes is between idiopathic pulmonary fibrosis (IPF) and the other interstitial pneumonias which include non-specific interstitial pneumonia (NSIP), desquamative interstitial pneumonia (DIP), respiratory bronchiolitis-associated interstitial lung disease (RB-ILD), acute interstitial pneumonia (AIP), cryptogenic organizing pneumonia (COP), and lymphocytic interstitial pneumonia (LIP). Over the years the diagnostic gold standards have become increasingly multi-disciplinary and dependant equally upon the skills of the pathologists, radiologists and clinicians.

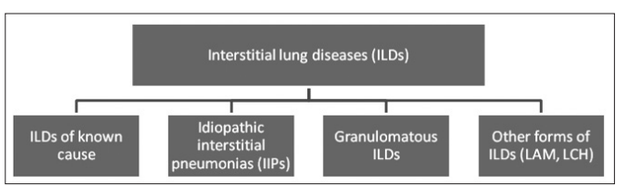

Figure 1a: Classification of interstitial lung diseases.
Abbreviations: LAM - Lymphangioleiomyomatosis, LCH - Langerhans' cell histiocytosis.

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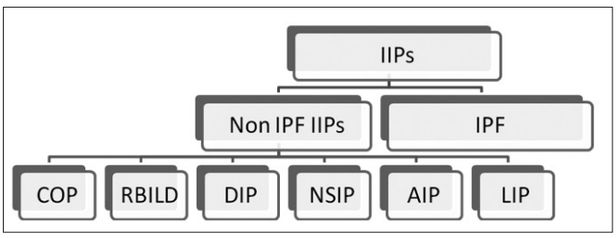
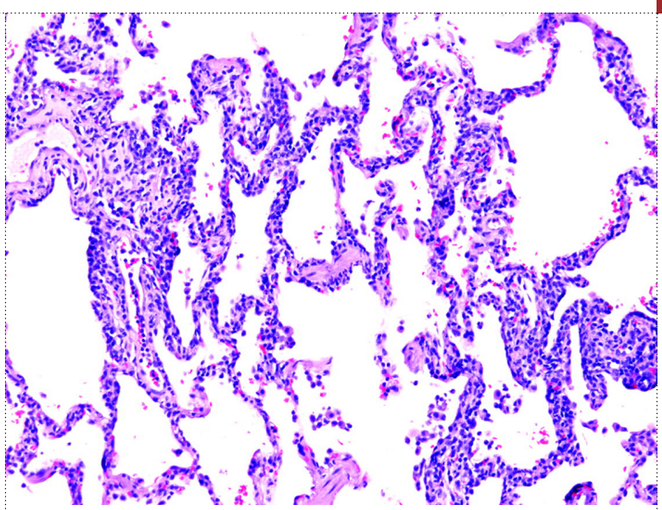


Figure 1b: Classification of Idiopathic Interstitial Pneumonias.
Abbreviations: IIPs - Idiopathic Interstitial Pneumonias, IPF - Idiopathic Pulmonary Fibrosis, COP - Cryptogenic Organising Pneumonia, RBILD - Respiratory Bronchiolitis-associated Interstitial Lung Disease, DIP - Desquamative Interstitial Pneumonia, NSIP - Non-specific Interstitial Pneumonia, AIP - Acute Interstitial Pneumonia, LIP - Lymphocytic Interstitial Pneumonia.

Type of ILD	Description
ILD of known causes	• Medications • Asbestos, Beryllium, Silica • Hypersensitivity pneumonitis • Radiation • Fumes, Gases • Aspiration pneumonia • Residual of acute respiratory distress syndrome
ILD associated with other disorders	1. Connective tissue diseases • Systemic Lupus Erythematosus • Rheumatoid Arthritis • Systemic Sclerosis • Polymyositis/Dermatomyositis • Ankylosing Spondylitis • Pulmonary haemorrhage syndromes • Goodpasture's syndrome • Idiopathic pulmonary haemosiderosis • Isolated pulmonary capillaritis 2. Vasculitides • Wegener's granulomatosis • Churg-Strauss syndrome 3. Inherited diseases • Tuberous Sclerosis • Gaucher's disease • Niemann-Pick disease • Neurofibromatosis • Hermansky-Pudlak syndrome 4. Gastrointestinal or Liver diseases • Crohn's disease • Ulcerative colitis • Primary Biliary Cirrhosis • Chronic Active Hepatitis

Table 1: Description of interstitial lung diseases (ILD) related to the underlying cause.



Diagnosis of ILD

Clinical History and Examination

The clinical history should focus on the three main aspects, namely chronology of the symptoms, aetiological factors and assessment of the severity of the disease. The differential diagnosis of ILD can be based on whether the symptoms have been acute e.g. acute interstitial pneumonia, episodic that may be more characteristic of eosinophilic pneumonia, hypersensitivity pneumonitis or cryptogenic organising pneumonia or chronic as is the case in IPF. Smoking habits or occupational and environmental exposure should always be recorded[3].

For example, RB-ILD and DIP occurs almost exclusively on the background of tobacco smoking. The history of occupational or environmental exposure provides important information in conditions such as asbestosis or in hypersensitivity pneumonitis including farmer's or bird fancier lung. Travel history may suggest eosinophilic lung disease secondary to parasite infection. As many ILD may be associated with rheumatological disorders the symptoms associated with those conditions should be inquired about including Raynaud's phenomenon, rashes, arthralgia or ocular symptoms. Other points in history may be of assistance such as recurrent pneumothoraces that may suggest cystic lung disease associated with LAM or Langerhans'cell histiocytosis, previous chemotherapy or radiotherapy may suggest pulmonary fibrosis or history of asthma, rhinitis and vasculitis may point towards Churg-Strauss syndrome.

Finally, as many medications such as Amiodarone or Nitrofurantoin may cause interstitial lung diseases, a careful drug history should be taken including over the counter or herbal medications. The assessment of disease severity should be quantified in terms of exercise tolerance as well as a baseline performance status and disability, which subsequently can be used as markers of disease progression. The most common symptoms associated with ILD are dyspnoea, initially on exertion or with diseases progression also at rest and dry cough.

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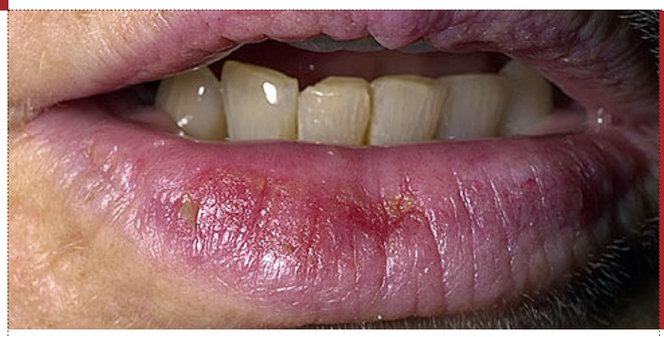

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Physical examination should include assessment for multisystem disorders including skin lesions, arthlargia and ocular inflammation (uveitis or conjunctivitis) as they may suggest sarcoidosis or connective tissues diseases. Fine end inspiratory crackles described as dry 'Velcro' like are commonly present in IPF and other conditions such as ILD associated with connective tissue diseases or asbestosis[4]. Mid-inspiratory high-pitch squeaks are associated with bronchiolitis but can also be present in NSIP or sub-acute hypersensitivity pneumonitis. Finger clubbing, which is present in up to 65% of patients with IPF can also be a feature of chronic hypersensitivity pneumonitis or rheumatoid arthritis associated ILD[5]. The signs of pulmonary hypertension and right ventricular failure may assist in establishing the severity of ILD.

Investigations

In simple terms, investigations of patients with ILD may be divided into non-radiological, radiological and invasive tests such as fibre-optic bronchoscopy or surgical lung biopsy.

Non-radiological Investigations

The patients with suspected ILD should have routine blood tests such as full blood count, urea and electrolytes and liver function tests as well as the urine analysis for proteinuria and haematuria. Thus presence of eosinophilia may suggest chronic eosinophilic pneumonia, Churg-Strauss syndrome or drug reaction, leukopenia or thrombocytopenia may suggest connective tissue disease or sarcoidosis and renal abnormalities or presence of haematuria could point towards Wegener's granulomatosis. The more specific tests should also be considered such as an autoantibody screen including rheumatoid factor, antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCA) levels, creatine kinase, serum calcium, serum angiotensin converting enzyme (ACE) levels, specific precipitins and inflammatory markers C-reactive protein or plasma viscosity. Electrocardiogram and echocardiogram may be required to assess the left and right ventricular function.

Lung function tests have an important role in assessing disease severity and progress. Spirometry testing usually reveals a restrictive pattern and is helpful in assessing of progression of the disease by monitoring forced vital capacity (FVC). Pulmonary function tests, which require more sophisticated technology allow for more advanced assessment of lung physiology. The pulmonary function tests can provide information regarding gas transfer at the alveolar level in terms of diffusion capacity of carbon monoxide (DLCO), lung volume measurements and distance covered during a six-minute-walk test. The latter may provide important prognostic features as median survival in patients with IPF with oxygen desaturation to 88% or below during the six-minute-walk test compared with those without evidence of oxygen desaturation to this extent was 3.21 years and 6.63 years respectively6.

Radiological Investigations

All patients investigated for ILD should have a chest radiograph, which is usually abnormal and may reveal changes such as honeycombing or reticulo-nodular shadowing (Figure 2a). The pattern and the distribution of the abnormalities may differentiate between the types of ILD. Mainly basal distribution of reticulo-nodular shadowing may be associated with asbestosis, IPF or connective tissue diseases. Conversely, mainly upper lung zones distribution of reticulo-nodular shadowing may be more in favour of sarcoidosis, silicosis or coal worker pneumoconiosis. The presence of mediastinal lymphadenopathy may be associated with sarcoidosis or silicosis. The evidence of pneumothorax may suggest LAM.

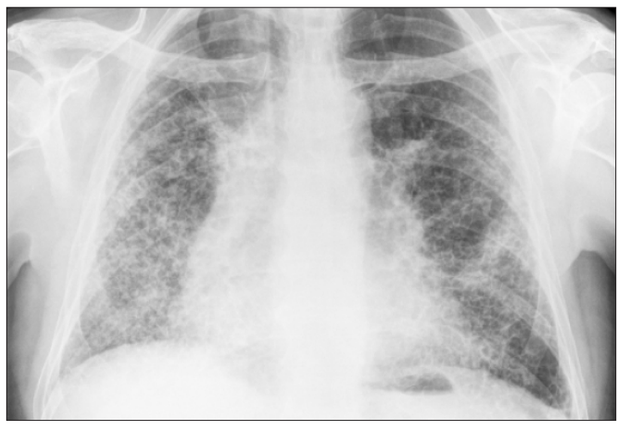

Figure 2a
Chest radiograph appearances in Idiopathic Pulmonary Fibrosis (IPF) showing mainly basal distribution of reticulo-nodular shadowing.

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The presence of pleural plaques or pleural thickening on the background of occupational exposure to asbestos may suggest asbestosis. The chest radiograph is also invaluable in identifying the secondary complications of ILD including pneumothorax, malignancy, infection or cardiac failure. However, correct diagnosis of ILD based solely on chest radiograph appearances can be made confidently in only a half of cases[7]. Therefore, High Resolution Computed Tomography (HRCT) of the thorax forms an important part of investigations of patients with ILD. HRCT of the thorax is more sensitive in detecting ILD than chest radiograph; 94% compared with 80% respectively[8]. The characteristics and the distribution of the changes on the HRCT of the thorax may suggest specific ILD.

For example, the HRCT of the thorax in IPF may show sub-pleural and basal predominance mainly, honeycombing, traction bronchiectasis, reticular component and occasionally ground glass component (Figure 2b). Other ILD which often exhibit characteristic HRCT of the thorax appearances are sarcoidosis, hypersensitivity pneumonitis, Langerhans' cell histiocytosis and LAM. The HRCT of the thorax may also be of assistance in assessing the extent of the disease or potential responsiveness to the treatment.

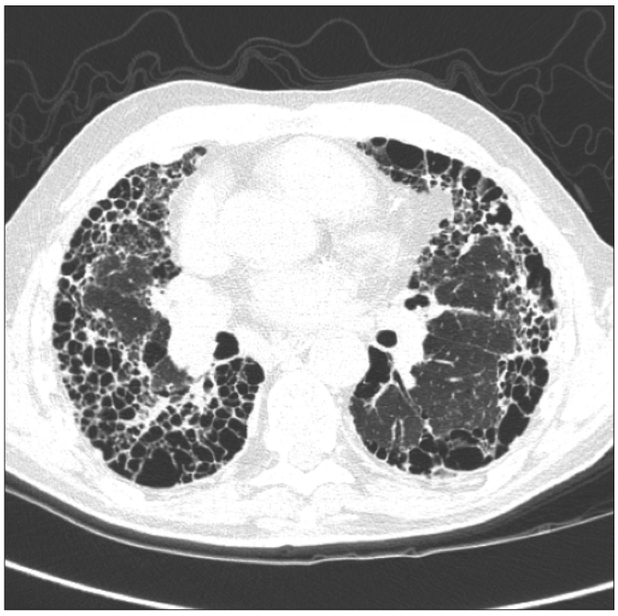
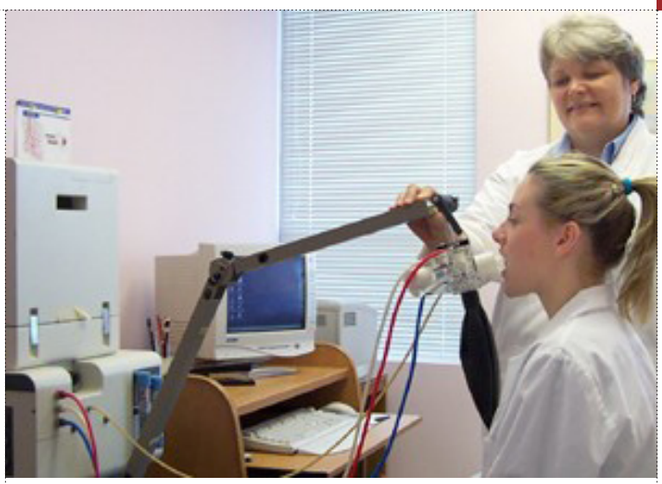


Figure 2b
Typical High Resolution Computed Tomography (HRCT) of the thorax appearances of Idiopathic Pulmonary Fibrosis (IPF) showing sub-pleural and basal predominance of reticular component, honeycombing and traction bronchiectasis.



Invasive tests

In many cases, ILD may be confidently diagnosed based on clinical presentation, pulmonary function tests and HRCT of the thorax findings. However, when there is diagnostic uncertainty more invasive tests should be considered, such as fibre-optic bronchoscopy with bronchoalveolar lavage (BAL) and trans-bronchial lung biopsy (TBLB) or surgical lung biopsy. These procedures should be performed ideally before the initiation of treatment. The BAL can be analysed for the presence of infection, cytological and fluid cell profile. BAL and TBLB are relatively safe procedures with a very small overall mortality and complications rate.

For example, major complications of TBLB are pneumothorax, which may occur in approximately 10% of procedures and the risk of haemorrhage. The main disadvantage of TBLB is related to the fact that the amount of lung tissues obtained during the procedure is relatively small. Therefore, the gold standard for histological diagnosis of ILD is a surgical lung biopsy, which allows collection of a larger sample of lung tissues for analysis. Due to potential risks of surgical lung biopsy patients have to be assessed and selected carefully. Video assisted thoracoscopic surgery (VATS) is comparatively less invasive as compared to the open lung biopsy. However, the accurate diagnosis of ILD requires a multi-disciplinary approach whereby all the data are integrated and a consensus diagnosis is reached by close communication between respiratory physicians, thoracic surgeons, pathologists and radiologists.

INTERSTITIAL LUNG DISEASES

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General management of ILD

It is currently recommended that a multi-disciplinary approach is applied to management of patients with ILD. In general, patients with well established and advanced ILD should receive supportive care and symptomatic relief including domiciliary and ambulatory oxygen, analgesia and palliative care team involvement. All patients with ILD who are smokers should stop smoking and receive smoking cessation advice. In cases of RB-ILD and DIP smoking cessation is the main aspect of treatment. In cases of hypersensitivity pneumonitis, identification and antigen avoidance form important aspects of the treatment. Corticosteroids are the mainstay of treatment in ILD such as COP, advanced and progressive sarcoidosis and hypersensitivity pneumonitis. Immunosuppressive therapy including cyclophosphomide or azathioprine in addition to corticosteroids is used in connective tissue diseases related ILD. The duration of treatment varies in different conditions. Patients should also be assessed for pulmonary hypertension, which is a recognised complication of chronic ILD.

Specific Conditions

It is beyond this article to discuss all of the ILD so we will discuss IPF, NSIP, DIP, RBILD, AIP, COP, LIP and sarcoidosis. Patients with these conditions are more likely to be encountered during an acute medical take or on medical or surgical wards.

Idiopathic Interstitial Pneumonias (IIPs)

The guidelines divided IIPs into Idiopathic Pulmonary fibrosis (IPF) and non IPF IIPs (COP, cellular NSIP, DIP, LIP and RB-ILD)[1,2]. The non-IPF IIPs are associated with better overall prognosis as they are often more inflammatory rather than fibrotic in their nature. Previously in the United Kingdom the term 'Cryptogenic Fibrosing Alveolitis'(CFA) was used as a blanket term for all IIPs but the guidelines made it clear that CFA and IPF were synonymous terms[1,2].

Idiopathic Pulmonary Fibrosis (IPF)

IPF is the commonest of the IIPs with 2,000 new cases reported in England and Wales every year[1]. The IPF has the worst overall prognosis with a median survival of 3 years from diagnosis[9]. Moreover, patients with IPF have a markedly increased risk of developing lung cancer. The histological correlate of IPF is usual interstitial pneumonia (UIP) (Figure 3). Currently there is no cure for IPF. Several medical treatment modalities have been tried. One such approach includes a combination of Prednisolone, Azathioprine and N-Acetyl Cysteine (NAC).

In a randomised controlled study comparing Prednisolone and Azathioprine alone or with NAC, there was an observed reduction in decline of FVC and DLCO in favour of NAC group but no difference in mortality between the two groups[1]. Several other agents including Interferon gamma 1b, Cyclophosphamide, and Cyclosporine have been tried but unfortunately none of those agents has given any ground breaking results.

Patients aged less than 65 years with IPF may be considered for lung transplantation although it is not easy to judge the optimal time for referral[1]. Best supportive care aimed in managing symptoms of breathlessness with ambulatory and domiciliary oxygen forms an integral part of the management strategy for patients with IPF. During the end stage of the disease frequently palliative care support may be required.

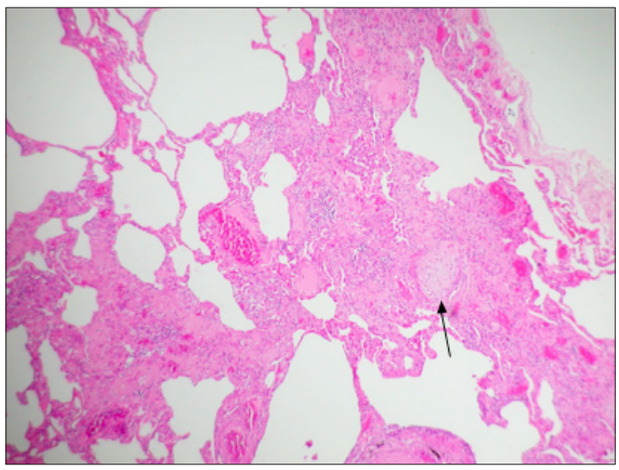

Figure 3
Histopathology of usual interstitial pneumonia (UIP) seen on a video assisted thoracoscopic surgery (VATS) lung biopsy from a patient with Idiopathic Pulmonary Fibrosis (IPF). There is patchy interstitial fibrosis interspersed with normal lung tissue with a fibroblastic focus being demonstrated (arrow). (Photomicrograph provided by Dr A. Campbell).

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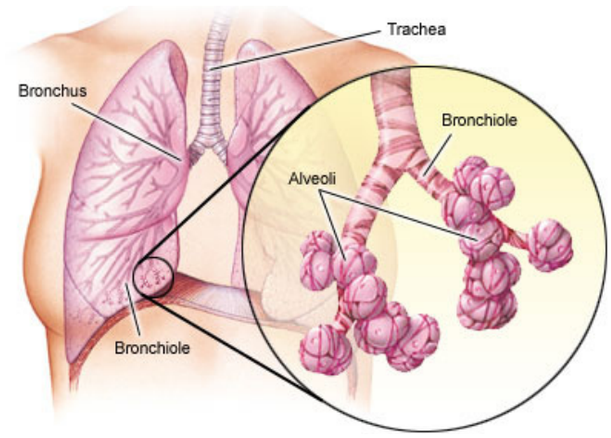


Non-Specific Interstitial Pneumonia (NSIP)

NSIP is a histological diagnosis based on lung biopsy. Broadly there are two types of NSIP namely; 'fibrotic' NSIP, which is very difficult to distinguish from IPF and 'cellular' NSIP, which has better prognosis. The radiological appearances may resemble those of IPF but ground glass changes are usually more extensive and traction bronchiectasis is less common. Diagnosis of NSIP requires a multi-disciplinary approach with careful assessment of clinical radiological and histopathological features. Corticosteroids remain the mainstay of treatment of NSIP.

Desquamative Interstitial Pneumonia (DIP)

This is a form of IIP which is more common in men and usually affects smokers in their fourth or fifth decades. The radiological findings are not specific, and surgical lung biopsy is required to make a confident diagnosis. The overall prognosis in DIP is good. Treatment in majority of cases is smoking cessation. If the condition progresses oral corticosteroids may be considered.

Respiratory Bronchiolitis Interstitial Lung Disease (RBILD)

Respiratory bronchiolitis is the physiological response to smoking with a majority of patients remaining asymptomatic. A small minority of smokers develop RBILD and become symptomatic. Similarly to DIP, RBILD is seen more commonly in current or ex-smokers in their fourth or fifth decades. The diagnosis can be made confidently based on clinical and radiological appearances although in some cases a surgical lung biopsy may be required. The HRCT of the thorax may show ground glass changes, micronodules and bronchial wall thickening[1]. Treatment as in DIP is smoking cessation.

Acute Interstitial Pneumonia (AIP)

AIP is also known as Hamman-Rich syndrome, which is a type of idiopathic acute respiratory distress syndrome (ARDS). It presents as rapidly progressive respiratory failure. AIP can occur in previously healthy individuals and presents with a fairly short duration of cough and dyspnoea. Unfortunately mortality remains very high.

Cryptogenic Organising Pneumonia (COP)

COP usually presents with symptoms suggestive of respiratory tract infection that do not respond to antibiotics and may persist over many months. Chest radiograph or HRCT of the thorax may reveal peripheral often migratory consolidation[1]. The lung biopsy shows changes of organising pneumonia. Corticosteroids remain the treatment of choice. Overall prognosis is good although COP can occasionally relapse.

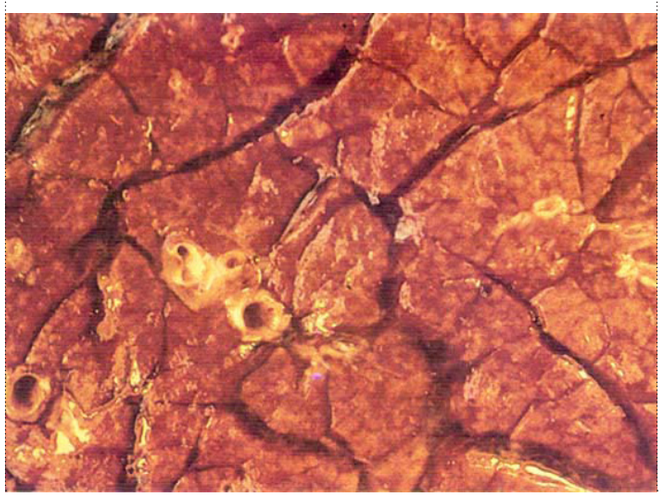
Lymphoid Interstitial Pneumonia (LIP)

The pathogenesis of LIP is unknown. It is characterised by diffuse lymphocytic infiltration of lung interstitium. It is usually seen in association with connective tissues diseases or autoimmune disorders such as Sjogrens syndrome, Systemic Lupus Erythematosus (SLE), rheumatoid arthritis, pernicious anaemia or primary biliary cirrhosis. Corticosteroids are the most commonly used treatment. The overall mortality was reported at 38%[1].

Sarcoidosis

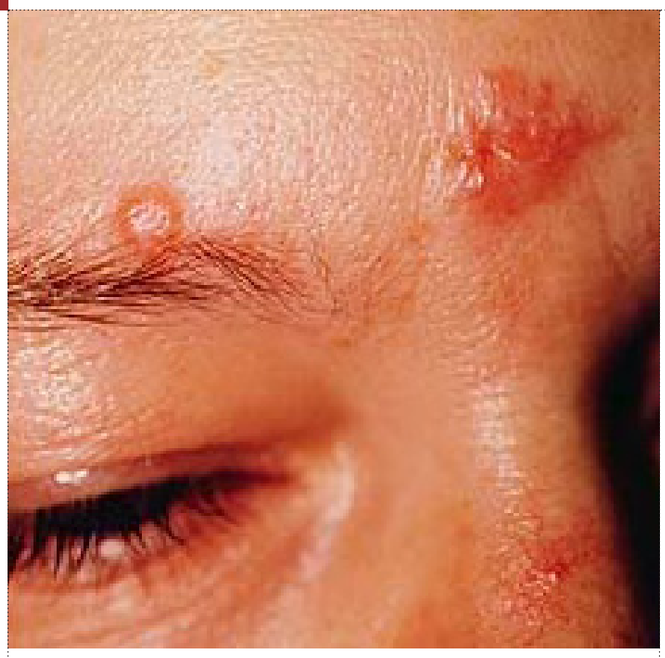
Sarcoidosis is a multisystem granulomatous disease of unknown aetiology[10]. In the majority of cases sarcoidosis involves the respiratory system[11]. Sarcoidosis can also affect other organs such as the skin e.g. erythema nodosum or the ocular system e.g. uveitis and less commonly the central nervous system and the heart. The baseline investigations for sarcoidosis should include full blood count to assess for anaemia or leukopenia and serum biochemistry, which may reveal hypercalcaemia. Lung function tests may be normal or may show a restrictive lung defect or reduced DLCO especially in cases with pulmonary infiltrates and pulmonary fibrosis.

The chest radiograph findings have been classified into four stages. Stage I is defined as bilateral hilar lymphadenopathy, stage II as bilateral hilar lymphadenopathy and pulmonary infiltrates, stage III as pulmonary infiltrates only and stage IV as pulmonary fibrosis. The HRCT of the thorax is helpful in detecting any parenchymal involvement. Commonly a diagnosis of sarcoidosis can be made based on clinical presentation as is the case in the common variant of sarcoidosis called Lofgren's syndrome that presents with a triad of erythema nodosum, arthlargia and bilateral hilar lymphadenopathy. In other cases histological tissue diagnosis may be required.



INTERSTITIAL LUNG DISEASES

I Aslam, SP Hart, JA Kastelik



Overall sarcoidosis has a good prognosis. Spontaneous remission for stage I and II of sarcoidosis occurs in 90% and 70% of patients respectively[12]. Stage III disease has less favourable outcomes with only 20% patients having reported spontaneous remission[12]. Therefore, many patients with mild asymptomatic disease will not require any treatment. Oral corticosteroids are indicated in patients who report noticeable deterioration in symptoms, lung function or radiological appearances or in cases of extra-pulmonary sarcoidosis[1]. In more severe disease other treatments can be considered including Methotrexate, Cyclosporine or Azathioprine.

Conclusions

ILD form a very interesting group of diseases. The majority of patients with ILD are managed through a multi-disciplinary team approach that involves close co-operation between respiratory physicians, radiologists, thoracic surgeons and pathologists. From the junior doctor's perspective, the knowledge of the different types of ILD may be useful on acute medical take or on general medical or surgical wards. The understanding of the treatment options, potential complications and prognosis should be of help when managing patients with ILD in those settings. However, due to relative complexity of these diseases specialist advice from a respiratory physician is required to provide appropriate management of patients with ILD.

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Questions

1. Are the following statements regarding interstitial lung diseases (ILD) true or false?

a) Amiodarone and Nitrofurantoin are known to cause ILD.
b) Idiopathic Pulmonary Fibrosis (IPF) is the commonest Idiopathic Interstitial Pneumonia.
c) Spirometry shows obstructive pattern.
d) Median survival for Idiopathic Pulmonary Fibrosis (IPF) is less than 6 months.
e) Lung transplantation should be offered to all patients with Idiopathic Pulmonary Fibrosis (IPF).

INTERSTITIAL LUNG DISEASES

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2. Can the following occur in the context of ILD?

a) The presence of pulmonary fibrosis on a chest radiograph suggests stage IV of sarcoidosis.
b) Chest radiograph changes of reticulo-nodular interstitial shadowing do not occur in Idiopathic Pulmonary Fibrosis (IPF).
c) Cryptogenic Organising Pneumonia usually responds to oral corticosteroids.
d) Fine inspiratory 'velcro' like crackles are commonly present on auscultation of the chest in patients with ILD.
e) Diagnosis of ILD cannot be made without surgical lung biopsy.

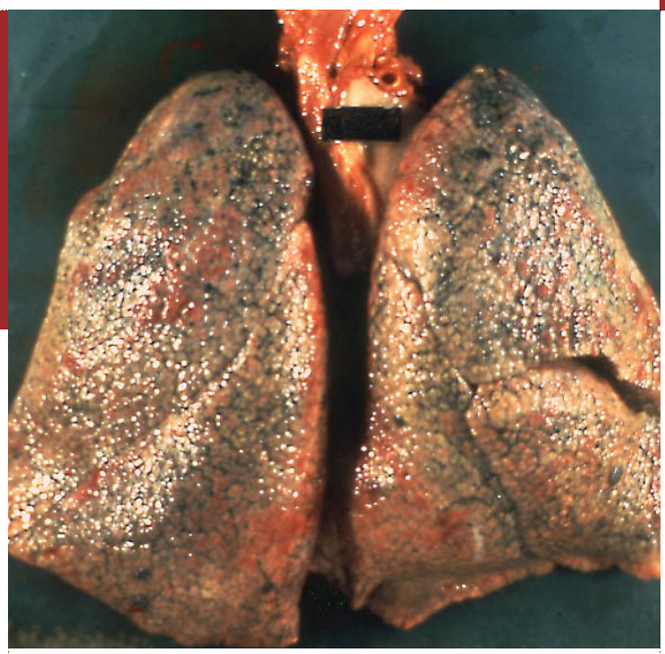
Answers

Question 1

a) True. Both Amiodarone and Nitrofurantoin can cause ILD.
b) True. IPF is the commonest of the Idiopathic Interstitial Pneumonias with 2,000 new cases reported in England and Wales every year.
c) False. Spirometry testing usually reveals a restrictive pattern.
d) False. The IPF has the worst overall prognosis with median survival of 3 years from diagnosis.
e) False. Patients' with IPF aged less than 65 years may be considered for lung transplantation although it is not easy to judge the optimal time for referral.

Question 2

a) True. The chest radiograph findings in sarcoidosis have been classified into four stages. Stage I is defined as bilateral hilar lymphadenopathy, stage II as bilateral hilar lymphadenopathy and pulmonary infiltrates, stage III as pulmonary infiltrates only and stage IV as pulmonary fibrosis.
b) False. Chest radiograph in IPF is usually abnormal and may reveal honeycombing or reticulo-nodular changes.
c) True. In Cryptogenic Organising Pneumonia corticosteroids remain the treatment of choice.
d) True. Fine end inspiratory crackles described as dry 'Velcro' like are commonly present in Idiopathic Pulmonary Fibrosis (IPF), although crackles may also be present in other conditions such as ILD associated with connective tissue diseases or asbestosis.
e) False. Not all ILD require surgical lung biopsy to confirm the diagnosis. For example diagnosis of IPF can be confidently made as based on clinical presentation, findings and radiological appearances of HRCT of the thorax.



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We would like to thank Dr A Campbell Consultant Histopathologist, Castle Hill Hospital, Castle Road, Cottingham, East Yorkshire HU 16 5JQ, UK, for providing a photomicrograph of histopathology of usual interstitial pneumonia (UIP), (Figure 3).

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid

**Disorders of the Pleura –
Case Based Discussion.
Good Clinical Care.**

Abstract

Diseases affecting the pleura represent challenges to both acute/general physicians and respiratory specialists alike. The presentation occurs in the young and old, the previously healthy and those with chronic illness. Pleural disease can reflect terminal illness or acute reversible pathology. Using a case based discussion approach this article looks at three common presentations of pleural disease; unilateral pleural effusion, pleural infection and pneumothorax.

Pleural effusion

Case 1: *A 68 year old female, is admitted with a 4 week history of increasing exertional breathlessness, fatigue and cough. Her GP arranges admission to hospital after a chest X-ray in the community has shown a large left-sided pleural effusion.*

Discussion

The lung and the inside of the chest wall are both lined by pleural membranes. That surrounding the lung is termed the visceral pleura and that lining the inside of the chest wall is termed the parietal pleura. The pleural space – the space between the parietal and visceral pleura - normally contains a small amount of fluid, usually less than 1ml, which acts to facilitate the smooth egress of the lung over the chest wall during respiration. The accumulation of larger amounts of fluid within the pleural space is termed pleural effusion. In general, pleural fluid accumulates as a result of either increased hydrostatic pressure or decreased osmotic pressure ('transudative effusion' as seen in cardiac, liver or renal failure), or from increased microvascular pressure due to disease of the pleural surface itself, or injury in the adjacent lung ('exudative effusion'). A number of potential diagnoses may present with a pleural effusion including malignant disease, infections such as tuberculosis and pneumonia, pulmonary thromboembolism, connective tissue disorders and cardiac failure. The cause of the majority of pleural effusions can usually be identified through a thorough history, examination and relevant investigations but some remain undiagnosed.

What are the important points to elicit in the history?

As with many medical problems, important clues to the underlying pathology may lie within the history. Typical symptoms include cough, breathlessness and chest pain but their nature, character and onset may provide clues as may the time period over which symptoms have developed and the presence of absence of systemic upset. For example, respiratory infections typically present in an acute fashion (days-weeks) accompanied by cough, mucopurulent sputum, pleuritic chest pain, breathless and marked systemic upset with loss of appetite and fever, whereas malignant disease classically presents with a more indolent course (weeks-months) where cough is persistent, chest pain persistent, breathlessness slowly evolving and systemic symptoms less apparent. Haemoptysis may suggest malignancy which may also be accompanied by weight loss but both of these features may also be a feature of tuberculosis; although in the latter, systemic symptoms such as fever and night sweats may be much more prominent. Chest pain is a particularly important symptom. As suggested above, the occurrence of pleurisy may be typical of infection but may also be reported in pulmonary embolism. A longer history of dull chest pain associated with ipsilateral effusion may be more suggestive of an underlying malignant pathology such as carcinoma or mesothelioma. Mesothelioma may also be accompanied by night sweats.

Elsewhere in past medical history co-morbidities such as previous malignancy (e.g. breast), rheumatoid arthritis or other connective tissue disease (Table 1) might suggest an underlying cause. A history of cardiac, renal or liver disease may suggest the presentation of a transudate. Systemic enquiry may reveal an unrecognised cause for the effusion i.e. full gastrointestinal and genitourinary history could point to an underlying malignant process. A detailed occupational history may often be necessary to uncover exposure to asbestos which is not always easily recalled by the patient. A comprehensive drug history should be taken as, albeit uncommonly, a number of medications have been reported to cause pleural effusion. A smoking history is mandatory but care should be taken not to dismiss malignancy in non-smokers as metastatic adenocarcinoma of the lung is common in non-smokers.

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid

	Exudate	Transudate
Common	Malignancy Parapneumonic	Heart failure Liver failure
Less common	Tuberculosis PE/infarction Rheumatoid arthritis SLE Pancreatitis Benign asbestos effusion Post MI/CABG	Hypoalbuminaemia Nephrotic syndrome Peritoneal dialysis
Very rare	Yellow nail syndrome	Hypothyroidism

Table 1: Causes of pleural effusion (not exhaustive)

What should I look for on examination?

The signs of pleural effusion depend on its size and typically 500ml are required before an effusion becomes clinically obvious. The classical features of a size significant effusion are reduced chest expansion, a stony dull percussion note and reduced breath sounds all on the side of the effusion. Occasionally a small area of bronchial breathing may be located at the top of the effusion. A thorough clinical examination may also reveal signs of underlying malignancy such as cachexia, finger clubbing, and lymphadenopathy, or manifestations of rheumatoid or connective tissue disease, and signs of cardiac, renal or hepatic failure. Examination of other systems for extra-pulmonary malignancy should always include a breast examination in females.

Case 1: *Our patient has smoked 20 cigarettes per day for 50 years. Her GP has recently started her on inhalers but she is on no other medications. She normally keeps well but complains of fatigue, exertional dyspnoea and dry cough over 6 weeks. She has been off her food for the last few months and thinks her clothes have become loose. There is a past history of mastectomy and radiotherapy for a right-sided breast tumour 2 years earlier. Examination was unremarkable other than chest signs consistent with a moderately large pleural effusion.*

What investigations should follow?

In this particular case, the time course of presentation, smoking history, the absence of infective symptoms suggest that malignancy should be strongly suspected. A late presentation with metastases from breast cancer is as likely a cause as underlying pulmonary malignancy.

Simple blood tests should be performed. An infective process may be indicated by a leucocytosis and elevated c-reactive protein. Malignant disease may be accompanied by anaemia, deranged liver function tests, hypoalbuminaemia or hypercalcaemia. Anti-CCP (anti-cyclic citrullinated peptide antibody) / rheumatoid factor or autimmune screen may suggest an underlying rheumatoid or connective tissue disease. A coagulation screen should be performed in case a diagnostic or therapeutic procedure is required. In unexplained transudative effusion thyroid function tests should be checked looking for hypothyroidism.

In this case, a chest X-ray has already been performed. Appearances of pleural effusion on a plain x-ray can be varied and the appearances depend on the size of effusion. It takes around 200-300ml of fluid to be visible on a standard PA film although a lateral film is more sensitive (50ml).[1] Depending on the volume of fluid present appearances may be as subtle as blunting of the costophrenic angle (Figure 1) to complete opacification of the unilateral hemithorax (Figure 2). The appearance of free pleural fluid as a homogeneous opacity with a concave upper border ascending towards the axilla is called the pleural meniscus sign (Figure 3) but is in fact an artifact as in reality, the fluid surrounds the whole lung, but casts a radiological shadow only where the X-ray beam passes tangentially across the fluid against the lateral chest wall.

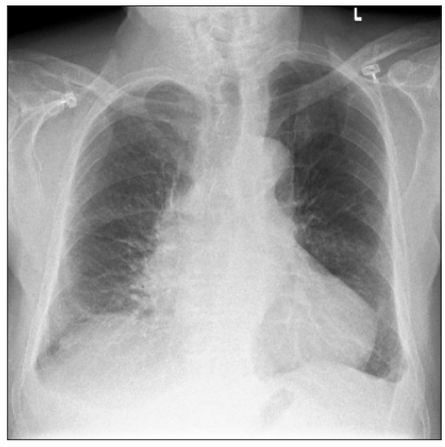


Figure 1: Small bilateral effusions with blunting of the costaphrenic angles.

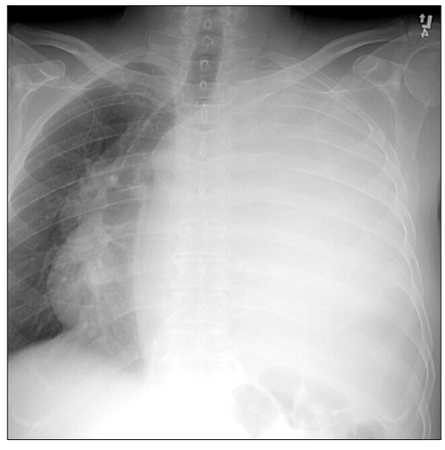


Figure 2: Massive left effusion with mediastinal shift.

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid

Disorders of the Pleura – Case Based Discussion. Good Clinical Care.

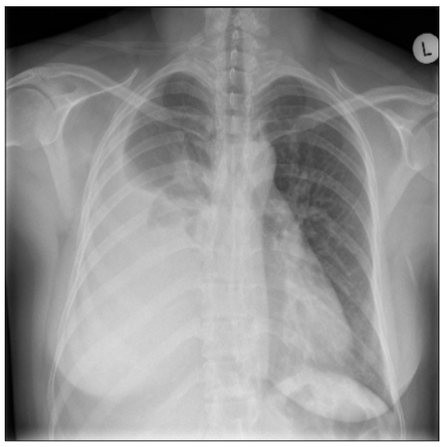


Figure 3: Large right effusion with meniscus.

A diagnostic pleural aspiration is invariably required. Pleural ultrasound (USS) is recommended prior to intervention to assist safe aspiration.[2] USS is very sensitive for pleural fluid providing an estimation of volume and allowing determination of the position of the diaphragm thereby preventing the operator from inadvertently damaging the liver or spleen. It may also detect the presence of loculation (complicating empyema). Ideally USS should be performed at the bedside as the potential safety benefits may be lost when an 'x marks the spot' process occurs distant in location and time to intervention later on the ward.[3]

Inspection by the naked eye provides information on the colour and texture of fluid (Table 2). The fluid should then be sent to biochemistry (total protein, LDH and glucose), microbiology (routine culture, AAFB stain and mycobacterium culture) and cytology. Fluid can be sampled using a 21G needle and a 50ml syringe. Samples should be sent in universal containers. Where malignancy is suspected the largest volume of fluid should be sent to cytology. In cases where pleural infection is suspected the pH should also be measured (see Case 2). A post procedure CHEST X-RAY is not always necessary but should be performed if air is aspirated, the procedure has been technically difficult or multiple attempts have been made or if the patient becomes symptomatic post procedure.

Fluid appearance	Likely cause of effusion
Frank pus	Empyema
Blood stained	Malignancy, pulmonary infarction, Post cardiac injury syndrome, Infection, TB
Frank blood	Haemothorax
Milky	Chylothorax (due to thoracic duct disruption)
Food particles	Oesophageal rupture
Bile stained	Biliary fistula (Cholothroax)

Table 2: Pleural fluid appearances and underlying causes[4]

Case 1: *Blood tests showed borderline anaemia (Hb106mg/l) and hypoalbuminaemia (Alb 28g/l). Diagnostic aspiration revealed straw coloured pleural fluid, with a protein count of 32g/l, LDH 780 and glucose[3,4]. The microbiological culture and gram stain was negative. Cytology exam found atypical cells but no evidence of malignant.*

Is this an exudate or a transudate?

Estimation of the protein content in the pleural fluid allows differentiation between a transudate and an exudate: transudates are generally regarded as having a protein level less than 30g/l and exudates a level greater than 30g/l. However, when the pleural fluid protein is in the range of 25-35 g/l, or the serum protein level is low, it is good practice to employ Lights criteria (Table 3) which requires the simultaneous measurement of serum protein and LDH.

Lights criteria: An effusion is an exudate if any of the following criteria are met
• Pleural protein divided by serum protein > 0.5
• Pleural LDH divided by serum LDH <0.6
• Pleural LDH > 2/3 upper limit of normal serum LDH level

Table 3: Lights criteria

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid

What further investigations are required?

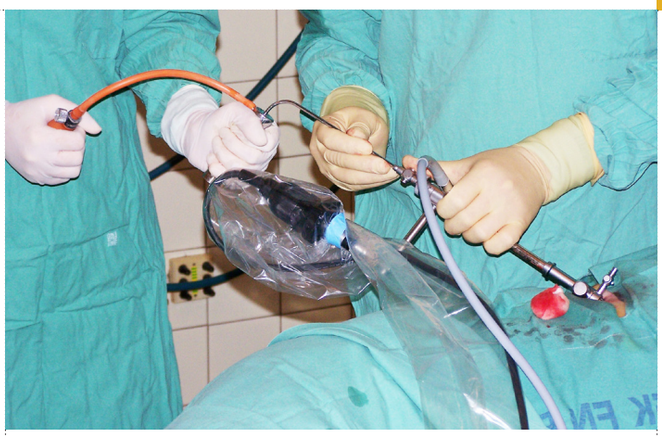
Further imaging is appropriate with a contrast enhanced CT for exudative pleural effusions of uncertain aetiology. In this case, where malignancy is strongly suspected, it is appropriate to perform a CT scan of the thorax, abdomen and pelvis (although in male patients a CT scan of the chest and abdomen it is usually sufficient). A CT scan typically adds to the information gleaned from USS on the appearances of the pleura but provides additional information on the underlying lung parenchyma and may suggest spread from a primary malignant process. The presence of pleural fluid often assists with visualisation of an underlying primary pleural process aiding differentiation between benign and malignant pleural thickening, however large volumes of fluid may compress the underlying lung making comments on an underlying pulmonary process challenging.

How do we proceed to a diagnosis?

In cases of malignant effusions, pleural fluid cytology will establish the diagnosis in around 60% of cases.[5] Diagnostic yield does not improve with repeated sampling if the second sample fails to establish the diagnosis. A variety of further investigations may be considered. For many years it has been common to perform a blind pleural biopsy; usually with an Abrams needle. This test can be performed at the bedside but it is not possible to visualise the pleura or any potential abnormalities and the diagnostic yield for malignancy is seldom increased significantly beyond pleural aspiration alone.[6] Techniques, such as medical thoracoscopy or video assisted thoracoscopic surgery (VATS) allow the operator to directly visualise the pleural surface provide much greater diagnostic yields.

Case History: *Thoracoscopy is currently considered the investigation of choice in unexplained exudative effusions where cytology is negative and malignancy is suspected.[4] Medical thoracoscopy can be performed under sedation and local anaesthetic but requires a large volume of fluid to be safely performed. It allows direct visualisation of the parietal and visceral pleura with subsequent drainage of the effusion and potential for talc pleurodesis. In cases where a focal area of pleural nodularity is identified on CT, image guided biopsy, after discussion with the radiologists, is often a sensible next investigation. This carries a higher yield than blind pleural biopsy. Bronchoscopy is not a routine investigation in the management of pleural effusion and is reserved for when there are associated parenchymal or endobronchial abnormalities seen on CT.*

In this case the pleural fluid is an exudate and CT scan chest, abdomen and pelvis identifies a moderately large pleural effusion without additional evidence of bronchogenic malignancy, lymphadenopathy, distal metastatic disease or alternative primary disease. The patient underwent medical thoracoscopy following which, she returned to the ward with an intercostal drain in situ. The biopsy confirmed the presence of an adenocarcinoma and immunohistochemistry stains which suggested a lung primary.



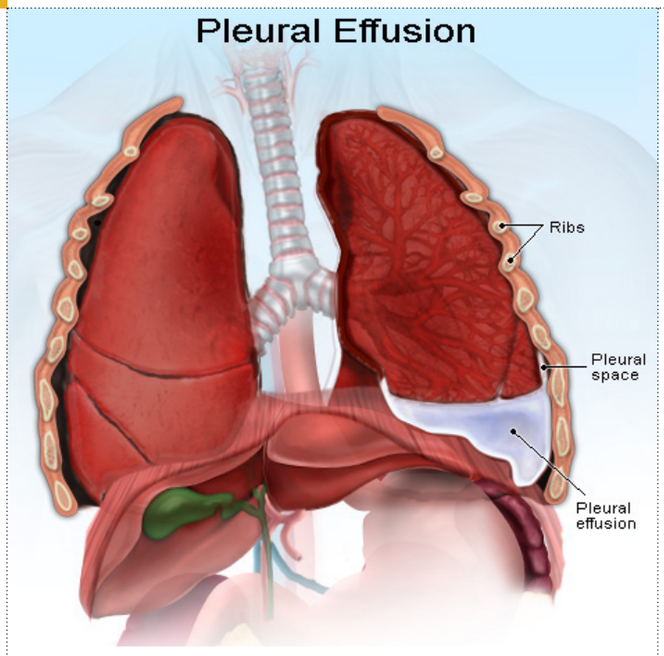
Should we perform intercostal drainage and pleurodesis?

Before deciding whether to perform pleurodesis the first question is often whether the effusion requires formal intercostal drainage. In cases of small or asymptomatic pleural effusions it may be appropriate to observe the patient and defer intervention. Where symptoms have developed the choice lies between therapeutic aspiration and intercostal drainage and the decision should include the patient's wishes. A therapeutic aspiration (removal of up to 1.5L of fluid at one time) is a relatively simple procedure, which may be performed as a day case and may be the most appropriate choice to provide symptomatic relief in patients with a very short life expectancy. However, malignant effusions re-accumulate quickly with a recurrence rate approaching 100% at 1 month.[7] Repeat thoracocentesis is often unacceptable and in such cases intercostal drainage and pleurodesis is more definitive. Small bore drains (size 12-14F) are usually sufficient. Pleural effusions should be drained in a controlled fashion (e.g. 1-1.5L at one time or 500ml/hr). This is to prevent the rare but significant complication of re-expansion pulmonary oedema. More commonly patients can become symptomatic with cough and pleuritic pain when a lung that has been compressed under a vast quantity of fluid re-expands rapidly. It is seldom good practice to perform non-urgent pleural procedures out of hours.

Successful pleurodesis causes a diffuse inflammatory reaction to obliterate the space between the parietal and visceral pleural surfaces and is best performed within 24 hours of radiographic lung reinflation.[8] This appears to be more important than delaying the procedure until the volume of pleural fluid drained in 24 hours falls below 150ml.[7] Pleurodesis must not be performed in cases of 'trapped lung' where there is complete failure of lung apposition to chest wall, but may be attempted if only partial apposition is achieved. There is little evidence to back up popular belief that larger drains are required for successful pleurodesis.[9] Each centre is likely to have its own specific pleurodesis protocol. In the majority of centres sterile talc is the sclerosing agent of choice.[7] Pain and fever are common post pleurodesis and appropriate analgesia and anti-pyretic therapy should be prescribed. After the talc slurry is injected intra-pleuraly (through the drain), the drain should be clamped for an hour before being allowed to drain freely. The drain should be removed within 12-72 hours as long as the lung remains inflated and there is satisfactory cessation of pleural fluid flow.

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid



Pleural infection

Case 2: *A 46 year old male smoker with a background of alcohol excess is admitted with a 3 week history of fever, shortness of breath, purulent sputum and left-sided pleurisy. His CHEST X-RAY showed a left-sided pleural collection. His bloods show leucocytosis, elevated C - reactive protein and acute renal impairment.*

Discussion

In contrast to the previous case this patient has a shorter history and symptoms consistent with infection; hence the index of suspicion for pleural infection is high. When pleural effusion occurs as a complication of pneumonia it is termed 'parapneumonic'. The development of pleural fluid in pulmonary infection is understood to go through a progressive process from 'simple parapneumonic effusion' to 'complicated parapneumonic effusion' and finally empyema where frank pus is present in the pleural space.

A parapneumonic effusion may develop even when the initial assessment CHEST X-RAY showed no fluid and should be considered in any patient who fails to improve despite 48-72 hours of appropriate antibiotic therapy. It is difficult to predict who will develop pleural complications in pneumonia but those at greater risk include those with a history of intravenous drug or chronic alcohol abuse.[10] Personal experience suggests the complication is often more common is those with marked pleural pain.

Should the fluid be sampled?

When infection is suspected, the threshold for aspiration of pleural fluid should be low. It may be permissible to observe a small effusion, particularly when aspiration may place the patient at greater risk from a pneumothorax; however, if the effusion is large (Figure 4) and/or empyema is suspected, pleural fluid should be aspirated as matter of urgency. As discussed in case 1, pleural ultrasound is helpful in marking a suitable site for aspiration and providing information on the volume of fluid present. A fluid depth >10mm is usually sufficient to facilitate safe aspiration. As outlined in case 1 the aspirate should be sent for biochemical, microbiological and cytological assessment although here measurement of pH assumes greater importance as the presence of pleural fluid acidosis (pH<7.2) is an indication for prompt drainage. pH may be measured in a blood gas analyser using a heparinised syringe.

Take care to remove all air from the syringe as its presence may result in a falsely high pH; similarly, the presence of lidocaine a false low pH. The measurement of pH is not necessary when the fluid aspirated is frank pus. Other biochemical markers of infection include a high pleural LDH and low pleural glucose.

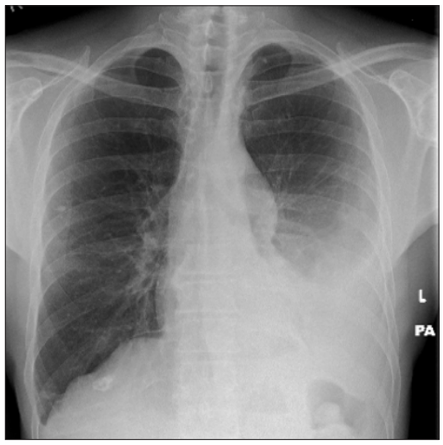


Figure 4: Parapneumonic effusion.

What is appropriate antibiotic management?

All patients should receive broad spectrum antibiotic treatment, including anaerobic cover, until further guidance from sputum, blood or pleural fluid culture becomes available.[11] Streptococcus and staphylococcus species are the commonest community acquired pathogens. Empirical treatment regimes for hospital acquired pleural infection should cover MRSA.[12] Intravenous antibiotics and prolonged oral courses of antibiotics are frequently required although there is no clear evidence to guide the ideal length of antibiotic course with parapneumonic effusion. A variety of antibiotic combinations may be appropriate and choice is often determined by local policies.

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid

Any other management issues?

A chest physician should be involved in all cases of pleural infection. Further imaging beyond CHEST X-RAY and pleural US is occasionally required. CT thorax (Figure 5) may be of value in a number of examples as outlined below in table 4.

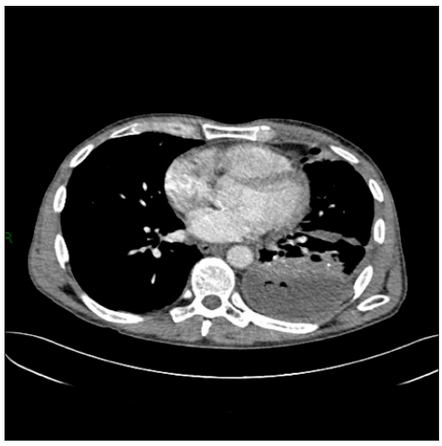


Figure 5: Corresponding CT appearances of pleural collection.

Indications for CT scanning in pleural infection
• Diagnostic difficulty (sub-pulmonary collections may not be obvious on plain CHEST X-RAY)
• Differentiate pleural collection from parenchymal abscess
• Outline complex loculated pleural collections
• Guidance for drain insertion
• Determine further management in those failing to improve (i.e. surgical intervention required)

Table 4: Indications for CT scan in pleural infection

Ensure any nutritional issues, particularly in the elderly, have been addressed and involve the dietician if necessary. Patients should be on appropriate venous thromboprophylaxis.

Case 2: *An USS confirms the presence of a 6x7x8cm fluid collection in the right hemithorax. A site is marked for aspiration and this reveals cloudy straw coloured fluid. Its pH is measured at 7.15 and the fluid is sent off for further laboratory analysis. The patient remains symptomatic and has shown no improvement in 24 hours of hospital treatment.*

Should the fluid be drained?

Indications for early drainage include the aspiration of frank pus or a pleural fluid pH of less than 7.2.[13] Other potential indications for chest drainage include fluid with positive microbial culture and the demonstration of loculated fluid which, is associated with a poorer outcome.[14] In cases of simple parapneumonic effusions, narrow bore (12-14F) drains are usually sufficient although larger drains are often required when frank pus is present. Regular flushing ought to be performed to avoid blocked drains. Smaller effusions will often resolve with appropriate antibiotic therapy but careful supervision should be undertaken.

Case 2: *A 14F chest drain is inserted and 650 ml of fluid is drained 3 days later. The drain is still swinging but no further fluid has drained in 48 hrs. The patient remains pyrexial, with a CRP of >100. A CT thorax is performed which shows two further small loculated collections separate from the initial collection drained.*

How do we manage pleural infection that fails to resolve?

Empyema is often complicated and complete resolution may not always be possible with intercostal drainage alone. In these situations the decision usually rests between conservative management and surgical input taking into consideration several factors including volume of residual collection, the presence of sepsis and fitness of the individual for surgery. Conservative options include a prolonged antibiotic course or insertion of a further drain under radiological guidance into the remaining collections. There has been some interest in the use of intrapleural fibrinolytic therapy.[11] Despite allowing an increase in pleural fluid flow rate, a large randomised trial with streptokinase failed to show an associated reduction in mortality, requirement for surgery, length of hospital stay or radiological or functional outcome.[15] A combination of fibrinolytic (tPA) and deoxyribonuclease (DNAse) may produce superior drainage to fibrinolytic agent alone and the results of such trials are eagerly awaited.

Pneumothorax

Case 3: *A 24 year old male was admitted with a 24 hour history of acute right-sided pleuritic pain. The CHEST X-RAY shows a clear lung edge and loss of lung markings peripheral to this in the right lung. The diagnosis is a spontaneous right-sided pneumothorax.*

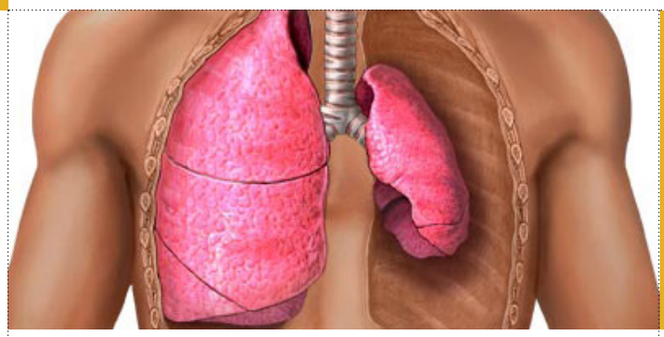
Discussion

Pneumothorax is the presence of air in the pleural space, which can either occur spontaneously, or result from iatrogenic injury or trauma to the lung or chest wall. (Fig. 6).

Primary spontaneous pneumothorax occurs in patients with no history of lung disease. It principally affects males aged 15–30 in whom smoking, tall stature[16] and the presence of apical subpleural blebs[17] are additional risk factors. Secondary pneumothorax affects patients with pre-existing lung disease, is most common in older patients, and is associated with higher mortality rates.

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid



Disorders of the Pleura – Case Based Discussion. Good Clinical Care.

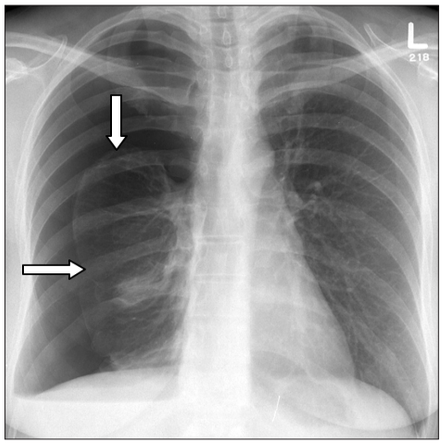


Figure 6: Large right pneumothorax. Arrows showing lung edge

What is important from the history?

The typical symptoms of spontaneous pneumothorax are sudden-onset unilateral pleuritic chest pain or breathlessness. However, it is important to appreciate that the history is not a reliable indicator for the size of pneumothorax. Symptoms in primary spontaneous pneumothorax, particularly if they occur in an otherwise fit individual with good respiratory reserve, may be minimal or even absent, whereas in cases of secondary pneumothorax (where underlying lung disease pre-exists) the symptoms are likely to reflect both the size of the pneumothorax and the extent to which the underlying lung disease has encroached on respiratory reserve. Where very severe breathlessness and respiratory distress are present the clinician should consider the possibility of tension pneumothorax in which large amounts of trapped air accumulate progressively in the pleural space causing intrapleural pressure to rise sufficiently to displace the mediastinum, compression to the opposite normal lung and impair systemic venous return, with resulting cardiovascular compromise.

It is also very important to consider whether this is the first presentation of pneumothorax as the management plan will be altered if this is the second event. Smoking is a significant risk factor for pneumothorax. The lifetime risk of smoking males is 12% compared to 0.1% in non-smoking males.[18] When considering subsequent recurrence rates smoking cessation advice should be offered to all smokers. In secondary pneumothorax where management may differ from that of primary pneumothorax underlying lung disease may be undiagnosed. Common causes of secondary pneumothorax include emphysema, bronchiectasis and pulmonary fibrosis.

Clinical signs of a pneumothorax may be very subtle but include reduced expansion, hyper-resonant percussion and reduced (or absent) breath sounds on the side of the pneumothorax. In cases of tension pneumothorax tracheal and mediastinal shift may be detectable along with tachycardia and hypotension.

Are any other investigations required?

In most cases a CHEST X-RAY is sufficient to establish the diagnosis and guide initial management. CHEST X-RAY features include a visible lung edge confirming collapse of the lung with loss of lung markings peripheral to this (Figure 6). CT scanning may be required in cases where the differential diagnosis includes an emphysematous bulla or when pleural tethering renders the ideal site for intervention unclear.

When managing pneumothorax the most important considerations are the size of pneumothorax and the presence of breathlessness and/or adverse physiological consequences.

British Thoracic Society guidelines[19] define a "small" pneumothorax on the basis that the distance between the visible lung edge and the chest wall at the level of the hilum is less than 2cm; however, it is almost universally acknowledged that sizing pneumothoraces on a plain CHEST X-RAY is notoriously inaccurate as they frequently underestimate the extent of the condition and, in clinical practice, management is most often dictated by the consequence of the pneumothorax to the patient.

Medical management options include

1) Observation
2) Needle aspiration
3) Intercostal drainage

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid

Case 3: *There is no history of prior lung disease. The patient's respiratory rate is 18 breathes/min, SpO_2 on air is 96%. He complains of pleuritic pain and has a sinus tachycardic of 110bpm but is normotensive. On closer inspection of the chest X-ray the pneumothorax is measured at 4cm from chest wall to lung edge.*

The patient has a primary pneumothorax. He is symptomatic but there is no evidence of significant respiratory or haemodynamic compromise; however, the size of the pneumothorax suggests that intervention is required. Observation could have been considered if the pneumothorax was small and there was no associated breathlessness (see Figure 7).

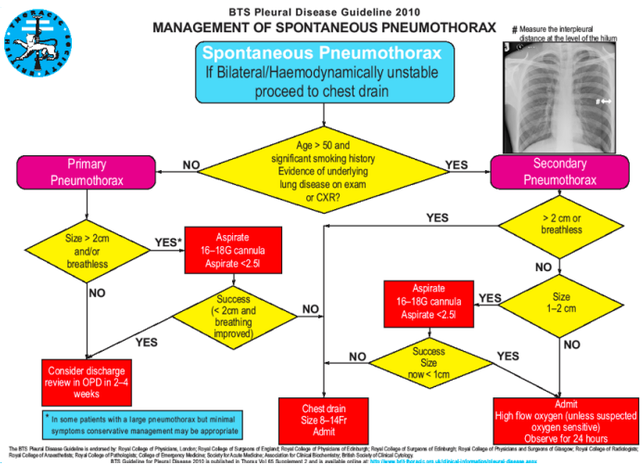


Figure 7: BTS guidelines on management of spontaneous pneumothorax[18]

The first step in management would be an attempt at needle aspiration. This involves the insertion an intravenous cannula through the 2nd intercostal space in the midclavicular line (not a suitable site in loculated non apical pneumothorax) under local anaesthetic. After withdrawal of the needle from the cannula a three way tap can be attached to the end of the venflon. A 60ml syringe is then attached to the other end of the three-way tap and air aspirated from the pleural cavity and expelled to the atmosphere. Air should continue to be aspirated until the operator is no longer able to evacuate air or if the patient becomes symptomatic with cough or chest discomfort.

The advantage of aspiration is perhaps greatest in terms of complications, particularly if the clinicians involved have less experience inserting chest drains. Provided the volume of air removed is no more than 1.5L complications are rare. The advent of newer fine bore chest drains which are inserted by a seldinger technique has meant that guidelines recommending needle aspiration are often not followed by clinicians who prefer a more definitive initial intervention.[20]

Case 4: *A post procedure chest X-ray shows a significant improvement in the size of pneumothorax with only a small apical rim remaining. The patient is well enough to be discharged home from A+E but is asked to return the following morning for a repeat CHEST X-RAY. He returns and reports having suffered a recurrence of the pain; the repeat CHEST X-RAY confirms that the lung has deflated to its original position.*

Experience suggests there is little merit in attempting a further aspiration. Repeat aspiration at this point should only be reattempted if there were technical difficulties (i.e. catheter kink) during the initial attempt.[19] In this case it is best to proceed to intercostal tube drainage. Smaller drains tend to be easier to insert and are more comfortable for patients such that they are generally considered first line. [21] There is no convincing evidence to justify larger drains.

Intercostal drains should be inserted in the 4th, 5th or 6th intercostal space in the mid-axillary line (so called 'triangle of safety') and advanced in an apical direction. Most drains are connected to an underwater seal although one-way valves may be employed. If not already done so, the patient should now be referred for specialist respiratory input.

Successful resolution of a pneumothorax leads to re-inflation of the lung which is usually heralded by a cessation of bubbling in the underwater seal drain. A CHEST X-RAY should be obtained to confirm the lung has re-expanded and, if so, the drain should be removed 24 hours later (preferably first thing in the morning rather than later in the day!).

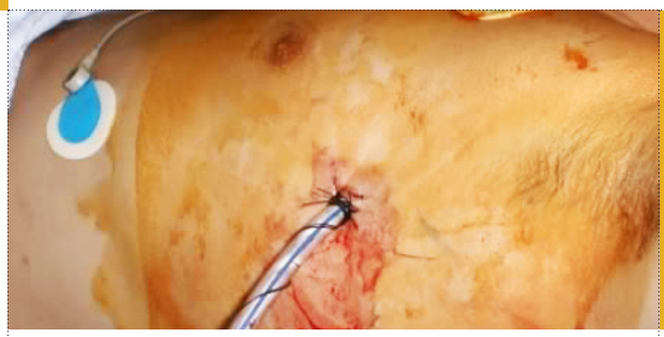
A persistent air leak is defined as the presence of bubbling in the drain bottle 48 hours after drain insertion. In the first instance, this can be managed conservatively by applying suction (pressures of -10 to 20 cm_2 H20) to the drain. A further option is to consider the insertion of a larger bore drain which may facilitate better drainage. All hospitalised patients should receive supplemental oxygen which is thought to improve the rate of resolution by reducing the partial pressure of nitrogen in the pleural space relative to oxygen, which is more readily absorbed.

When should a spontaneous pneumothorax be referred to the thoracic surgeons?

The optimum time for referral to thoracic surgery remains debatable. However, it is generally considered good practice to discuss patients with a primary pneumothorax who are failing on intercostal drainage after 72 hours and probably earlier in patients with secondary pneumothorax.[19] Indications for referral to thoracic surgery include failure of lung re-expansion and persistent air leak. Other indications are summarised in table 5. In these other examples it is common practice for the pneumothorax to be treated medically with outpatient surgical review for consideration of elective surgery to prevent recurrence. Surgical options include open thoracotomy with pleurectomy which although most invasive has the lowest recurrence rate. Less invasive techniques are more common practice now and this can be done by video assisted thoracoscopy (VATS). In patients not fit or unwilling to undergo thoracic surgery, medical pleurodesis with talc slurry may be attempted.

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid



Disorders of the Pleura – Case Based Discussion. Good Clinical Care.

Indications for thoracic surgical referral in spontaneous pneumothorax
• Failure to re-expand or persistent air leak despite adequate attempt at intercostal drainage.
• Bilateral pneumothorax
• Second ipsilateral pneumothorax
• First contra lateral pneumothorax
• First ipsilateral pneumothorax in professionals at risk (divers, pilots)

Table 5: Surgical referral in pneumothorax

Case 5: *A chest drain is suitably placed and the drain is swinging and bubbling. The patient complains of chest discomfort around the site of insertion. On examination there is subcutaneous swelling and audible crackling on palpation.*

What, if anything, should be done?

The drain appears to be functioning appropriately but the patient has developed subcutaneous (surgical) emphysema i.e. the presence of air in the subcutaneous tissue. This is usually obvious clinically and easily identified on CHEST X-RAY. It is important to ensure it has not occurred due to one of the ports of the drain sitting in the subcutaneous tissue or that the drain is not sealed tightly at the point of insertion in the chest wall. However, whilst unsightly, the condition usually only requires observation and reassurance.

The patient's lung has fully re-inflated on repeat CHEST X-RAY and after 4 days it is noticed on the evening ward round the drain has stopped bubbling. The patient is well and asymptomatic.

How do we manage the patient from here?

These findings suggest that the lung has healed and the pneumothorax has resolved; particularly if there is no bubbling when the patent coughs or takes deep breathes in and out. Even then, the drain should not be removed immediately as bubbling may be intermittent. Rather, it is sensible to leave the drain in overnight and if by the morning no further bubbling has been observed and radiographic resolution is confirmed, the drain should be removed. Repeat the CHEST X-RAY roughly four hours after drain removal to ensure there has been no relapse and if there are no complications the patient can be discharged.

What advice do we need to give the patient on discharge?

Patients who have suffered one pneumothorax should be informed that they are at risk of recurrence; hence, they should return to hospital if breathlessness or pleuritic chest pain recurs. The risk is generally held to be around 30% for a primary pneumothorax (most occurring within 2 years from the first event), and increases further if the patient suffers a second or third event e.g. 40% after a second and >50% after a third.[23] Recurrence rates in secondary pneumothorax are higher still.

If appropriate, smoking cessation advice should be given.

The time between resolution of spontaneous pneumothorax and safe air travel is potentially contentious. Air travel does not cause pneumothorax, but will aggravate a pre-existing pneumothorax. All patients should have a CHEST X-RAY that confirms lung condition before air travel is allowed.[19] Traditionally commercial airlines had set an arbitrary 6 week interval between resolution of a pneumothorax and air travel but this has been relaxed to 1 week. Nonetheless, these rules may vary according to the airline and patients should be advised to check with their carrier before travelling. As there is a high initial risk of recurrence that only falls after 1 year[24] patients may wish to wait longer than the recommended interval. All patients should be advised that a history of pneumothorax should be regarded as a contraindication to scuba diving unless definitive surgical intervention has been undertaken.

How is the management different in secondary pneumothorax?

Observation is only recommended in very small pneumothoraces (less than 1cm) that are asymptomatic. Pleural aspiration can still be attempted in secondary pneumothorax if its size is less than 2cm and is associated with mild breathlessness at worst; but, in contrast to a patient with primary pneumothorax, the need for a full hospital admission may be avoided, but patients should be observed in hospital for up to 24 hours post procedure[19] even if the procedure is successful. Therapeutic aspiration is less likely to be successful in those with pre-existing lung disease, particularly in those aged over 50 years.[19] If an attempt at aspiration fails, the patient should proceed to intercostal drainage.

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid

Pleural Procedures: Good Clinical Practice[18]
• All doctors should be able to insert chest drains but must first observe and be observed in this practice (DOPS). Doctors must be signed off as competent in this procedure prior to performing without supervision.
• Unless in emergency, pleural procedures should not be performed out of hours.
• All procedures should be performed with aseptic technique.
• Prior to intervention for pleural effusion a recent CHEST X-RAY should be available and pleural USS guidance is strongly recommended.
• Non-urgent pleural procedures should be delayed until INR <1.5 in anticoagulated patients and platelets >50x10^9/l.
• The preferred site for pleural procedures, where possible, should be the 'triangle of safety'. This is bordered anteriorly by the lateral edge of pectoralis major, laterally by lateral edge latissimi dorsi, inferiorly by the line of the 5th intercostal space and superiorly by the base of the axilla.
• Written informed consent should be obtained in all non-emergency chest drain insertions.
• Analgesia should be considered as premedication and should always be available post procedure. Lidocaine 1% should be infiltrated prior to intercostal drainage.
• A chest drain may be withdrawn but never pushed in further due to the risk of introducing infection. Similarly a further drain should never be inserted through the same hole as a previous site.
• Drainage of fluid should be in a controlled manner to prevent complications of re-expansion pulmonary oedema.
• A bubbling chest drain should never be clamped.
• All chest drains should be managed on wards where the nursing staff are experienced in chest drain management.

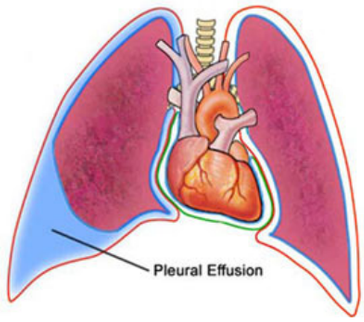
Table 6: Good pleural procedure practice

Test Yourself

Question 1

Which of the following is not a recognised cause of an exudative pleural effusion?

A: Parapneumonic effusion
B: Metastatic bronchogenic malignancy
C: Liver cirrhosis
D: Pancreatitis
E: Pulmonary embolus



Question 2

Which of the following statements on the investigation of pleural effusion is true?

A: Diagnostic pleural aspiration is necessary for all pleural effusions
B: Pleural fluid cytology is positive in 90% of cases of pleural malignancy
C: Pleural USS is required prior to aspiration only in effusions that are too small to accurately detect clinically
D: Flexible bronchoscopy should be performed in all cases of exudative effusions where malignancy is strongly suspected
E: The pleural fluid pH should be measured via blood gas analyser in cases of suspected pleural infection.

Question 3

Which of the following is not an indication for intercostal tube drainage in pleural infection?

A: Pleural fluid pH < 7.2
B: Frank pus aspirated from pleural space
C: Serum CRP > 100
D: Failure to improve despite adequate antibiotic therapy
E: Large parapneumonic effusion causing breathlessness

Question 4

Which of the following statements regarding spontaneous pneumothorax is false?

A: Symptoms correlate poorly with the size of pneumothorax
B: The presence of breathlessness is the most important influence in management
C: Observation is appropriate in small (<2cm) primary pneumothorax without breathlessness
D: The presence of pleuritic chest pain is an indication for intercostal drainage
E: After needle aspiration in secondary pneumothorax the patient should be observed as an inpatient for 24 hours

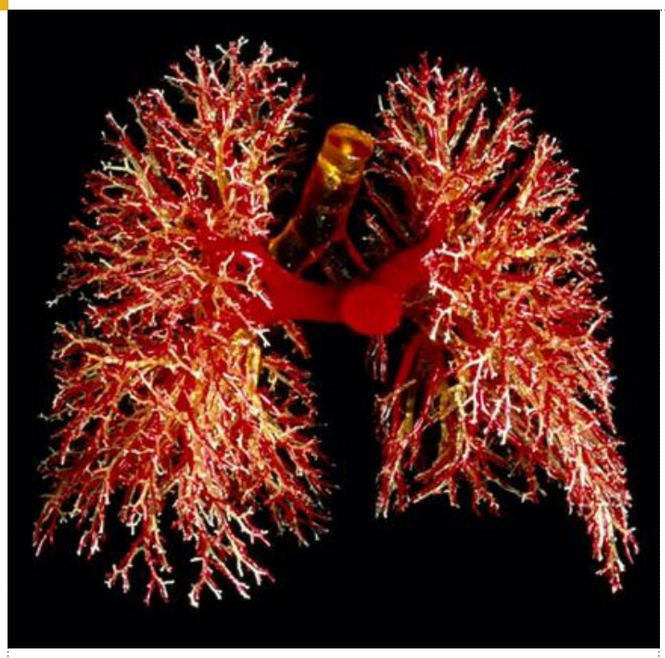
Question 5

Which of the following is an indication for surgical referral in spontaneous pneumothorax?

A: Second occurrence of pneumothorax on the same side
B: Failure to resolve after second needle aspiration
C: All cases of secondary pneumothorax
D: Failure to resolve after 48 hours of intercostal drainage
E: Patients who are due to fly within four weeks of occurrence

DISORDERS OF THE PLEURA – CASE BASED DISCUSSION

PA Reid and PT Reid



Answers

1. Answer C:
Parapneumonic and bronchogenic malignancy are by far the two commonest causes of exudative effusions. Pancreatitis along with other inflammatory conditions below the diaphragm (e.g. liver abscess) can cause exudative effusions. Pulmonary embolus can cause both exudate and transudate effusions. Liver cirrhosis is a common cause of transudate effusion and often occurs with ascites.

2. Answer E:
Bilateral effusions are commonly transudates and the cause may be obvious from the history and examination e.g. heart failure. Often further investigation is unnecessary and it may be more appropriate to treat with diuretics and reassess response. Pleural fluid cytology is positive in 60% of malignant effusions. Pleural USS is recommended prior to intervention in all cases of effusion. Bronchoscopy is not routinely indicated in pleural effusion. This should be performed if there is a suspicion of underlying mass or collapse on CHEST X-RAY or CT, a history of haemoptysis.

3. Answer C:
A rising or persistently elevated CRP may raise the suspicion of the development of a parapneumonic effusion in pneumonia or may be a marker of failure to improve but alone is not an indication for a chest drain.

4. Answer D:
The presence of symptoms is relevant in management of pneumothorax but dyspnoea is of more significance than pleuritic chest pain. The presence or absence of dyspnoea in pneumothorax can be the difference between observation and intervention.

5. Answer A:
A second occurrence of pneumothorax on the same side is an indication for definitive surgical intervention as there is an estimated 40% risk of recurrence. Thoracic surgery should be involved in cases where the pneumothorax fails to resolve despite adequate intercostal drainage rather than failed needle aspiration. The timing of this is uncertain but in practice tends to be around day 3 to 5. Secondary pneumothorax itself is not an indication in itself unless again it does not resolve with a chest drain. Unfortunately many people with chronic lung disease such as pulmonary fibrosis may not be fit for surgical intervention. Secondary pneumothorax has a higher mortality than primary at 10%. Planned air travel is not an indication. It is now recommended that patients do not fly for at least a week after successful resolution. Professionals at risk such as pilots or divers may be referred for surgical input after a solitary pneumothorax.

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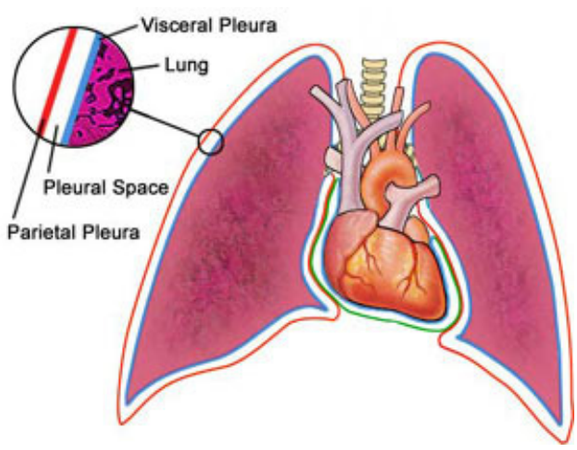
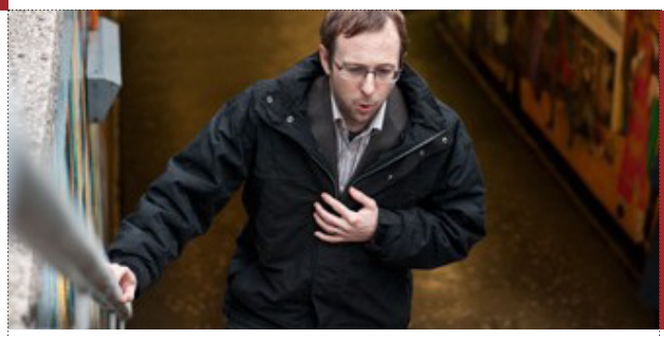


FUNCTIONAL AND PSYCHOLOGICAL ASPECTS OF BREATHLESSNESS

N Pargeter, L Stonehewer and AH Mansur



Functional and psychological aspects of breathlessness. Patient Management.

Acute dyspnoea or breathlessness is one of the commonest presenting complaints to emergency or acute medical departments. The causes vary widely from respiratory to cardiac or haematological diseases. However, functional disorders often associated with anxiety or depression or other psychological diseases can present with breathlessness. This is not uncommon, but often not appropriately diagnosed and mistreated with harmful side-effects, due to general lack of recognition of this aspect of breathlessness. Some of the common presentations are the clinical entities of vocal cord dysfunction (VCD), hyperventilation syndrome (HVS) and dysfunctional breathing (DB). Any of these may present alone or as an epiphenomena to another disease such as refractory asthma. Awareness of foundation doctors of these conditions and what would be required to make diagnosis and arrange treatment plans is crucial to the initiation of proper management and the avoidance of harmful inappropriate interventions. In this article we present some illustrative cases and provide general tips to foundation doctor trainees on this subject.

Case history one

A 26 year old woman, presented to a refractory asthma clinic with high maintenance/stress personality (there was history of childhood bullying at school and parental divorce). She had a history of mild exercise induced asthma treated with occasional short acting beta 2 receptor agonist inhaler since teen years and family history of atopy. At the age of 25 years she developed a sudden and stormy period of ill health, leading to an initial diagnosis of idiopathic anaphylaxis and refractory asthma.

For a period of 12 months she suffered very frequent attendances to accident and emergency (A&E) and acute medical wards including one intensive care and 2 high dependency unit admissions. However she did not require intubation or ventilation. During these acute episodes she was treated for presumed acute anaphylaxis/asthma with injected adrenaline, nebulises bronchodilators parental and oral corticosteroids.

The main features of these 'choking attacks' were cough, dyspnoea, throat tightening/closing down, feeling that something bad was going to happen, tight chest and inability to speak. There was no rash, lip or tongue swelling or facial oedema, but inspiratory and expiratory upper chest wheeze could be heard on auscultation. Peak expiratory flow rate (PEFR) was often normal as well as oxygen saturation (>97%). Spirometry was also normal with forced expiratory volume in one second (FEV1=99% predicted), forced vital capacity (FVC = 97% predicted), FEV1/FVC ratio = 89%.

She was treated for asthma and anaphylaxis with 250/25 µg seretide evohaler 2 puffs twice daily, montelukast 10mg once daily, cetirizine 10mg once daily, as required salbutamol 100 µg in addition to adrenaline auto-injector (Epipen 0.3mg) for emergency use. The treatment was ineffective in controlling daily symptoms or in preventing acute attacks. She had received multiple courses, and was considered for maintenance corticosteroids treatment. The substantial time off-work caused difficulty with her employer.

During assessment at a refractory asthma clinic, a skin prick test inadvertently provoked an acute attack which was observed by the medical team and appeared atypical of acute anaphylaxis or acute asthma. She displayed predominant upper airway wheeze and normal vital signs apart from sinus tachycardia (pulse = 110 beats /min). A planned second attack was provoked with skin prick test again (with full resuscitation measures available). During this provoked episode, nasendoscopy showed inspiratory vocal cord adduction and posterior diamond-shaped glottic chink, associated with inspiratory wheeze and coughing consistent with diagnosis of vocal cord dysfunction.

Once diagnosis was established, the patient received counselling and treated by specialised speech and language therapist (SLT), that included throat relaxation exercises and breathing manoeuvres "see below". The patient was prescribed Heliox cylinder (Oxygen 21%/Helium79% gas mixture), for acute symptoms relief at work or home. Whilst on holiday, the patient gained much confidence from successfully aborting an attack using SLT exercises, without resorting to Heliox. Symptoms became gradually less severe and less frequent with no further hospital admission. Stress was a major driver of her VCD attacks for which she received counselling. She has remained asymptomatic and off all asthma medication.

Case history two

A 49 year old woman, who worked as a college cleric, was diagnosed with asthma at the age of 17 years. Her mother and older sister had asthma. She was sexually abused as a teenager and physically assaulted by her first husband. She subsequently remarried and had two children. Her asthma dramatically worsened by age 36 and she stopped work due to ill-health at age 42.

FUNCTIONAL AND PSYCHOLOGICAL ASPECTS OF BREATHLESSNESS

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In the following two years, she reported approximately 60 A&E and acute medical admissions including 6 intensive care episodes and 2 intubation/ventilation. Of note her airway pressure was normal during mechanical ventilation. Blood gases were often normal. On background of chronic cough she experienced choking, sudden dyspnoea, upper chest and throat tightness, sensation of suffocation and poor response to asthma medication. Her treatment comprised of seretide 500/50µg 2 puffs twice daily, phyllocontin 450mg am, 250mg pm, as required salbutamol and ipratropium bromide nebulisers and maintenance dose of 10mg/day prednisolone (as well as monthly increases to 40mg/day).

She appeared cushingoid during examination with increased BMI at 32. Because of refractory symptoms bronchoscopy was conducted, during which symptoms were reproduced by Valsalva manoeuvre. A characteristic paradoxical vocal cord adduction during inspiration with posterior glottic chink was observed (see figure 1) in keeping with a diagnosis of vocal cord dysfunction.

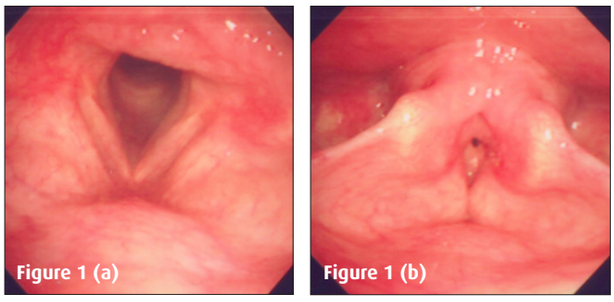

Figure 1
(a) showing vocal cord abduction during normal breathing
(b) paradoxical vocal cord adduction with posterior chinking during VCD attack

She received counselling and speech therapy (SLT) for treatment of VCD. The psychological counselling focused on coping strategies and handling of childhood abuse experience. SLT and Heliox helped her to control VCD attacks and general symptoms. There was dramatic reduction in hospital admissions and reduced exposure to oral steroids. However, because of late diagnosis and severity of underlying disease she continued to experience significant limitation to her quality of life.

Vocal Cord Dysfunction

Epidemiology and pathophysiology

VCD is a poorly understood condition characterised by episodic, sudden onset paradoxical vocal cord closure during inspiration (and sometimes expiration). The true prevalence of VCD in the general population is not known though it is more common in females than males (ratio 4:1), athletes and army recruits. It often co-exists with asthma and chronic cough (Table 1).

VCD was seen largely as a conversion disorder of psychogenic origin. The larynx is innervated by a complex neurological network and the association between stress and co-morbid psychology and VCD attacks strengthened this view. More recently it became apparent that VCD exists outside the conversion disorder prototype. Laryngeal closure is a normal physiological reaction to exposure to irritants (e.g. aspiration), but this reaction normally only lasts for few seconds. Acute (e.g. toxic fume inhalation) or recurrent irritation (e.g. repeated extreme cold air exposure) may lead to laryngeal hypersensitivity manifesting as vocal cord adduction and airflow limitation. Laryngeal hypersensitivity may form part of unified allergic airway syndrome with asthma and rhinitis. The association of laryngeal hypersensitivity with altered autonomic balance status maintained by central brain activity have been postulated to underlie development of VCD.

Table 1 - VCD prevalence in different patient groups

Patient Group	Prevalence %
Refractory asthma	5–10
Dyspnoea	2.8
Army recruits with stress-induced asthma	15
Olympic athletes	5
Childhood acute asthma#	14

#: presenting to emergency department. The reported mean age at VCD diagnosis is 14.5 yrs in children and 33 yrs in adults

Clinical Features

VCD and asthma share many common features and triggers (Tables 2 & 3). Getting a clear description of symptoms from the patient is key to diagnosis. When a patient describes difficulty breathing in with restriction at throat level, further investigation is warranted. VCD is frequently misdiagnosed and mistreated as asthma. Often a diagnosis of VCD is made after treatment for asthma stretching over a period of few years has been unsuccessful. These patients may display cushingoid features due to long-term high dose steroids.

Table 2 - Symptoms of Vocal Cord Dysfunction

Difficulty breathing in (and sometimes out)
Inspiratory (and sometime expiratory) wheeze and stridor
Dyspnoea
Cough
Tight throat / 'strangled' sensation
Episodic, sudden onset attacks
Symptoms difficult to reproduce in test environment

Table 3 - Common Triggers of Vocal Cord Dysfunction

• Cough	• Exertion
• Stress	• Food
• Reflux	• Laughter
• Inhaled Irritants	• Temperature change
• Smoke	• Allergy (rhinitis)

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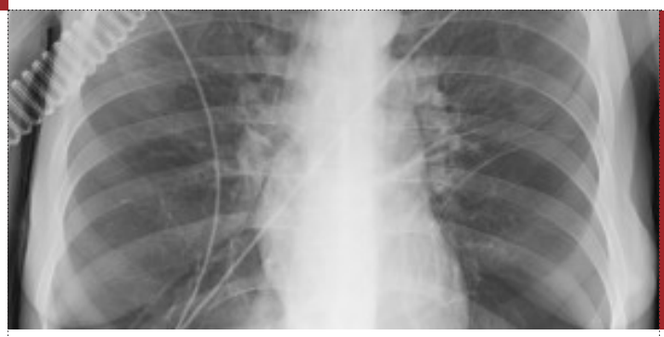
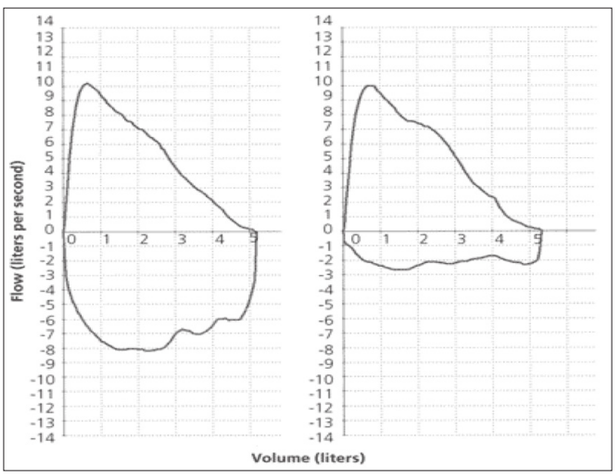


Functional and psychological aspects of breathlessness. Patient Management.

Assessment and Diagnosis of VCD

Direct visualisation of the larynx during nasendoscopy or bronchoscopy when symptomatic remains the gold standard test for VCD. (Figure 2). Characteristically, the anterior two thirds of the vocal cords close with a small posterior 'diamond-shaped' glottic chink remaining through which to breathe. VCD attacks are unpredictable and often difficult to reproduce in a controlled environment. Ideally, therefore laryngeal visualisation should be conducted during acute attacks or after symptoms provocation (e.g. inhalation of strong perfumes or after exercise depending on patients history). Assessment when asymptomatic usually show normal laryngeal function and does not exclude diagnosis. Flow-volume loops can show (Figure 3) truncation of the inspiratory limb reflecting variable extra-thoracic airway obstruction suggestive of VCD. However, lung function is frequently poorly tolerated and non-reproducible in patients with VCD. Normal flow-volumes loops are not sensitive enough to exclude diagnosis.



Treatment of VCD

Critical to VCD management is patient education. Video or photographic demonstration of cause of a patient's symptoms enables proper understanding and allows patient engagement with therapy. Identifying specific triggers and how to avoid them; techniques to prevent, control and resolve attacks as they occur form the mainstay treatment which is usually led by specialised Speech & Language Therapist working in close cooperation with respiratory physician, Ear Nose and Throat specialist and a psychologist.

Treatment of acute attacks

The treating physician should adopt a calm, reassuring manner, asking the patient to focus on expiration with an "S" sound that helps in diverting patient's attention. Sniffing and panting manoeuvres can abort acute attacks by inducing vocal cord abduction. Where hypoxaemia and hypercapnia has been excluded, sedation with benzodiazepines may help patient relaxation. Heliox gas mixture can alleviate symptoms by enhancing upper airway laminar air flow and reducing dyspnoea feeling.

Long term treatment

SLT and psychotherapy form the mainstay of VCD treatment. SLT teaches patients to relax upper airways and control the laryngeal area. The aim is to enable the patient to practice breathing techniques to abort or treat acute attacks. The role of the SLT extends to making diagnosis, identification and treatment of triggers and relaxation techniques. Psychotherapy includes management of stress and anxiety, psycho-behavioural therapy and coping strategies.

Key Points:

- VCD is a poorly understood condition, frequently masquerading and co-existing with asthma.
- Typically VCD attacks occur and resolve abruptly and do not respond to asthma medication.
- Visualisation of the larynx while symptomatic remains the gold standard means of diagnosis.
- Speech & Language Therapy and Psychotherapy are the treatments of choice for this condition.

Hyperventilation Syndrome and dysfunctional breathing

Prevalence and pathophysiology

Hyperventilation syndrome (HVS) is a debilitating condition that affects up to 10% of the population with female preponderance (female/male ratio = 7 to 1), has wide ranging symptoms and is defined as increased minute ventilation in excess of the body's metabolic demands. It has had many names over the years from Da Costa's Syndrome or Soldiers' Heart to dysfunctional breathing. Psychogenic dyspnoea or behavioural breathlessness are other terms indicating that hyperventilation is result rather than cause of HVS. HVS is frequently associated with panic disorders.

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Dysfunctional breathing is any variation from the normal breathing pattern (table 5). It is extremely common and in many cases totally symptom free. Causes vary from respiratory diseases such as bronchiectasis, asthma and chronic obstructive pulmonary disease; neurological disorders such as multiple sclerosis, muscular dystrophy and stroke; musculo-skeletal conditions such as kyphoscoliosis; psychological disorders and pregnancy.

A change in breathing pattern is a normal reaction to physical and emotional stress or strain and only becomes abnormal when it becomes symptomatic. Acute symptoms such as fainting are easily recognised but chronic symptoms can be insidious and hard to diagnose initially.

The cause of all HVS symptoms is not fully understood (Figure 4). Slight changes in CO2 levels cause blood and extra-cellular alkalosis, buffer depletion, cerebral glucose deficit, calcium imbalance, magnesium deficiency. These can cause cerebral and coronary vasoconstriction, bronchospasm, gut dysmotility and localised ischemia. Hyperventilation also stimulates sympathetic nervous system with increased adrenaline release, lactic acid production, and increased oxygen affinity to haemoglobin predisposing to relative tissue hypoxia.

Clinical features

Acute HVS usually presents dramatically with symptoms wide ranging such as pins and needles, dizziness, syncope, increased respiratory effort, bloating, muscle cramp, pain and pseudotetany (carbopedal spasm). The recognition of acute HVS in the patient presenting with acute dyspnoea may mimic acute asthma. Over use of asthma medication may exaggerate bronchodilation and lead to increasing over breathing and its consequential hypocapnia. Arterial blood gases inevitably show respiratory alkalosis. Failure to make appropriate diagnosis will lead to a cycle of repeat admissions which in severe cases can lead to unnecessary intubation and ventilatory support (Table 5).

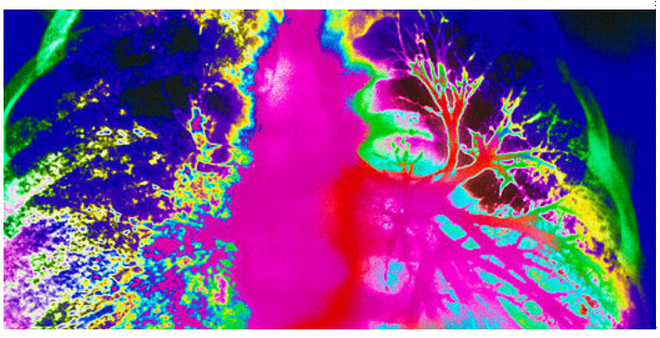
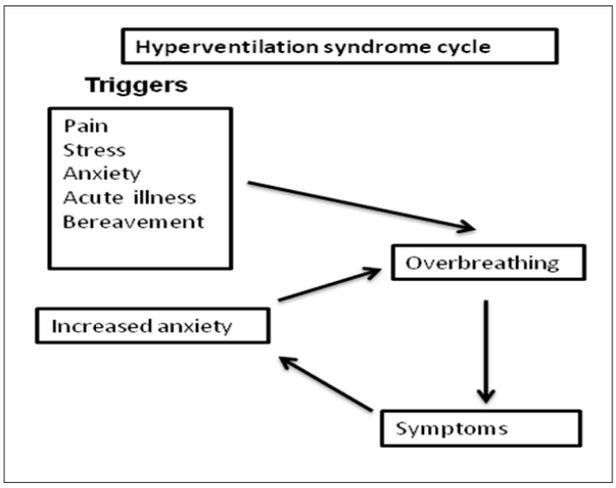


Table 5: A case of acute HVS	
Symptoms	Severe acute breathlessness, chest tightness and dizzy feeling Treated as acute asthma with no response.
Blood gases	PO2 = 18.3 kPa, PCO2 = 1.5 kPa, pH = 7.65, and HCO3 = 23.
Treatment	Relaxation physiotherapy, breathing control retraining

Figure 3



Chronic HVS

If acute HVS is not recognised and managed appropriately a pattern of fear and over-breathing quickly develops into a vicious cycle of increasing symptoms leading to decrease in function and fitness with associated depression and dependence on medical support. The cost to the patient in terms of quality of life is immense and the health costs will continue to spiral upwards with ever more expensive and invasive diagnostics leading to more expensive drugs.

The features chronic HVS are diverse and can manifest in many ways (Table 6), the most common are:

- Breathlessness: varied, undue and often described as "air hunger" or inability to take a satisfying breath in and usually not relieved by bronchodilators.
- Cough: unproductive, irritable.
- Fatigue: poor sleep and lack of concentration.
- Musculoskeletal: aches, pains and weakness.
- Neurological: pins and needles, dizziness.
- Gastrointestinal: irritable bowel syndrome.
- Cardiac: pseudo-angina.
- Signs of HVS: rapid speech pattern, frequent sighing, yawning, coughing or giggling (all ways of reducing CO_2), noisy breathing, inability to relax with poor posture and hunched shoulders.
- Characteristically patients have multiple complaints without much supportive physical evidence of disease.

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Diagnosis

Assessment of chronic HVS is both subjective and objective. Of the few validated objective measures available the Nijmegen Questionnaire (van Steeke et al. 1991) is quick and simple to use and is therefore perhaps the one used the most. The use of breath-hold as an indicator for intolerance to CO2 has not been validated. Blood gases may show reduced CO_2 level with increased compensatory renal excretion of HCO_3 to maintain normal pH.

Treatment

Traditional treatment of acute HVS using paper bag re-breathing is not recommended because of reported cases of death and suffocation. It is also unnecessary as effective reversal of respiratory alkalosis can be achieved by reassurance and explanation of how symptoms of HVS develop. It is essential to exclude potentially life threatening causes of hyperventilation such as acute renal failure, metabolic acidosis or pulmonary oedema.

Treatment of chronic HVS is usually delivered by specialised physiotherapists and comprises patient education of causes and effects of hyperventilation, breathing re-training, relaxation, management of underlying conditions such as pain and general advice on life-style. Often patients have an overinflated chest, using the upper thorax for breathing at a high lung volumes. Breathing retraining using a diaphragmatic technique helps exhalation and chest deflation and is usually effective in ameliorating symptoms of HVS. There is often a history of depression or anxiety which will require specialist psychological or psychiatric involvement. Careful use of benzodiazepines, beta-blockers and breathing retaining can help in reducing stress, hyperventilation attacks and chronic HVS symptoms.

Key Points

- HVS is a poorly recognised condition associated with multiple physical symptoms.
- HVS presents in acute and chronic forms.
- If unrecognised, many diagnostics and treatments are conducted unnecessarily and usually come back negative.
- HVS should be differentiated from tachypnoea which is a normal response to stimuli and often has no side-effects.

Further reading

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INVASIVE AND NON-INVASIVE VENTILATION

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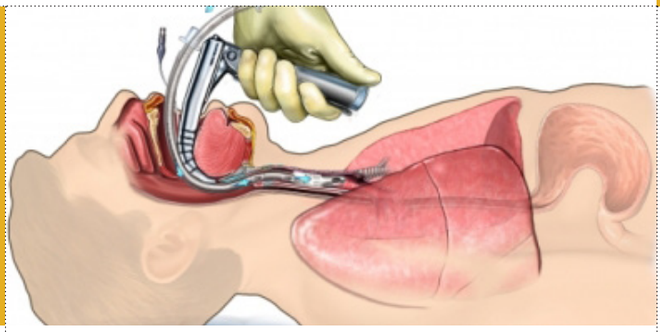
Good Clinical Care.



Abstract

Respiratory failure is one the commonest medical emergencies. Many patients improve with standard medical therapy but some need respiratory support with non-invasive or invasive mechanical ventilation. Bi-level non-invasive ventilation (NIV) is effective if used correctly for type 2 respiratory failure due to the exacerbations of chronic obstructive pulmonary disease but can be dangerous if used inappropriately. The use of NIV in other conditions such as pulmonary oedema is less established. Some of the dangers of NIV can be reduced by appropriate prior consideration of a plan in case NIV fails. Invasive ventilation is another option which protects against some of the problems of NIV but has its own complications. In this article we discuss these issues with reference to two illustrative cases.

Case One

You are asked to see Mrs B, a 64 year old lady in A&E with shortness of breath and wheezing. She is in significant respiratory distress, tachypnoeic with low finger-probe oxygen saturations. She is sitting upright on the bed using her accessory muscles of respiration. She has a past medical history of COPD and osteoporosis. She has been unwell with a purulent cough for the past few weeks. On auscultation there is reduced air entry bilaterally, scattered wheeze and a few crackles at the right lung base. Her pulse is regular at 102 bpm and blood pressure 126/88. GCS is 15/15.

She is immediately given salbutamol and ipratropium nebulisers, oral prednisolone and 35% O2 via a venturi mask followed by an ECG, chest radiograph and further assessment. The chest radiograph shows hyperinflated lung fields but no focal consolidation. Arterial blood gas (ABG) shows a pH of 7.30, pO_2 7.8, pCO_2 7.4, HCO_3 32 and BE of 3.4. An aminophylline infusion is started.

After one hour, a repeat ABG shows a pH of 7.26, pO_2 7.6, pCO_2 7.8 on 28% oxygen. Her finger probe O_2 saturation is 85%. What should you do? Would your plan be different if the chest radiograph showed pneumonia?

The patient has an exacerbation of chronic obstructive pulmonary disease (COPD) and is deteriorating with type 2 respiratory failure despite optimal medical management and controlled oxygen. What should you do? After senior review the decision is taken to start Non-Invasive Ventilation (NIV).

Definition Of Respiratory Failure
Type 1: paO_2 < 8.0 kPa on room air with low or normal $paCO_2$
Type 2: paO_2 < 8.0 kPa on room air with elevated $paCO_2$ > 6.0 kPa

Ventilation is a term used to describe the application of different levels of pressure during the patient's inspiration and expiration to aid movement of air into the lungs on inspiration. Most commonly different levels of positive air pressure are applied to the airway. It is non-invasive when given via a mask, nasal prongs or helmet (as compared to invasive mechanical ventilation when a pressurised flow of oxygen is through an endotracheal tube or tracheostomy). The development and role of NIV has become more prominent in the treatment of respiratory failure over the past decade.

Continuous positive airway pressure (CPAP) is the application of a flow of air at a constant pressure throughout both inspiration and expiration – it is not considered a true form of ventilation as it does not provide an increased pressure during the inspiratory phase to specifically increase air flow in to the lungs during inspiration. We will however discuss its use alongside NIV in the following paragraphs.

There is little standardisation between manufacturers of ventilators, which means that unfortunately different machines may have different names for similar modes of ventilation. NIV can also be called Bilevel Positive Airways Pressure (BIPAP). Commonly, the pressure during inspiration is called the Inspiratory Positive Airways Pressure (IPAP) and the pressure during expiration is called the Expiratory Positive Airways Pressure (EPAP) – see figure 1.

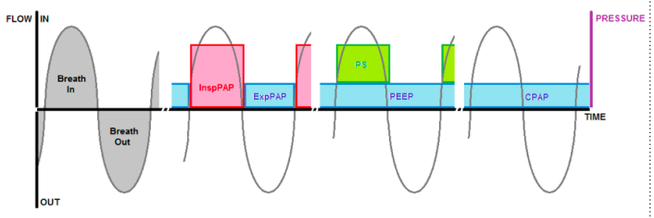


Figure 1: Diagram showing the different terminologies for pressure applied during ventilation and also CPAP.

InspPAP = Inspiratory Positive Airways Pressure, ExpPAP = Expiratory Positive Airways Pressure, PS = Pressure Support, PEEP = Positive End-Expiratory Pressure, CPAP = Continuous Positive Airways Pressure.

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The terminology used with invasive mechanical ventilation is often different. The low pressure supplied during expiration is called PEEP (positive end-expiratory pressure). During inspiration extra pressure (Pressure Support) is supplied on top of continuing PEEP. NIV is a well-established treatment for acidotic type 2 respiratory failure due to exacerbations of COPD.

How does NIV work?

The increased pressure during inspiration (the Pressure Support) causes an increased tidal volume for each breath with reduced work of breathing on inspiration. This increases the amount of air that moves through the lung with each breathing cycle, helping to bring oxygenated air to the alveolar surface and blow off carbon dioxide. It allows patients to take deep breaths without working so hard. The inspiratory pressure can help open up collapsed lung units, recruiting more lung surface for gas transfer.

The relatively low positive pressure during expiration (EPAP) also has benefits – it stops small airways collapsing on expiration and reduces work of breathing by moving it to a more compliant part of the pressure-volume curve.

Does it really work?

There is significant evidence to show that NIV is beneficial when used for patients in type 2 respiratory failure due to COPD. A Cochrane meta-analysis looking specifically at NIV for exacerbations of COPD with hypercapnic respiratory failure (compared with usual medical care) showed a significant improvement in mortality, reduced need for intubation and reduced length of stay.[1] For every 4 patients treated with NIV, 1 patient avoids intubation. The wealth of evidence for NIV in exacerbations of COPD under study conditions has sometimes seemed in contrast to many doctors' personal experience – this has led to national guidelines for the safe and effective use of NIV in exacerbations of COPD.[2] In particular, patients with severe acidosis (<7.26) or high complexity should have a low threshold for being intubated as the treatment failure rate is higher.

NIV is also used in patients with acute cardiogenic pulmonary oedema. A recent meta-analysis of NIV for acute cardiogenic pulmonary oedema showed that both CPAP and NIV reduce mortality though the result was only statistically significant for CPAP.[3] The lack of statistical significance for NIV was likely the result of smaller patient numbers. Both reduce the need for intubation. The 3CPO trial looked at patients presenting to Accident & Emergency with acute severe cardiogenic pulmonary oedema. It showed NIV and CPAP improved many end-points such as breathlessness and acidosis. However, there was no significant difference in the primary outcome of 7 day mortality when compared with standard oxygen therapy.[4]

It is therefore suggested that NIV can be used as an adjunct to medical therapy or in the event that pharmacological intervention fails, but not as a substitute for medical treatment. Although theoretically NIV improves CO_2 clearance better, studies have shown no difference in outcomes between NIV and CPAP for respiratory failure due to cardiogenic pulmonary oedema - if anything, CPAP is tolerated better and is less expensive.

Patients with respiratory failure due to chronic neuromuscular disease can experience benefit from NIV, however, bulbar weakness can cause problems. Home ventilation in these patients has been shown to improve long term survival. Another condition benefiting from NIV is obesity-hypoventilation syndrome – again long-term domiciliary NIV may be necessary. What is in common in these conditions that respond well to non-invasive ventilation is that the respiratory failure is due to an acute decompensation of chronic mechanical problems impairing their breathing. The patients are in respiratory failure but relatively haemodynamically stable.

Would your plan be different if the chest radiograph showed pneumonia?
There is conflicting evidence for the use of NIV in patients with pneumonia. These patients are often haemodynamically unstable and this can be worsened by positive pressure. Also their hypoxia is partly due to shunting of blood through consolidated lung and NIV will not improve this shunting. In one small study of NIV for community acquired pneumonia two thirds of patients went on to require intubation and invasive ventilation.[5] It should therefore be used in caution with these patients and preferably in an ITU setting where facilities to step-up treatment are available.

So how is it used?

The decision to use non-invasive ventilation always needs to be made carefully. Although it can be effective, particularly in exacerbations of COPD and pulmonary oedema, it does have complications. Most importantly it can fail to improve ventilation but delay necessary intubation while the patient continues to deteriorate. The positive pressure reduces venous return to the heart which is beneficial in left ventricular failure causing pulmonary oedema but in other conditions it can decrease cardiac output and blood pressure. The tight fitting mask can be very uncomfortable (see below) and can also stop the patient expectorating sputum.

Golden Rules For Successful Non-Invasive Ventilation

- Make sure the patient has a condition that is likely to respond to NIV.
- Firstly give appropriate medical therapy and controlled oxygen.
- Have a plan for what you will do if they fail on NIV before you start NIV.
- Invest time in explaining and starting the patient comfortably on NIV.

Before starting NIV on the ward make sure that the patient is a suitable candidate for NIV:

(1) they have type 2 respiratory failure with a respiratory acidosis due to a condition likely to respond to NIV;
(2) all medical therapy and controlled oxygen have been started and generally given an hour to work;
(3) there are no contra-indications to NIV.

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Also before starting NIV always have a plan for what you will do if they do not tolerate or fail to improve on NIV. Patients who fail on NIV can deteriorate very quickly so you need a plan before you start NIV. If your plan in the event of NIV failure is intubation on ITU (the next step up in management) then speak to ITU before starting NIV. Similar considerations must be made before starting a patient on CPAP.

Contra-Indications To NIV

- Unsafe airway including reduced conscious level and facial trauma
- Undrained pneumothorax
- Vomiting
- Inability to clear secretions
- Confusion / agitation
- Cardio-vascular instability
- Acute asthma

Once you have considered the above then you can start NIV. Explain the machine to the patient, select the correct mask size, fit the mask tightly but comfortably, and start the machine at low settings. The mask needs to be tight fitted to stop leakage (when assessing leakage make sure you don't block the mask expiratory port). Typical settings to start the patient on are an inspiratory pressure of 15cm H_2O and expiratory pressure of 5cm H_2O. Supplemental oxygen can be entrained through the NIV circuit to achieve desired oxygen saturations.

A repeat blood gas must be checked after one hour.

Non-invasive ventilation was started with an IPAP of 15 cm H_2O and EPAP of 5 cm H_2O with 1L/min supplemental oxygen. ABGs after one hour showed slight improvement with pH of 7.28, pO_2 8.1, pCO_2 7.4 on NIV 15/5 with 1L O_2 entrained oxygen.

Based on how well the patient is tolerating NIV and any improvement on ABGs the settings can be adjusted. You should see the patient taking deeper breaths on NIV and the machine responding in time with the patient's breaths (synchronising well). Increasing IPAP will help to blow off CO_2 and improve a respiratory acidosis as long as it is tolerated. Excessively high pressure should be avoided as it can cause trauma to the lungs.

Repeat ABGs one hour later showed a pH of 7.31, pO_2 8.2 and pCO_2 6.9.

ABGs after one hour should show some improvement but it will take many hours for the blood gasses to fully correct. The patient should stay on NIV for as much of the next 24 hours as possible with breaks for medical therapy, comfort, and to eat & drink. Then the patient's time each day on NIV can be reduced over the next few days (staying on NIV each night).

For some patients as the underlying acute illness is treated their ability to breathe improves and after a few days they no longer have hypercapnic respiratory failure and do not need NIV. Other patients have severe underlying disease and although the respiratory acidosis will resolve the patient will remain in hypercapnic respiratory failure. Specialist centres can assess these patients for long-term domiciliary non-invasive ventilation.

Case Two

A 78 year old man is admitted with acute community acquired pneumonia. Chest radiograph shows dense right lower lobe pneumonia and a few patches of consolidation in the left lung. Oxygen saturations on 60% O_2 via a venturi mask are 88%, blood pressure is 98/68 and heart rate is 124 bpm. The patient is managing to take deep breaths and talk short sentences. The patient is given intravenous antibiotics and fluids. After one hour the blood pressure and heart rate have improved, oxygen saturation is 91% on 60% O_2 but the patient is tiring with rapid shallow breaths. ABGs show a pH 7.36, pO_2 7.8 and pCO_2 4.6. Should you give the patient NIV?

There is no reason to give the patient NIV – they have type 1 respiratory failure not type 2 respiratory failure. In fact NIV may well be detrimental as most NIV machines cannot supply the high flow oxygen this patient is requiring. The patient is critically unwell and needs high dependency support.

The patient is discussed with the intensive care team and transferred to the High Dependency Unit and started on Continuous Positive Airways Pressure (CPAP) at 7.5 cm H_2O with 75% entrained oxygen.

CPAP is started as it decreases the work of breathing, allowing the patient to breathe easier and helping to hold open the small airways. High-flow oxygen (high percentages of oxygen) can be delivered by CPAP machines. A similar tight-fitting mask is used in CPAP and NIV.

After one hour the patient is reviewed. He is now drowsy, oxygen saturations are falling as is his blood pressure. He is intermittently agitated and pulling at the mask.

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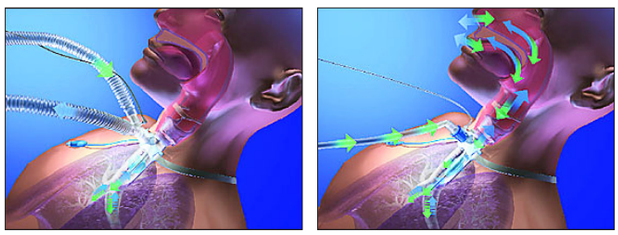

When NIV or CPAP fails there are only really three choices – intubation with invasive ventilation, stopping NIV / CPAP but continuing medical therapy, and stopping NIV / CPAP but starting palliation. If the patient is a candidate for intensive care or resuscitation in the event of cardiac arrest then intubation should be the next step. The option of stopping NIV / CPAP but continuing medical therapy is often difficult as the patient is likely to deteriorate.

The patient is intubated and started on invasive ventilation with a PEEP of 7.5 and Pressure Support of 15. He is sedated so that he can tolerate the endotracheal tube. His blood pressure drops and he is started on inotropes. His own breathing pattern interferes with the supported ventilation and he is paralysed for mandatory mechanical volume controlled ventilation. Over the next few days he initially improves but at one week he is still requiring significant pressure support. As slow weaning is expected he has a tracheostomy which allows sedation to be reduced and faster weaning off the ventilator.

Invasive ventilation by endotracheal tube has advantages. It maintains a safe airway, allows precise ventilator control, high pressures and high flow oxygen, but it also has disadvantages. Endotracheal tubes require heavy sedation to be tolerated. This is possible as the tube also maintains a safe airway but heavy sedation reduces the patient's blood pressure and their ability to cough. Sick patients often become haemodynamically unstable after intubation, requiring inotropes, and can deteriorate before improving. Non-invasive ventilators are nearly always used in a patient triggered mode providing supplemental inspiratory pressure when the patient themselves starts a breath in.

Invasive mechanical ventilators are used in different modes depending on circumstances. If the patient is doing well then the ventilators are used in a patient triggered mode. However if the patient is not breathing on their own (is apnoeic) then pressure-controlled or volume-controlled ventilation at a mandatory rate is necessary. If their own breathing is synchronising poorly with the machine causing poor ventilation then they need to be paralysed for mandatory controlled ventilation. The sedation for tube tolerance often slows down their recovery – if the patient has a tracheostomy then sedation can be lightened and recovery may be faster.

Summary

Non-invasive ventilation, CPAP and invasive ventilation are vital tools for treating unwell patients in respiratory failure. However they all have complications. NIV is a successful treatment for type 2 respiratory failure with respiratory acidosis due to exacerbations of COPD but certain golden rules must be followed to use NIV safely.

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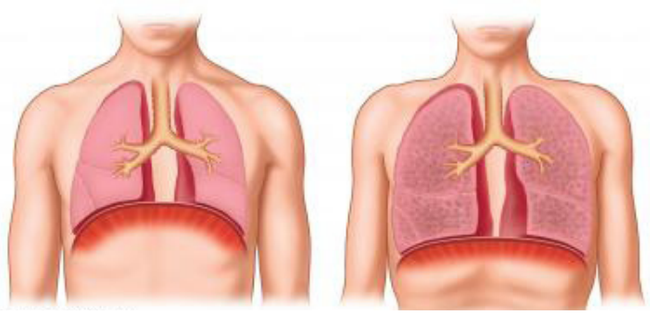
Assessment Questions

1. A 63 year old man with known emphysema is admitted by ambulance. He has severe breathlessness, cough and wheeze that has worsened over the last week. Initial arterial blood gasses on 8L O_2 via mask are: pH 7.29, paO_2 14.8, $paCO_2$ 8.7. Which of the following is not an appropriate part of initial management:

a. Nebulised salbutamol
b. Oral prednisolone
c. Nebulised ipratropium
d. Non-invasive ventilation
e. Controlled oxygen



INVASIVE AND NON-INVASIVE VENTILATION

K Panesar, P Pfeffer and H Makker

2. A 32 year old lady with no past medical history is admitted with a short history of a fever and cough of green sputum. On presentation she is drowsy GCS 9/15, her blood pressure is 94/62, heart rate 132 bpm and hypoxic. A chest radiograph shows diffuse consolidation. Arterial blood gasses on 10L O_2 via a non-rebreathing bag and mask are: pH 7.27, paO_2 9.2, $paCO_2$ 6.8, BE -4.8. What is the most appropriate route for oxygen delivery in her case:

a. Bi-level non-invasive ventilation
b. Mechanical ventilation via an endotracheal tube
c. Continuous positive airways pressure by mask (CPAP)
d. High-flow oxygen via non-rebreathing mask
e. High-flow humidified oxygen via mask

3. You are reviewing a patient on the respiratory ward with a medical student. The patient is on NIV with an IPAP of 15 and EPAP of 5. The student has recently done their intensive care attachment and asks how these relate to the Pressure Support (PS) and PEEP settings used on ICU. You reply the IPAP & EPAP correspond to:

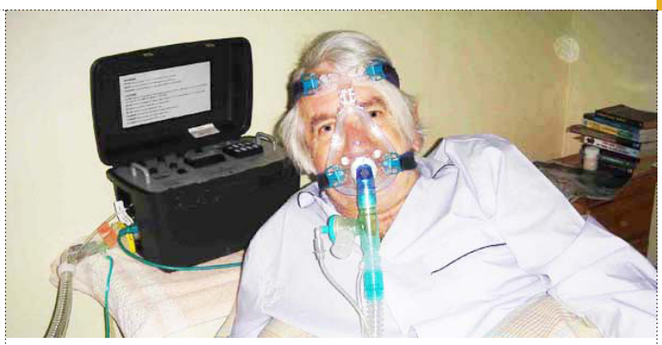
a. PS 10, PEEP 5
b. PS 15, PEEP 5
c. PS 20, PEEP 5
d. PS 5, PEEP 10
e. PS 7.5, PEEP 7.5

4. Which of the following is a contra-indication to non-invasive ventilation:

a. Previously broken nose
b. Pneumothorax with surgical chest drain in situ
c. Nausea and vomiting
d. Tachycardia
e. Undrained pleural effusion

5. An elderly lady with an exacerbation of COPD is breathless with a respiratory acidosis despite optimal medical therapy and controlled oxygen. She is a good candidate for NIV but is concerned whether she will tolerate the mask given her claustrophobia. What is the best way to manage this situation:

a. Sedate her with lorazepam so she is relaxed and accepts NIV
b. Spend time explaining the mask to her and gently introducing her to NIV with low pressures before increasing to full pressures
c. Start NIV without sedation but restrain her if she does not tolerate NIV and tries to remove the mask
d. Sedate and intubate her for invasive ventilation
e. Try CPAP instead of NIV as this may be better tolerated



Answers

1. Answer: d. This gentleman has an exacerbation of COPD. Initial management even in the presence of a respiratory acidosis is good medical therapy and controlled oxygen. Non-invasive ventilation should only be considered if it is needed after medical therapy has been started.

2. Answer: b. This lady has pneumonia and is critically unwell with multi-organ dysfunction. She needs ventilatory support. Non-invasive ventilation would be dangerous given her drowsiness and would likely cause further haemodynamic compromise. She needs invasive ventilation and likely haemodynamic support with inotropes on the intensive care unit.

3. Answer: a. The PEEP setting corresponds to EPAP. Pressure Support is the difference between the IPAP and EPAP.

4. Answer: c. Vomiting is a contra-indication to NIV as the tight mask means the vomit is trapped in and around the mouth, and may well be inhaled into the lungs. A drained pneumothorax is not a contra-indication as long as the drain is working. Tachycardia in itself is not a contra-indication to NIV although it should prompt you to assess whether the patient is haemodynamically stable.

5. Answer: b. She needs ventilatory support with a higher pressure on inspiration, rather than CPAP, as she has type 2 respiratory failure with a respiratory acidosis. The cause of her respiratory failure is an exacerbation of COPD – a pathology known to respond well to NIV. Although she may go on to need invasive ventilation, it would be wrong not to try NIV as invasive ventilation has its own complications. Sedation would be wrong as it may worsen her respiratory failure and make her prone to aspiration. Restraint of patients intolerant of NIV is completely unacceptable. The best way to get patients to tolerate NIV is spending time explaining and introducing them to the mask and sensation of positive pressure.

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MANAGEMENT OF ACUTE TYPE 2 RESPIRATORY FAILURE

S Paramothayan

Management of Acute Type 2 Respiratory Failure. Patient Management.

Abstract

Acute type 2 (hypercapnic) respiratory failure is a potentially life-threatening complication that is more likely to develop in patients with certain underlying conditions. The morbidity and mortality from the consequent disturbance in acid-base balance can be significant. In hospital it can develop as the result of inappropriate oxygen therapy and is therefore often preventable. Awareness of those at risk and an understanding of the principles of oxygen therapy can prevent it from developing in many cases. Patients with type 2 respiratory failure may develop confusion, irritability and decreased consciousness although the diagnosis can only be made by arterial blood gas (ABG) interpretation. The precipitating cause can be determined by routine investigations, including chest X-ray and bloods tests. The immediate management includes treatment of the underlying cause, careful prescribing and monitoring of oxygen therapy (by serial ABGS) and the commencement of non-invasive positive-pressure ventilation (NIPPV), usually Bi-level Positive Airways Pressure (BiPAP), the use of which is supported by evidence from randomized controlled trials (RCTs) and included in national guidelines. Although NIPPV has significantly improved mortality and morbidity in patients with type 2 respiratory failure, there are contraindications. When BiPAP is contraindicated or not tolerated, respiratory stimulants can be administered. As many patients who develop type 2 respiratory failure have severe, chronic disease, there are ethical issues regarding escalation of treatment and invasive ventilation in the Intensive Care Unit (ICU).

Definitions

Hypoxaemia is arterial oxygen level that is below normal and can result in hypoxia. Hypoxia is a reduction in the oxygen delivery to tissues despite adequate perfusion.

Respiratory failure is due to inadequate gas exchange resulting in abnormal oxygen (O_2) and carbon dioxide (CO_2) levels in blood and can be acute or chronic.

Respiratory failure is defined as hypoxaemia, with a partial pressure of oxygen (PaO_2) of < 60 mmHg or 8.0 kPa. Type 1 respiratory failure is hypoxaemia with normo or hypocapnoea and can be the result of any acute respiratory illness, such as pulmonary embolus, acute asthma, heart failure or pneumonia.

Type 2 respiratory failure is defined as hypoxaemia (PaO_2 < 60 mmHg or 8.0 kPa) with hypercapnoea, with a partial pressure of carbon dioxide (pCO_2) of > 48 mmHg or 6.5 kPa. Patients who develop type 2 respiratory failure are at risk of developing respiratory acidosis (pH < 7.35) which can be life-threatening.

	Normal	Type 1 Respiratory Failure	Acute Type II Respiratory Failure
PaO_2 mmHg (kPa)	80-100 (10.5-13.3)	<60 (8.0)	< 60 (8.0)
$PaCO_2$ mmHg (kPa)	35-45(4.5-6.0)	35-45 (4.5-6.0)	>48 (6.5)
pH	7.35-7.45	7.35-7.45	<7.35
HCO_3^- mmol/L	24	22-26	22-26

Table 1 depicts the measurements of PaO_2, $PaCO_2$, pH and bicarbonate (HCO3-) in normal subjects and those with Type 1 and Type 2 respiratory failure.

Case Presentation

A 73 year old man was admitted to hospital with an exacerbation of his severe COPD (FEV1 25% predicted). He was on maximal therapy and 2L of oxygen via a concentrator at home. Clinical examination and investigations confirmed a left basal pneumonia. As he was hypoxic, he was given 4L oxygen via nasal cannula with no documentation of his ABGS on air. ABGS done 20 minutes later were: PaO_2 59 mmHg (7.84 kPa), PCO_2 of 78 mmHg (10.4 kPa), pH of 7.31 and HCO_3^- of 22.3 mmol/L indicating CO_2 retention and acute type 2 respiratory failure. He was commenced on intravenous antibiotics and fluids, regular nebulisers, corticosteroids and controlled oxygen via a 28% venturi mask, with a target oxygen saturation range of 88%-92%. He improved slightly but ABGS showed rising CO_2 levels and a drop in pH. He was commenced on BiPAP with improvement in his clinical condition and ABGS over the next 12–24 hours. The BiPAP was weaned off gradually and stopped after 48 hours, with the patient maintaining oxygen saturations between 88-92%. He was discharged home after a week on oral antibiotics and oral corticosteroids.

MANAGEMENT OF ACUTE TYPE 2 RESPIRATORY FAILURE

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The Regulation of Breathing

The respiratory centre consists of neurones in the medulla which produce automated breathing activity under the regulation of chemical and physical reflexes. This can be overridden by voluntary cortical control.[1]

Carbon dioxide has a major influence on the control of breathing. Pfluger (1868) was the first to show that the CO_2 content of arterial blood affected breathing in animals and Haldane and Priestley (1905) later established that the respiratory centre was extremely sensitive to small changes in alveolar CO2 concentrations. The chemoreceptors on the anterolateral surfaces of the medulla are responsible for the majority of the response to inhaled CO_2, which crosses the blood-brain barrier and are very sensitive to hydrogen ions (H+) which directly increase ventilation.[1]

CO_2 is carried in blood dissolved in plasma in equilibrium with HCO_3^-, and is important in buffering the plasma. The Henderson-Hasselbalch equation shows this:

$$CO_2 + H_2O \overset{CA}{\rightleftharpoons} H_2CO_3^- \rightleftharpoons H^+ + HCO_3^-$$

The peripheral chemoreceptors in the carotid and aortic bodies are also sensitive to CO_2 and pH but are activated substantially only when there is a significant fall in the O_2 level of arterial blood (< 60 mmHg) and not important under normal physiological conditions.[2]

Patients with type 2 respiratory failure have chronically elevated levels of CO_2 in their blood and in the extracellular fluid surrounding the central chemoreceptors in the respiratory centre, which become relatively insensitive to the raised levels. The response to hypoxia by the peripheral chemoreceptors becomes the key stimulant to breathing. Correcting the hypoxia by giving too much oxygen can stop the hypoxic drive and worsen the hypoventilation, eventually resulting in respiratory arrest.

Diagnosis of Type 2 Respiratory Failure

It is important to have a low threshold of suspicion of patients who may be at risk of developing type 2 respiratory failure. Generally patients will be hypoventilating rather than hyperventilating so may not present with an increased respiratory rate or appear dyspnoeic. However, patients who are tachypnoeic may become tired and thus begin to retain CO_2. Symptoms and signs of CO_2 retention include drowsiness, confusion, irritability, a CO_2 retention flap, a bounding pulse (caused by vasodilation) and ultimately coma and death when the CO_2 level rises to very high levels. Acute respiratory failure can develop within hours: there is insufficient time for the renal buffering system to work and the pH drops. Chronic respiratory failure develops over several days allowing the kidneys to compensate by excretion of carbonic acid and reabsorption of bicarbonate. The pH is only slightly reduced.

	PaO_2	$PaCO_2$	pH	HCO_3^-
Acute Respiratory Acidosis	↑	↑↑	↓↓	Normal
Compensated (Chronic) Respiratory Acidosis	↑	↑	Normal but <7.40	↑
Metabolic Acidosis	Normal	Normal	↓	↓
Compensated Metabolic Acidosis	Normal	Normal or ↓	Normal but< 7.40	↓

Table 2 gives a quick and simple guide to working out ABGS in acute and chronic respiratory and metabolic acidosis.

Immediate investigations include a chest X-ray to exclude pneumothorax and infection, measurement of oxygen saturation and ABGS, if possible on air as a baseline. The initial ABG measurement will act as a guide to how much oxygen should be prescribed. Further regular ABGS once the patient is commenced on oxygen is compulsory.

Patients at risk of Type 2 Respiratory Failure

1. Chronic Lung Disease: Chronic Obstructive Pulmonary Disease (COPD), severe chronic asthma, bronchiectasis (including cystic fibrosis)
2. Chest Wall disease: kyphoscoliosis, thoracoplasty
3. Neuromuscular disorders: muscular dystrophy, motor neurone disease, spinal cord injury
4. Obesity hypoventilation
5. Reduced central nervous system stimulation: post anaesthetic, narcotics and sedatives

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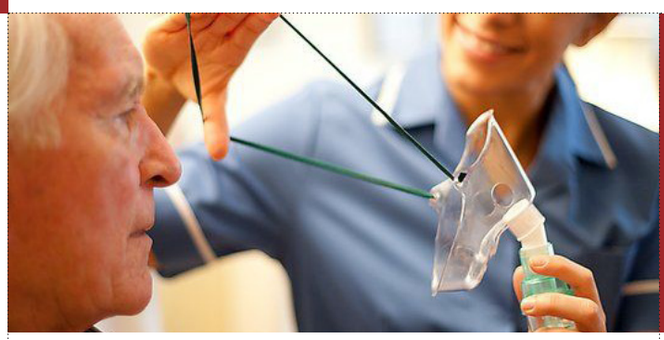

Management of Acute Type 2 Respiratory Failure. Patient Management.

Immediate Management of Type 2 Respiratory Failure

Once it has been established, on the basis of ABGS, that the patient has type 2 respiratory failure it is essential to treat it without delay. This includes managing the underlying condition with bronchodilators, antibiotics, corticosteroids, theophyllines, diuretics and anticoagulants to prevent veno-thromboembolic disease.

The key point in the management of type 2 respiratory failure is the use of controlled oxygen, which should be prescribed on the drug chart. Controlled oxygen should be given by the use of a venturi (fixed performance) mask, which gives controlled inspired oxygen at 24%, 28%, 35% or 40% oxygen. These are colour coded to make it easier to identify which one to use. If the patient is tachypnoeic with a respiratory rate of > 30 breaths/minute, the oxygen supply should be increased by 50%: this does not increase the amount of inspired oxygen. If patients are unable to tolerate a venturi mask then small concentrations of inspired oxygen can be given by nasal cannula. The aim in these patients is to maintain the oxygen saturation between 88%-92%. Once the patient has been prescribed and commenced on oxygen therapy, the ABG should be repeated in twenty to thirty minutes and the oxygen prescribed adjusted as appropriate.

Despite optimal management of the underlying condition, careful oxygen therapy and monitoring, some patients will deteriorate, will retain CO2 and the respiratory acidosis will worsen. These patients will need to be commenced on NIPPV usually with a BiPAP machine and should ideally be managed in a respiratory High Dependency Unit (HDU) by trained doctors and nurses. Patients may require supplemental oxygen together with the BiPAP in order to correct their hypoxaemia without worsening their CO2 level and acidosis.

Oxygen Therapy and Monitoring

Oxygen is a drug and must be prescribed, just like any other drug. Oxygen is indicated for all patients with hypoxaemia but not for breathlessness in the absence of hypoxaemia. Hypoxia (PaO_2 < 60 mmHg or 8.0 kPa) must always be corrected to avoid the consequences, which includes respiratory arrest.

The British Thoracic Society (BTS) Oxygen Guidelines, with agreement from 21 other societies, including the British Association for Emergency Medicine, British Cardiovascular Society and the Royal College of Anaesthetists have been disseminated nationally.[3]

For most patients, even those who are acutely unwell, the aim is to maintain the oxygen saturation between 94% -98%. For those at risk of hypercapnic respiratory failure, the target saturation range should be maintained between 88% - 92%. Oxygen should not be prescribed to those with breathlessness without hypoxaemia, except in the palliative care setting.

Non-invasive positive-pressure ventilation (NIPPV)

Negative-pressure tank-type ventilators were first developed by Dalziel in 1832. Drinker-Shaw in 1928 used the iron lung for patients with respiratory failure secondary to poliomyelitis and the tank ventilator was developed by Emerson in 1931.1,4

Non-invasive positive-pressure ventilation (NIPPV) has revolutionised the management of type 2 respiratory failure in the past two decades and is the treatment of choice for patients who have not responded to optimal medical treatment. NIPPV reduces the respiratory rate and dyspnoea, increases tidal volume, reduces the work of breathing, improves oxygenation whilst allowing CO2 to be blown off, thus improving the acidosis. Improvements can be seen within a few hours.[2]

Prior to the introduction of NIPPV, patients required invasive ventilation on ICU with resulting complications.[5] NIPPV is also indicated for patients who are slow to wean from ventilation[6] and reduces the total length of time on a ventilator and reduces mortality.[7]

Several RCTs have shown that patients with type 2 respiratory failure commenced on BiPAP had reduced need for endotracheal intubation, had lower complication rates, lower mortality and shorter stay in hospitals compared to usual care.[8,9,10,11] This applied to respiratory failure from different aetiologies,[9] but especially secondary to COPD.[10,11]

MANAGEMENT OF ACUTE TYPE 2 RESPIRATORY FAILURE

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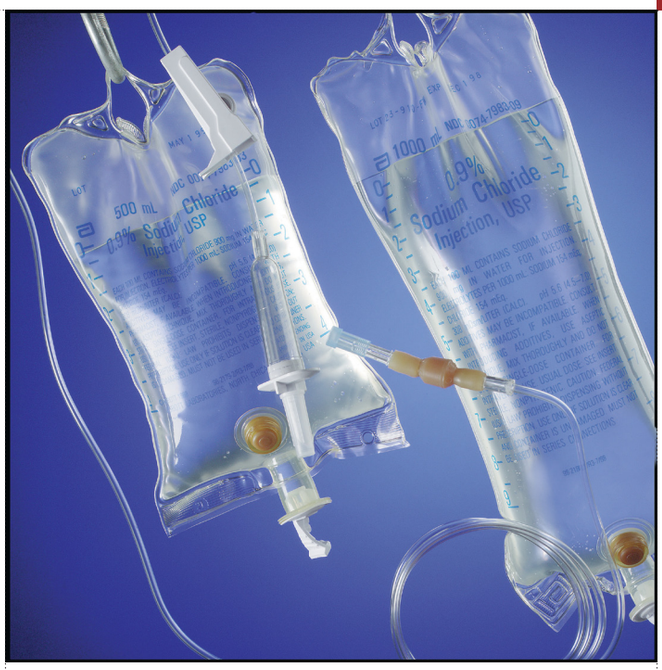
The Inspiratory Positive Airways Pressure (IPAP) which blows off the CO_2, is commenced at around 10 cm water (H_2O), and can be increased incrementally by 2 cm up to a maximum of 24 cm H_2O if there is persistent hypercapnia. The Expiratory Positive Airways Pressure (EPAP) is set between 4-10 cmH2O and improves oxygenation. The number of breaths per minute (BPM) is set between12–18 in the patient flow-triggered/time-trigger (S/T) mode. Monitoring of ABGS is essential and the limiting factor may be patient tolerability. The exact settings of the BiPAP will depend on the individual patient and includes factors such as the size of the patient and the severity of bullous disease.

There are a variety of masks. Orofacial and nasal are the commonest and come in small, medium and large sizes. Measurements should be taken to ensure that the mask fits properly. This will improve compliance, prevent the leakage of air (which will compromise the close circuit functioning of the system) and reduce pressure sores and skin lacerations from developing in areas of close fitting, such as the bridge of the nose. Other types of patient-ventilator interfaces include mouthpieces, nasal pillows, total face masks and helmet devices. Patients who feel claustrophobic should be given reassurance, encouragement and frequent (but short) breaks. Patients can become dry, so will need intravenous fluids, humidification and nasal saline. Gastric insufflations, aspiration and pneumothorax are rare complications.

Most patients with type 2 respiratory failure will require supplemental oxygen whilst on BiPAP. This is given through a port on the mask. The amount given depends on the level of hypoxia on the ABG. It must be emphasised that patients commenced on BiPAP need to have regular ABGS with adjustment of the oxygen given and of the BiPAP settings. Patients should be continued on BiPAP until their type 2 respiratory failure resolves and their acidosis improves. Patients are often weaned off BiPAP slowly, with breaks off BiPAP getting longer and longer until they no longer require it.

It is important to be realistic about the use of BiPAP in patients with severe type 2 respiratory failure. Patient selection is essential: patients who are ill but not critically ill are likely to benefit. Factors predicting a successful outcome include a cooperative patient with normal neurological function, a moderately high APACHE II score (acute physiology and chronic health evaluation) and a pH > 7.10.2 If the patient deteriorates despite optimal therapy there should be a clear decision regarding the ceiling of treatment. If it is felt that the patient is a candidate for invasive ventilation then referral should be made without delay.

Contraindications to BiPAP include confusion (with the inability of the patient to protect his airway), coma, vomiting, severe bullous disease, pneumothorax, severe hypotension and unstable cardiac status.



Respiratory Stimulants

Doxapram is a respiratory stimulant which increases the tidal volume and respiratory rate by stimulating the respiratory centre in the medulla. Although not used as first line treatment, Doxapram can be used in patients with type 2 respiratory failure who have respiratory acidosis, who have a contraindication to BiPAP, who are unable to tolerate BiPAP and/or have a reduced conscious level. Doxapram should be initiated after consultation with a senior doctor who has experience in using the drug. Doxapram is given intravenously at 1-3 mg/min and usually for short periods of time. Careful monitoring of the patient will be required.

Prevention of Type 2 Respiratory Failure

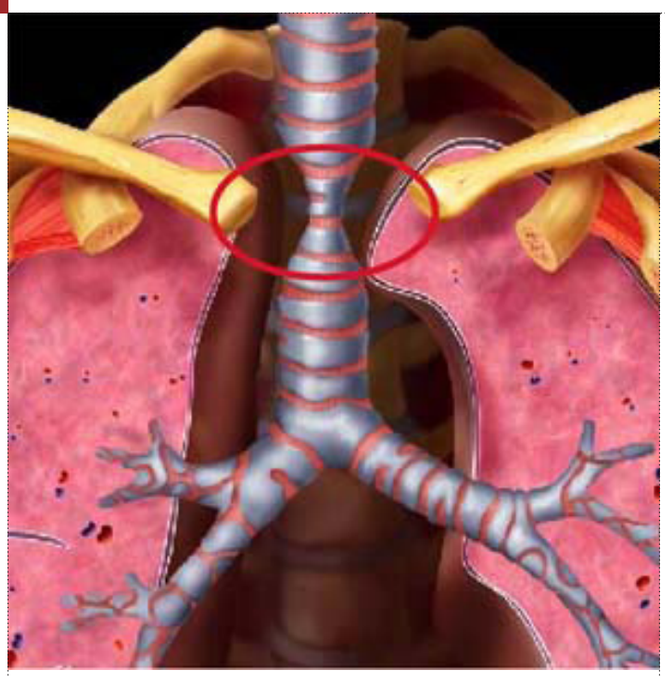
The risk of acute type 2 respiratory failure can be reduced by educating all healthcare professionals of those potentially at risk and by prescribing and monitoring oxygen therapy carefully.

The British Thoracic Society (BTS) Audit on oxygen prescribing and monitoring in 2008 highlighted concerns regarding the inappropriate prescription and monitoring of oxygen therapy.[13] The BTS Guidelines (2008) have been disseminated to all trusts with recommendations to complete regular audits to ensure compliance.[3] The National Patient Safety Alert has also emphasised the risk of oxygen therapy which can result in the development of type 2 respiratory failure.

Patients who are identified as at risk of developing type 2 respiratory failure should be made aware of this, given written information, an alert card specifying how much oxygen they should be given and in some instances given the appropriate venturi mask to use at home on in transit to hospital via ambulance.

MANAGEMENT OF ACUTE TYPE 2 RESPIRATORY FAILURE

S Paramothayan



Ethical Issues

Many patients who present with type 2 respiratory failure have exacerbations of severe COPD, possibly as a result of respiratory infections, which can be reversed with appropriate treatment. They will recover if their respiration is supported over the critical period. However, there are patients with end-stage COPD, often with a poor quality of life, who have a poor prognosis and who may not survive such an episode.

Most patients with severe COPD and type 2 respiratory failure are not considered suitable for ventilation on the Intensive Care Unit (ICU). Prior to the introduction of NIPPV most of these patients would have died without any form of ventilation or after intubation and ventilation.[2] These days, most patients would have a trial of BiPAP, often on a Respiratory high dependency unit (HDU), with a better prognosis.[2]

One of the most difficult decisions for doctors is whether to continue treating patients who are extremely unwell and who are not suitable for ventilation on ICU. In order to make this decision it is useful to have information about the patient which includes their pre-morbid state, their daily level of function (including exercise capacity), their performance status, whether they are on home oxygen and home nebulisers, their baseline spirometry (indicating severity of COPD), the number of exacerbations, the number of hospital admissions in the past year and their age.[6] Other factors which are relevant include significant co-morbidity and the wishes of the patient and the family.

Ideally the decision regarding the ceiling of treatment in patients with end-stage COPD should be made prior to an acute admission after clear and detailed discussion with the patient and their family. There should be clear documentation of such a decision in the notes. If it is clear that it is an "end of life" situation, palliative care should be the priority, with the aim of symptom control, especially relieving distressing breathlessness with medication such as opiates. Clear, careful and sympathetic communication with the family and other healthcare professionals is crucial.

Summary

Acute type 2 respiratory failure is a common presentation in hospitals and carries a significant morbidity and mortality. Awareness of those at risk and prevention is the key. Diagnosis of acute type 2 respiratory failure is easy with ABG measurements. Morbidity and mortality have improved significantly in the past two decades with the use of NIPPV. Ethical dilemmas are common in these patients who are often not suitable for invasive ventilation.

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A PATIENT PRESENTING WITH ACUTE ONSET BREATHLESSNESS, FEVER, RESPIRATORY FAILURE AND ABNORMAL CHEST X-RAY

S Mukherjee

A patient presenting with acute onset breathlessness, fever, respiratory failure and abnormal chest X-ray. Good Clinical Care.

Abstract

This case report is about a 38 year old teacher who presented with an acute febrile illness, dyspnoea and respiratory failure. Chest X-ray and CT scan revealed bilateral multifocal consolidations. A diagnosis of organising pneumonia was made after exclusion of community acquired pneumonia (CAP). Organising pneumonia can mimic CAP and early suspicion and diagnosis can lead to treatment with steroids which leads to rapid resolution of symptoms, clinical and radiological signs. Although the reported mean annual incidence is around 1.97/100,000 population, it is thought to be commoner than generally considered. If not treated early, it can progress rapidly and lead to respiratory failure needing ventilatory support. The differential diagnosis and specific investigations of multifocal consolidations followed by management strategies are discussed in the article.

Case History

A 38 year old female teacher presented with a 1 week history of cough productive of clear sputum, backache, fever and progressive breathlessness over 2 days. She had a history of recurrent colds and headaches for the previous 2 years. She is a lifelong non-smoker with occasional alcohol consumption.

On admission, she was pyrexial with a temperature of 38.4 degrees Celsius, a respiratory rate of 20/min, oxygen saturations of 94% on 2Litres/min, tachycardia, blood pressure of 107/62 mmHg and normal cardiovascular examination. Auscultation revealed reduced air entry to the left lung base with bilateral crackles.

Initial investigation results:

- ECG: Sinus tachycardia
- Arterial blood gases showed Type 1 respiratory failure.
- Neutrophilic leukocytosis, normal eosinophil counts
- C reactive protein >400
- Mildly deranged liver function tests with albumin of 28 G/L
- Renal functions and electrolytes were normal.

Chest radiograph is shown below (Fig 1)

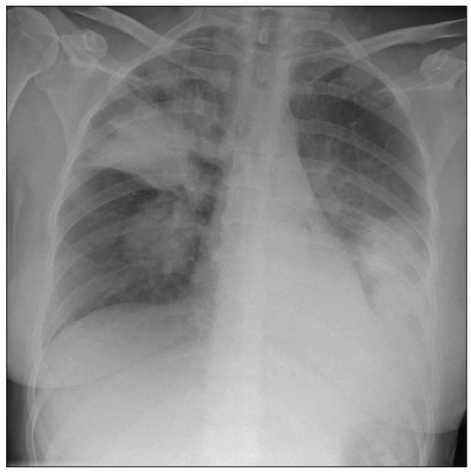


Fig.1

The chest X-ray showing multifocal consolidations, collapse/consolidation of the left lower lobe, consolidation in the right upper lobe and also areas of round consolidation at both bases.

Interpretation of the chest radiograph

Heart size is normal. There is collapse/consolidation of the left lower lobe, consolidation in the right upper lobe and also areas of round consolidation at both bases.

What is the differential diagnosis?

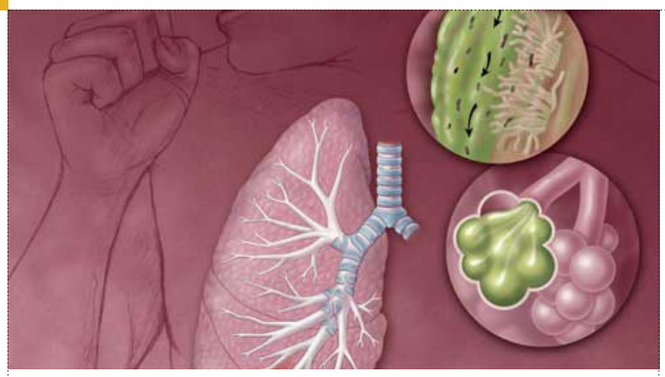
This lady has presented with acute onset breathlessness, pyrexia, markedly raised inflammatory markers and multifocal consolidation on chest radiograph.

The differential diagnosis include:

- Multifocal pneumonia
- Organizing pneumonia (OP)
- Acute eosinophilic pneumonia
- Vasculitis including Wegener's granulomatosis
- Bronchoalveolar carcinoma (least likely in a non-smoker at this age group)

A PATIENT PRESENTING WITH ACUTE ONSET BREATHLESSNESS, FEVER, RESPIRATORY FAILURE AND ABNORMAL CHEST X-RAY

S Mukherjee



Learning points

Organising Pneumonia is defined pathologically by the presence in the distal air spaces of buds of granulation tissue progressing from fibrin exudates to loose collagen containing fibroblasts. There is also associated inflammation of the bronchioles & surrounding tissue in the lungs. It is a non-specific inflammatory process resulting from lung injury; it may also result from a number of causes including vasculitis [1-3]. It can be classified as:

- Organising pneumonia of determined cause;
- Organising pneumonia of undetermined cause but occurring in a specific and relevant context;
- Cryptogenic (idiopathic) organising pneumonia: currently considered as one of the idiopathic interstitial pneumonias [4]

Some causes of secondary organising pneumonia[5]

Infective pneumonia	Streptococcus pneumoniae Mycoplasma pneumoniae Legionella sp, Opportunistic organisms, viruses
Radiation	Post breast-cancer radiotherapy
Connective tissue disease	Rheumatoid arthritis dermatomyositis/polymyositis systemic sclerosis systemic lupus erythematosus
Drugs	amphotericin, amiodarone, carbamazepine, mesalazine, sulphasalazine, sotalol, alpha interferon, Methotrexate, cocaine
Inflammatory bowel disease	Crohn's disease, ulcerative colitis
Neoplasms	In vicinity of bronchial carcinoma, in association with haematological Malignancies.

The presentation of COP is often indistinguishable from community acquired pneumonia. Failure to respond to antibiotic therapy and migratory chest X-ray changes or radiological multifocal consolidations should always raise the possibility of OP. Furthermore, there are no distinguishing clinical or radiological features between cryptogenic and secondary OP ([1-3, 5]).

There are no pathognomonic features on HRCT to distinguish OP reliably from infective consolidation. In COP, they are often peripheral and/or peribronchial and is present in 90% of patients. Typically they are associated with ground glass opacities and small nodules as shown in this case. Also commonly seen is bronchial wall thickening/dilation in involved areas ([1-3,5,7]).

Acute eosinophilic pneumonia is an acute febrile respiratory illness with hypoxaemia, diffuse pulmonary infiltrates/consolidation which can be migratory and an increase in broncho-alveolar lavage (BAL) fluid eosinophils. It has been suggested that it is an acute hypersensitivity reaction to an unidentified inhaled allergen. Infections with aspergillus, cocksackie A2 or pseudomonas maltophilia can predispose to this condition. Besides these, allergens, parasitic infections, human immunodeficiency virus (HIV) along with drugs like aspirin, penicillin, sulphasalazine, thiazides, isoniazid are often implicated as causes.

There can be an absence of peripheral eosinophilia.

Biopsy typically shows alveolar exudates predominantly consisting of eosinophils and diffuse alveolar damage with eosinophilic infiltration of the pulmonary interstitium. BAL fluid typically consists of >25% eosinophils [6].

Wegener's granulomatosis is a granulomatous vasculitis with multisystem involvement, predominantly lungs, kidney, upper airways. A chest radiograph shows nodules/masses with or without cavitations, infiltrates and ground glass changes. ANCA prevalence is present in up to 90% of cases [5].

What particular aspect of the history is important?

Drug history, because drugs are important causes of organizing pneumonia and eosinophilic pneumonia.

What further investigations are necessary?

- Sputum and blood culture
- Urinary pneumococcus and legionella antigens
- Auto antibodies including Anti nuclear-cytoplasmic antibodies (ANCA)
- Immunoglobulin levels
- Complement levels
- High resolution CT scan of the chest (HRCT) (Fig 2)

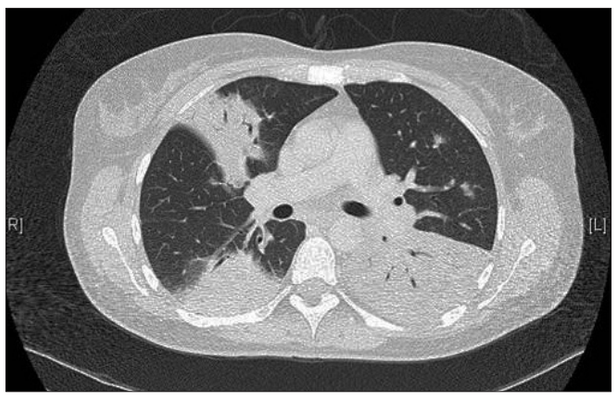


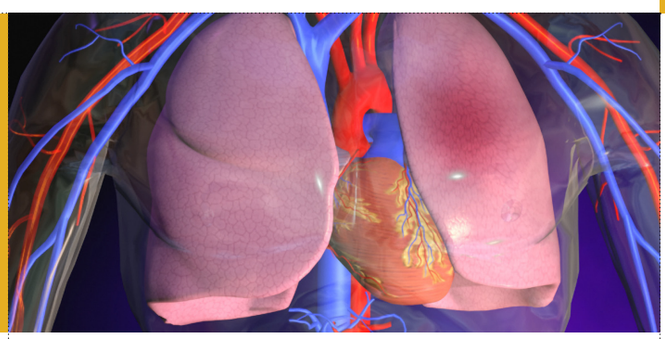
Fig. 2

The CT scan of the chest showing bilateral patchy air space opacifications varying from frank consolidation to ground glass opacity. It is important to exclude infections and therefore all relevant samples should be sent for microbiology. A CT scan of the chest (preferably HRCT) to look in detail at the lesions and also to look for any other abnormalities like ground glass opacities, pleural involvement and mediastinal lymphadenopathy.

A PATIENT PRESENTING WITH ACUTE ONSET BREATHLESSNESS, FEVER, RESPIRATORY FAILURE AND ABNORMAL CHEST X-RAY

S Mukherjee

A patient presenting with acute onset breathlessness, fever, respiratory failure and abnormal chest X-ray. Good Clinical Care.



What does the CT scan reveal?

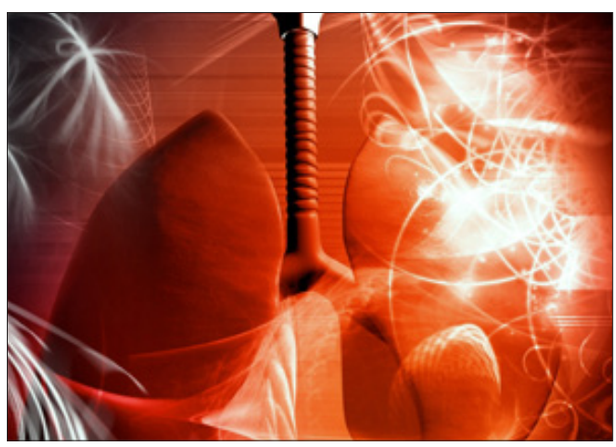
Bilateral patchy air space opacifications varying from frank consolidation to ground glass opacity. A few 'fluffy' pulmonary nodules on the left of similar character. Overall appearances suggest either cryptogenic or secondary organising pneumonia. A few mildly enlarged lymph nodes in the mediastinum seen which could be reactive. She was started treatment with intravenous antibiotics and intravenous fluids. Initial cultures were negative for organisms.

How can the diagnosis be confirmed?

The diagnosis of OP should be made on clinical, radiological and histological grounds but should never be made on the basis of histology alone as similar patterns can be sometimes seen in the vicinity of lung cancer.

Bronchoscopy with broncho-alveolar lavage and transbronchial biopsy is useful to obtain the histology. Occasionally a surgical lung biopsy may be needed. In this case, bronchoalveolar lavage did not show any increased eosinophil count. No organisms were identified on staining and culture. The biopsy was confirmatory of OP involving the alveolar ducts and alveoli with intraluminal polyps of granulation tissue associated with some interstitial inflammation.

She was started on prednisolone with clinical and radiological improvement and a fall in the inflammatory markers. She was also reviewed by rheumatologists who excluded any underlying connective tissue disorder. A follow-up chest-ray in 4 weeks revealed complete resolution of the radiological changes (Fig 3).



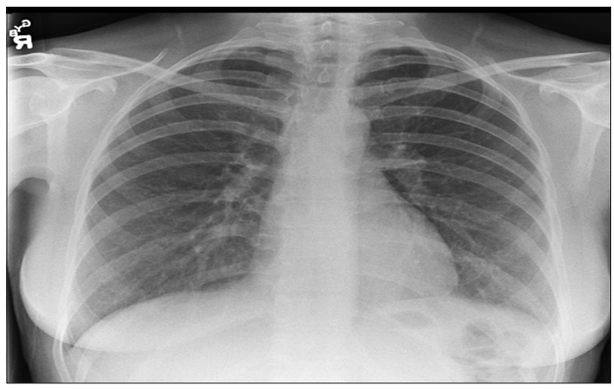


Fig.3

The follow-up chest X-ray after 4 weeks showing complete resolution of the consolidations.

Learning points

Corticosteroids are the mainstay of treatment and treatment may need to be continued for up to one year. However, there are no randomised controlled trials regarding the dose and duration of treatment. Most patients with OP respond very well to corticosteroid therapy. Relapses are common, both during treatment and particularly at the time of tapering of steroid dosage, but usually they can be controlled with moderate doses of prednisone. Relapses are not associated with increased mortality or progressive lung fibrosis. Relapses are as responsive to corticosteroids as the initial presentation. Occasionally, there can be asymptomatic radiological relapses and therefore, they might not need any further treatment [1-3, 5]. On occasions COP can progress rapidly to respiratory failure (fulminant COP) needing ventilatory support and therefore early suspicion and diagnosis is important so that appropriate treatment can be instituted.

A PATIENT PRESENTING WITH ACUTE ONSET BREATHLESSNESS, FEVER, RESPIRATORY FAILURE AND ABNORMAL CHEST X-RAY

S Mukherjee

Multiple choice questions

1. Which of the following are TRUE about organising pneumonia?

A. Fever, leukocytosis and raised C-reactive protein suggest infective aetiology.
B. Peripheral eosinophilia is commonly seen.
C. A CT scan is useful to differentiate cryptogenic organising pneumonia from secondary organising pneumonia.
D. Corticosteroids are the mainstay of treatment.
E. Relapses indicate worse prognosis.

2. Which of the following are causes of multifocal consolidations on a chest X-ray?

A. Infection
B. Organising pneumonia
C. Eosinophilic pneumonia
D. Wegener's granulomatosis
E. Bronchoalveolar carcinoma

3. A transbronchial lung biopsy is useful to confirm the diagnosis in which of the following?

A. Sarcoidosis
B. Organising pneumonia
C. Eosinophilic pneumonia
D. Miliary tuberculosis
E. Hypersensitivity pneumonitis

4. Which of the following are not associated with organising pneumonia?

A. Rheumatoid arthritis
B. Crohn's disease
C. Mycoplasma infection
D. Systemic lupus erythematosus
E. Sarcoidosis

5. Which of the following drugs can cause pulmonary eosinophilia?

A. Aspirin
B. Thiazides
C. Sulphasalazine
D. Nitrofurantoin
E. Methotrexate

Answers

Answer: C

Notes: Fever and neutrophilic leukocytosis is common in organising pneumonia; eosinophilia is absent. There are no distinguishing clinical or radiological features between cryptogenic and secondary OP. Relapses can be treated with another course of steroids and do not indicate worse prognosis or lead to progressive pulmonary fibrosis.

Answer: A, B, C, D, E.

Notes: Besides showing consolidations, B, C, D and E can also present with associated ground glass changes, nodules and infiltrates which can be migratory.

Answer: A, B, C, D, E.

Notes: Conditions with bronchocentric distribution can be diagnosed by transbronchial lung biopsy. Other conditions include lymphangitis carcinomatosa, cancer metastatic to lung, pulmonary alveolar proteinosis.

Answer: E

Notes: There is no known association of OP with Sarcoidosis; rest can be causes of secondary OP.

Answer: E.

Notes:: Methotrexate can cause drug induced OP. Sulphasalazine can cause both eosinophilic pneumonia and organising pneumonia.
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HOW AND WHEN TO PRESCRIBE OXYGEN FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

P Oppong, D Derry

How and when to prescribe oxygen for patients with chronic obstructive pulmonary disease. Good Clinical Care.

Abstract

Mild exacerbations of chronic obstructive pulmonary disease (COPD) may be treated in the community with bronchodilators, corticosteroids and antibiotics. Most patients with acute exacerbations of COPD who present to hospital will also require oxygen therapy. Generally, acutely breathless patients should be given sufficient supplementary oxygen to maintain oxygen saturations (SaO_2) in the range 94-98%. However, some patients with COPD will become hypercapnic and acidaemic when given this level of supplementary oxygen. They should be treated with controlled oxygen therapy to achieve a target SaO_2 of 88-92%. Junior doctors need to understand which patients with COPD require controlled oxygen therapy and how this should be administered, both during acute hospitalisation and on discharge.

Respiratory failure

Respiratory failure is conventionally categorised as type 1 (hypoxaemia alone; arterial pressure of oxygen (PaO_2) <8kPa with normal or low arterial pressure of carbon dioxide ($PaCO_2$) and type 2 (hypoxaemia with hypercapnia; $PaCO_2$ >6kPa).

Type 1 (hypoxic) respiratory failure arises primarily due to ventilation:perfusion (V/Q) mismatching and shunting (in which mixed venous blood bypasses ventilated alveoli). There are many causes including pneumonia, pulmonary embolism, asthma and COPD.

Type 2 (hypoxia with hypercapnia) respiratory failure is due to alveolar hypoventilation resulting from decreased ventilation (e.g. secondary to central nervous system depression) and/or failure to compensate for an increase in respiratory dead space or CO_2 production. Causes are addressed later in this article. Rises in $PaCO_2$ cause increased blood hydrogen ion concentration and so result in respiratory acidosis. If the onset of type 2 respiratory failure is slow, increased retention of bicarbonate by the kidneys compensates for the rise in hydrogen ions and blood pH remains normal. Clinical features of hypercapnia include headache, tachycardia, asterixis and drowsiness.

Why do some patients with COPD develop hypercapnia?

It is helpful to understand the physiology underlying why some patients with COPD become hypercapnic when given increased concentrations of inspired oxygen (FiO_2). A number of processes are involved:

- Many textbooks only mention the loss of "hypoxic drive", which results in a fall in ventilation when hypoxia is corrected. However, several studies[1, 2] suggest this is a minor factor, and this mirrors the clinical observation that COPD patients continue to have a strong respiratory drive until they develop central respiratory depression (CO_2 narcosis), which occurs when $PaCO_2$ rises above 12-16kPa.

- Impaired ventilation:perfusion matching is a more important factor (Figure 1).

- The Haldane effect. When haemoglobin binds more O_2, its ability to bind CO_2 falls. It is of minor importance as only around 20% of CO_2 in venous blood is bound to haemoglobin (the rest is carried as bicarbonate, or dissolved in solution)

- Nitrogen is not involved in gaseous exchange. Its presence in the alveoli prevents collapse. At high FiO_2, alveolar nitrogen is displaced. In areas of lung where ventilation is particularly poor, absorption of O_2 may result in collapse (atelectasis).

- $PaCO_2$ rises as a normal response to increased FiO_2. Central chemoreceptors respond to raised $PaCO_2$ by increasing respiratory effort. In patients with chronic hypercapnia, the threshold for this response is shifted upwards. Their $PaCO_2$ is therefore already closer to the threshold at which central respiratory depression, and thus ventilatory failure, occurs.

- Patients with COPD have hyperinflated lungs. At increased respiratory rates, there is less time for expiration, and their degree of hyperinflation increases. This increases the relative size of the respiratory dead space, changes the length of intercostal and diaphragmatic muscle, and makes ventilation less efficient. Patients are then unable to increase their ventilation sufficiently to 'blow off' the extra CO_2. A respiratory acidosis results and worsens as patients become fatigued.

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P Oppong, D Derry

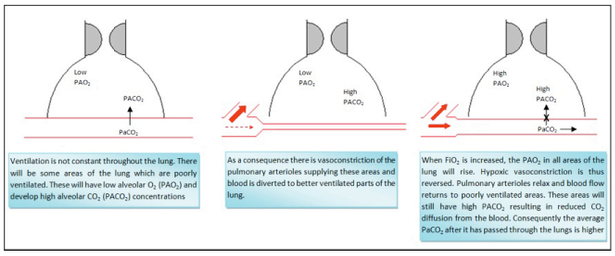


Figure 1. Reversal of hypoxic pulmonary vasoconstriction; reduced clearance of CO_2 from blood.

The 2008 National COPD Audit found that 44% of patients hospitalised with acute exacerbations of COPD were hypercapnic and 20% were acidotic. 30% had received high flow (≥35%) oxygen before their first arterial blood gas[3]. An earlier study of COPD admissions found that while overall 20% of patients were acidotic, in the hypercapnia cohort with PaO_2>10kPa, over 50% were acidotic with a proportion improving with the use of controlled oxygen without non-invasive ventilation (NIV), suggesting they may been made acidotic by injudicious use of oxygen[4]. Another study observed that patients with acute COPD exacerbations who have PaO_2>10kPa on admission have increased length of stay, more frequent admission to high dependency units and greater use of NIV[5].

For these reasons, the British Thoracic Society (BTS) recommends the use of controlled oxygen therapy, aiming for a target SaO_2 of 88-92%, in the quarter of patients with acute exacerbations of COPD who are at risk of hypercapnia[6]. The aim is to give sufficient oxygen to minimise the effects of tissue hypoxaemia, while limiting the rise in $PaCO_2$. In COPD patients with critical illness where risks of tissue hypoxaemia are greater, e.g. cardiac arrest or major trauma, ambulance staff are guided to use higher levels of FiO_2 aiming for a target SaO_2 of 94-98% pending an arterial blood gas (ABG).

Using controlled oxygen therapy

SaO_2 should be checked in all acutely ill or breathless patients and a target level set. Patients with COPD who require supplementary oxygen should be treated with 24-28% oxygen to a target SaO_2 of 88-92% pending the results of ABG analysis. Figure 2 outlines the appropriate action to take in response to the ABG result. As shown, the target SaO_2 can be safely increased to 94-98% in patients with COPD if they are normocapnic with no history of NIV requirement. It takes only a few minutes for SaO_2 to stabilise after a change in FiO_2; it takes 30-60 minutes for $PaCO_2$. Therefore an ABG should be taken 30-60 minutes following a change in oxygen therapy. Further ABGs are not required if the patient remains stable. An initial ABG is not usually required if patients have been breathing air and have SaO_2 >95%.

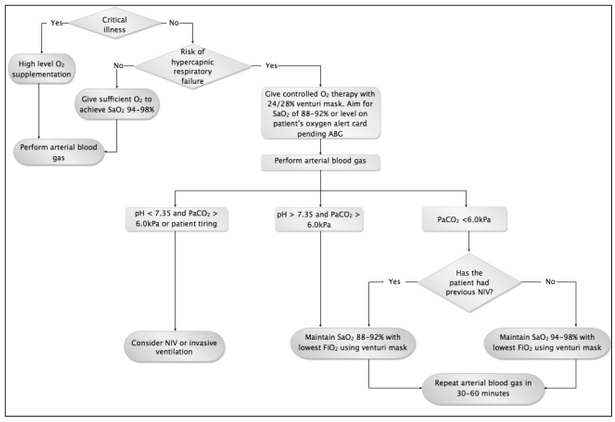


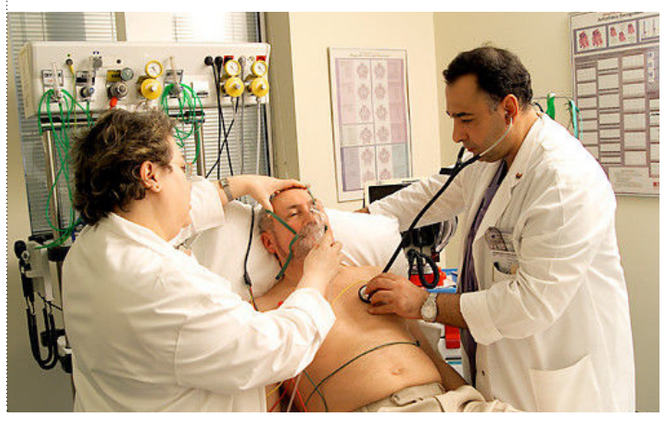
Figure 2. Guidance for the use of emergency oxygen. Adapted from BTS guideline[6].

If SaO_2 cannot be increased to the target range of 88-92% (or PaO_2 >8kPa) without the patient developing hypercapnia and acidosis, then NIV will be required[7]. Further discussion of NIV is outside the scope of this paper.

The diagnosis of COPD will not always have been made, but should be suspected in long-term smokers over the age of 50 years with a chronic history of breathlessness on minor exertion. Conversely, it should not be assumed that all cases of hypercapnic respiratory failure are due to COPD. Junior doctors must be alert to other possibilities including;

- sedatives, which may accumulate unexpectedly if there is acute renal dysfunction (check size of pupils and prescribed medications);
- neuromuscular disorders including Guillain-Barre syndrome and myasthenia gravis (check limb reflexes, although these can be depressed by high CO_2 levels);
- morbid obesity and chest wall disorders, such as kyphoscoliosis;
- patients in respiratory failure in whom $PaCO_2$ is rising as they become fatigued (e.g. those with life threatening acute asthma or severe pneumonia) and at risk of impending respiratory arrest.

The importance of these diagnoses is that there may be an antidote (naloxone or flumazenil) or patients need urgent assessment for ventilatory support (non-invasive or intubation), which may need to be continued on discharge.



HOW AND WHEN TO PRESCRIBE OXYGEN FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

P Oppong, D Derry

How and when to prescribe oxygen for patients with chronic obstructive pulmonary disease. Good Clinical Care.

How should you deliver oxygen?

Venturi masks (Figure 3) deliver predictable oxygen concentrations. 24% and 28% masks are suitable for patients with COPD, but only work when kept on the face. Nasal cannulae deliver a fixed rate. The effective oxygen concentration varies with minute ventilation. In respiratory distress the minute ventilation increases e.g. to 25 L/min, but nasal cannulae continue to supply a fixed flow rate e.g. 2 L/min and so the percentage of O_2 inspired falls. Conversely, as patients become drowsy and ventilation falls, FiO_2 increases. Nasal cannulae still work in patients who chose to mouth breathe, unless their nose is severely congested or blocked. Nasal cannulae are generally preferred by patients as they feel less claustrophobic, can be kept on while eating and stay in place more reliably overnight. For these reasons, venturi masks are preferred when patients are first admitted, with a change to nasal cannulae after stabilisation. You should prescribe oxygen on the drug chart indicating the device, concentration or flow rate and the SaO_2 target range.

Figure 3. The range of available venturi valves.

Beware rebound hypoxaemia

If you identify a patient with COPD who has been given too much oxygen, it may be tempting to immediately stop their supplementary oxygen in an attempt to rapidly correct their hypercapnia and acidaemia. However, if you do this, their SaO_2 will not just fall to its original level prior to any oxygen therapy; the SaO_2 will fall below its original level. You will just have made a bad situation worse. This dangerous situation occurs even in patients who are not CO_2 narcosed, and still have a strong respiratory drive. It occurs because total body CO_2 content rises during the period of excess oxygen therapy; more CO_2 is released into the alveoli; nitrogen is inert, so alveolar O_2 is displaced. The appropriate management is to gradually reduce FiO_2, by stepping down to a 28% venturi mask, while regularly rechecking the SaO_2 to ensure it does not fall below the 88-92% target range.

Weaning oxygen and prescribing on discharge

Oxygen should be weaned as patients with COPD recover from acute exacerbations. FiO_2 should be reduced if patients are above, or consistently towards the top end of their target SaO_2 range. After reducing FiO_2, SaO_2 should be monitored after 5 minutes and 60 minutes to ensure SaO_2 remains within the target range.

Patients with COPD are more symptomatic for many weeks after an acute exacerbation[8]. It follows that as the time for discharge from hospital approaches, many COPD patients will remain breathless and hypoxic at rest (SaO_2<88%; PaO_2<7.3kPa). They may be discharged with home oxygen pending formal assessment in respiratory clinic when stable. In this interim period, unless PaO_2 is very low (<6kPa), it is usual to recommend that they use oxygen for symptomatic relief. The survival benefit from long term oxygen therapy (LTOT) was only seen after 500 days[9], suggesting that this results from reducing right heart failure, rather than preventing deaths due to acute hypoxemia. If subsequent assessment in respiratory clinic confirms that they meet the criteria for LTOT (Table 1), they will then be advised of the need to use oxygen for at least 15 hours a day[9]. The majority of this can be overnight. This not only covers the period when PaO_2 levels are at their lowest but is also more convenient for the patient.

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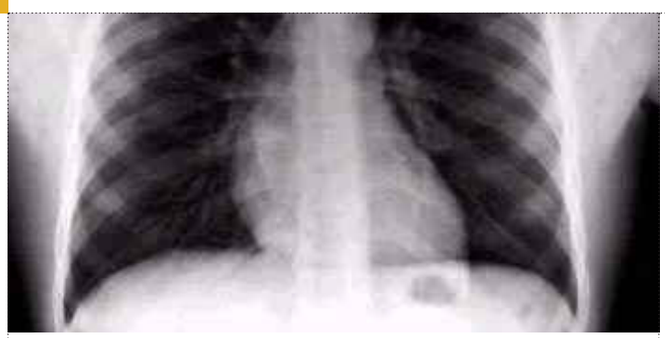

The efficacy of LTOT in COPD was demonstrated by randomised controlled trials conducted by the British Medical Research Council (MRC)[9] and Nocturnal Oxygen Therapy Trial (NOTT) Group[11]. The MRC trial showed an improvement in mortality over five years in those receiving fifteen hours of oxygen per day compared to those who received no supplementary oxygen. The survival benefit did not appear until after 500 days. In NOTT, after 24 months, the overall mortality rate in those who received a mean of 17.7 hours of oxygen overnight was almost half that of those who received 11.8 hours oxygen. A Cochrane review[12] concluded that LTOT did not appear to improve survival in patients with mild to moderate hypoxaemia or in those who desaturated at night.

COPD is the commonest condition for which LTOT is prescribed. Other conditions, with far less evidence, include interstitial lung disease, bronchiectasis, cystic fibrosis, primary pulmonary hypertension and chronic heart failure.

Figure 4. Oxygen flow meter. Read off flow rate from the centre of the plastic ball e.g. this valve is supplying 10L/min.

Which patients do not need home oxygen?

Oxygen is a treatment for hypoxaemia, not for breathlessness. Patients with COPD who have normal SaO_2 and $PaCO_2$ may still feel breathless because their lungs are hyperinflated and airway resistance increased. Supplementary oxygen will not have a significant effect on their symptoms and is not recommended. Other patients recovering from COPD exacerbations will have transient drops in SaO_2 and breathlessness on exertion; the prescription of supplementary oxygen in such patients is controversial and expensive. The authors do not consider short burst oxygen, unless the fall in SaO_2 is substantial and prolonged (e.g. >30 seconds with SaO2<85%). Even then, before arranging home oxygen you should ask the ward physiotherapist to determine whether patients can walk significantly further with supplementary oxygen than with air.

Often hypoxaemia is not the principle factor limiting the exercise capacity of these patients. You then have to consider the clinical relevance of a patient managing to walk just a few more metres. If significant exercise desaturation continues when the patient is stable, they may be considered for ambulatory oxygen when reviewed in respiratory clinic. There are no robust criteria for ambulatory oxygen therapy but the following has been suggested; evidence of exercise desaturation (at least 4% drop in SaO_2 to <90%) plus demonstration that the patient can walk 15% further with oxygen than with air delivered via nasal cannulae[10,13].

Table 2 includes alternative issues and treatments to consider in patients with COPD who remain breathless.

How to organise home oxygen

A standardised home oxygen order form (HOOF)[14] is used across England although an older version may still be found on some wards. The HOOF allows for prescription of LTOT, Ambulatory and Short Burst Oxygen therapy.

When patients are to be discharged on oxygen after an acute exacerbation, the duration (minutes or hours per day) requested on the HOOF will be influenced by the degree of hypoxaemia and frequency of the patient's breathlessness. If the patient has persistent breathlessness and clearly falls below the threshold for LTOT (Table 1) then "interim" LTOT should be selected on the HOOF. With lesser degrees of breathlessness or hypoxaemia, "interim" short burst oxygen should be selected. If less than 120 minutes per day are requested, the patient will be supplied with cylinders. With longer durations, the oxygen supplier will generally provide a concentrator (Figure 5a). Nasal cannulae are generally preferred by patients as discussed previously. Cannulae also require less oxygen flow than venturi masks, so if cylinders have been provided they will be depleted more slowly. A flow rate is selected which achieves a target waking SaO_2 of 88-92% (PaO_2 >8.0kPa). If a venturi mask is selected, then the flow rate should be appropriate for the mask (i.e. 2L/min for 24%; 4L/min for 28%)

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- PaO_2 ≤ 7.3kPa on room air on 2 separate occasions > 3 weeks apart
- On optimal medical management of their disorder for > 5 weeks prior to assessment
- Clinically stable (i.e. >6 weeks after an acute exacerbation of chronic lung disease)
- PaO_2 < 8kPa with secondary polycythaemia or clinical/echocardiographic evidence of pulmonary hypertension

Table 1. Criteria for LTOT[10]

Factor	Treatment
On optimal COPD treatment?	Review combination of inhalers; check inhaler technique; mucolytic; oral theophylline
Additional pathologies present?	Consider pulmonary emboli (potential role for d-dimer if inflammatory markers normal) and cardiac ischaemia
Deconditioned (loss of fitness)?	Enrol in pulmonary rehabilitation programme
Dysfunctional breathing syndrome (hyperventilation)?	Physiotherapy re-training of breathing pattern
Excessive drive from respiratory centre?	Suppress drive with low dose opiates (which have better evidence base than benzodiazepines) Use fan (as facial cooling reduces sensation of breathlessness)
Anxious or depressed?	Consider anti-depressant, such as citalopram
Unrealistic expectations?	Explain it usually takes a number of weeks for the increased symptoms experienced during an acute exacerbation to subside

Table 2. Factors and treatments to consider in patients with COPD who appear excessively breathless.

Figure 5a.
Oxygen is most commonly delivered by an oxygen concentrator. Room air is entrained into the concentrator and the nitrogen is filtered out by zeolite granules. Concentrators reliably produce up to 4L/min oxygen and a cylinder may be provided as backup. Images courtesy of Air Liquide UK

Figure 5b.
Portable liquid oxygen (LOX) systems are available which may be replenished from a supply kept in the patient's own home. LOX and portable cylinders may use an intermittent (oxygen conserving) delivery system which senses the patient's inspiratory effort and delivers oxygen at the beginning of inhalation thereby conserving the two thirds of oxygen that is usually wasted during the (prolonged) expiratory phase. The 36L LOX unit would fill 81 x 2L cylinders in gaseous form. Portable unit: weight - 2.5kg when full, duration – 5hours 40minutes at 2L/min (17 to 20 hours in oxygen conserving mode). Images courtesy of Air Liquide UK

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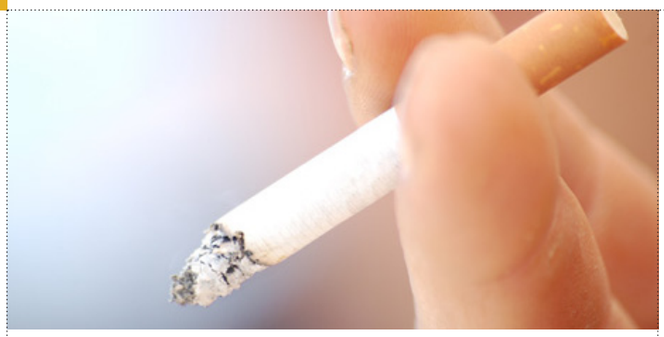
P Oppong, D Derry



Although emergency (supply within 4 hours) and next day supply options are more expensive than the standard 3 day service, it is cost effective to use these in cases where lack of home oxygen is all that prevents a patient's discharge. It is important to consider how the home oxygen service is going to gain access to the patient's home. Ambulatory oxygen is usually only prescribed once patients have been formally assessed in respiratory clinic. Lightweight cylinders are particularly expensive and so must only be prescribed by a specialist. Detailed guidance notes are provided with the HOOF. The patient's written consent[15] is required to comply with Data Protection Act 1998.

Smoking cessation should already have been recommended for the patient's underlying condition, however patients supplied with home oxygen should be strongly reminded of the associated fire hazard. Continued smoking is not an absolute contra-indication to the use of LTOT, but a risk assessment should be made.

Follow up

Patients commenced on home oxygen should have their oxygen requirements reassessed in respiratory clinic after 6-8 weeks. Patients with ambulatory oxygen should show evidence (e.g. via diary card) that they can leave the house for longer periods and have an improved ability to perform activities of daily living. Ambulatory oxygen should be withdrawn if there is no demonstrable benefit. Patients who have had hypercapnic respiratory failure should be issued with an "oxygen alert" card which advises on their optimal FiO_2, and instructed to show this to ambulance and emergency department staff. Patients may be given their own venturi mask and the need for controlled oxygen can be flagged on local ambulance control systems.

Conclusion

Junior doctors commonly have to prescribe oxygen for patients with COPD. They should recognise that a proportion of these patients are at risk of hypercapnic respiratory failure. They should be able to prescribe oxygen in a controlled, target orientated fashion. They should also be able to identify those patients who would benefit from home oxygen on discharge, and understand how to organise this.

The BTS guidelines for emergency oxygen use were published in 2008. The BTS home oxygen guidelines are due to be published in 2012/13.

Questions

1. A 59 year old lady with known COPD presents with a two day history of increasing breathlessness and a cough productive of green sputum. After assessment you diagnose an infective exacerbation of COPD. She has an initial respiratory rate of 32 breaths per minute. You obtain this initial ABG on nebulised air:

pH 7.36	(7.35-7.45)
pCO_2 8.03 kPa	(4.6-6.0)
pO_2 7.13 kPa	(10.5-13.5)
BE 7.6 mmol/l	(-2 +2)
HCO_3 28.8 mmol/l	(22-26)
SaO_2	84.2%

What is the most appropriate course of action?

a) commence oxygen at 2L/min with a simple face mask
b) commence oxygen at 15L/min via non re-breathe mask
c) commence non-invasive positive pressure ventilation (NIV)
d) commence oxygen at 3L/min via 24% venturi mask
e) commence oxygen at 2L/min via nasal cannulae

2. In which of the following scenarios would you consider Long Term Oxygen Therapy (LTOT)?

Patient with COPD and;

a) severe bilateral emphysema on CT scan
b) >3 exacerbations of COPD a year
c) PaO2 of 7.8kPa on ABG with polycythaemia
d) PaO2 of 7.8kPa after exercise
e) >5 apnoeic episodes during sleep

Answers

Answer: d

The ABG shows hypercapnic (type 2) respiratory failure with metabolic compensation. Controlled oxygen therapy should be used to improve the hypoxaemia aiming for a SaO_2 of between 88% and 92% with the lowest possible FiO_2. Delivering too much oxygen increases the risk of hypercapnia and acidaemia developing.

A minimum flow rate of 5L/min must be used with simple face masks to prevent rebreathing of exhaled air. Both simple face masks and nasal cannulae deliver 'uncontrolled' or variable concentrations of oxygen, dependent on the minute ventilation of the patient. Simple face masks typically deliver 40-50% oxygen with 5-10L/min oxygen. Nasal cannulae deliver 24%-40% oxygen with 1-6L/min oxygen, but the concentration will fall as minute ventilation increases.

NIV is not indicated because the patient is not acidaemic at this stage. It may become necessary if the patient subsequently develops hypercapnia and acidaemia when administered controlled oxygen.

HOW AND WHEN TO PRESCRIBE OXYGEN FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

P Oppong, D Derry

How and when to prescribe oxygen for patients with chronic obstructive pulmonary disease. Good Clinical Care.

The venturi mask delivers a fixed concentration of oxygen to the patient, as long as the flow of oxygen into the mask exceeds the minimum rate printed on the valve. A 24% mask requires a minimum oxygen flow rate of 2L/min. Increasing the rate of oxygen flow into the mask does not increase the oxygen concentration, but does increase the flow of 24% oxygen provided by the mask. The BTS guidelines recommend a 50% increase in oxygen above the minimum flow rate for a venturi mask when patients have a respiratory rate of over 30 breaths per minute[6].

Answer: c

LTOT is indicated in patients with:

- an arterial oxygen pressure (PaO_2) ≤7.3kPa (55mmHg) on room air;
- on two separate occasions at least three weeks apart;
- on optimal medical management of the disorder

for at least five weeks prior to assessment;

- during a period of clinical stability (i.e. at least

6 weeks after an acute exacerbation of chronic lung disease)[10].

If patients have either secondary polycythaemia or clinical and/or echocardiographic evidence of pulmonary hypertension, then the slightly higher threshold of 8kPa (60mmHg) is used.

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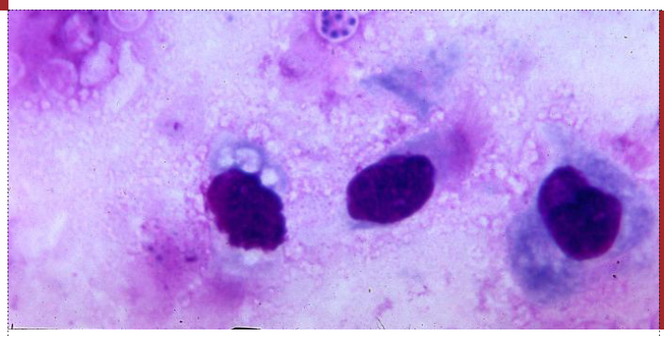
PNEUMONIA IN THE IMMUNOSUPPRESSED – A MEDICAL EMERGENCY!

G Hayes and N Withers



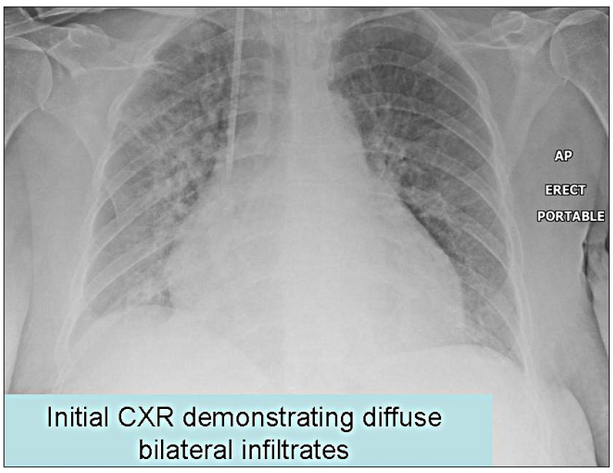
Pneumonia in the Immunosuppressed – a medical emergency!
Patient Management.

Case Study

A sixty one year old female with no significant past medical history, underwent cadaveric renal transplantation for end stage renal failure secondary to adult polycystic kidney disease. Following transplantation she was treated with prednisolone and tacrolimus to prevent graft rejection and the perioperative period was uncomplicated. Subsequently she suffered from intermittent neutropaenia due to heavy immunosuppression and the acquisition of cytomegalovirus. This caused further marrow suppression and two episodes of CMV pneumonitis, treated with valganciclovir.

Five months later she represented with intermittent fevers and mild breathlessness. Physical examination was unremarkable apart from saturations of 91% on air and an admission chest x-ray demonstrated no abnormality. Blood cultures grew a sensitive Staphylococcus aureus and she was treated with flucloxacillin and fucidic acid. During her treatment she became progressively more breathless and continued to have low grade fevers. It was subsequently noted that she desaturated to 82% on walking but remained otherwise asymptomatic.

Over the next few days she became progressively more oxygen dependent with a blood gas on air demonstrating a paO_2 of 6.7. There remained little to find on examination with a repeat CXR demonstrating diffuse patchy infiltrates (Picture 1) and blood tests revealing persistent neutropaenia.



Initial CXR demonstrating diffuse bilateral infiltrates

Picture 1

Pneumonia in the immunosuppressed – a big problem?

This case study highlights the significant problem of pneumonia in the immunocompromised. Although infections such a pneumocystis jirovecii (PCP) are often considered in patients who are immunocompromised due to Human Immunodeficiency Virus (HIV), with the increased success of organ and haematological transplantation, more effective cytotoxic chemotherapy and continuing use of high dose oral corticosteroids in the management of chronic disease, the pool of patients at risk of such infections is considerably broader.

Pneumonia in the immunosuppressed population is common and associated with high levels of morbidity and mortality. Pulmonary infection remains the commonest form of tissue invading infection in immunocompromised hosts[1-3]. Despite advances in antifungal therapy/prophylaxis, the incidence of fungal disease in immunocompromised patients is actually increasing[4,5]. Prompt investigation and treatment is vital as death can occur in hours from fulminant infection.

This article will discuss how to do to identify these patients at risk and steps to manage them on the acute take.

History taking in the immunocompromised individual – what do I need to ask?

As with all presentations on the acute take, a thorough history is a key element to reaching the correct diagnosis or differential diagnosis. Particular attention should be paid to the past medical history and the drug history.

Symptoms

Presentation in the immunosuppressed may be insidious and comparatively asymptomatic. Clues may be found in non-specific, constitutional features such as malaise and anorexia. Typical respiratory symptoms such as cough, chest pain and shortness of breath should be explored, particularly exertional dyspnoea. Elicit the speed of onset of symptoms, as this may act as guide towards the underlying infecting organism (Table 1).

PNEUMONIA IN THE IMMUNOSUPPRESSED – A MEDICAL EMERGENCY!

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Speed of Onset	Pathogens
24 hours or less	Bacterial pneumonia Viral pneumonitis – CMV, varicella
Days	Fungal – aspergillus, pneumocystis Atypical Bacterial – legionella, nocardia Viral - CMV
Weeks	Fungal or atypical mycobacteria

Table 1

Past Medical History

Ask specifically about: -

- Pre-existing lung disease – this increases susceptibility to infection
- Solid or haematological malignancy and ongoing chemotherapy
- Previous transplantation - when were they, were they successful and what drugs are they on?
- HIV and risk factors for HIV
- Pregnancy
- Co-morbid conditions associated with immunosuppression – chronic kidney disease, diabetes mellitus, liver failure, alcoholism, ischaemic heart disease, malnutrition.

Drug History

This is vital when assessing a patient who may be immunosuppressed and should include both current drugs and drugs taken in recent months.

When asking about chemotherapy and immunosuppression find out:

- What they are taking
- When they last took it
- How long they have been on it for and when they expect to complete it
- Should they be taking neutropaenic prophylaxis and are they?

In patients with HIV check which HAART (Highly Active Anti Retroviral Treatment) treatments they are taking and also which prophylactic drugs (such as Co-Trimoxazole) they have been prescribed. It is also important to check compliance, the HIV virus mutates rapidly and drug resistance can be a problem.

Record any treatments for other co-existing illnesses which might be contributing to the immunosuppressed state. Examples would be anticonvulsants such as phenytoin, carbamazepine and sodium valproate (agranulocytosis and pancytopaenia), antipsychotics such as clozapine (neutropaenia and agranulocytosis) and carbimazole (pancytopaenia and agranulocytosis).

Key questions

"Do you take your tablets?"

"How do you take them?"

Poor compliance or the wrong dosing can significantly alter the likely diagnosis and subsequent management.

Examination

Thorough physical examination is vital but in many cases, particularly in neutropaenic patients, the respiratory system may appear normal. Often the only features pointing towards respiratory pathology are an increased respiratory rate and low oxygen saturations. A fall in oxygen saturations on ambulation may be a useful sign indication pulmonary pathology even in the presence of a normal Chest Radiograph (CXR).

Remember to look elsewhere for extrapulmonary markers of infection including cutaneous manifestations such as pustules and vesicles, herpes simplex and varicella, and subcutaneous abscess from septic emboli, nocardia and staphylococcal infection.

Always elicit if the patient is febrile or has been prior to presentation (many patients who are immunosuppressed are asked to keep a temperature chart during periods of treatment/risk of neutropaenia).

Definition

Neutropaenic fever = a single temperature >38.3°C or a temperature > 38°C for > 1h and Neutropenia

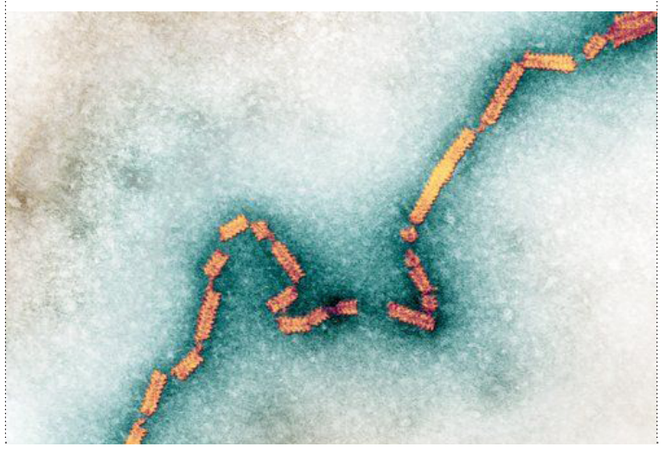
Investigations

Basic Blood tests

Take a full set of basic bloods to confirm or refute neutropaenia and to look for multisystem involvement. In most cases a full blood count, renal liver and bone biochemistry, C -Reactive Protein (CRP) and a clotting sample should be sufficient and will help direct your further management. In some patients, particularly those who have undergone solid organ or haematological transplantation, a further clotted sample for serology/Polymerase Chain Reaction to indentify reactivation of viruses such as Cytomegalovirus (CMV) and Epstein Barr (EBV) may be helpful.

Top Tip

High white cell counts do not always imply an adequate immune response. In haematological malignancies they can be abnormal and none functioning rendering patients effectively lympho or neutropaenic.



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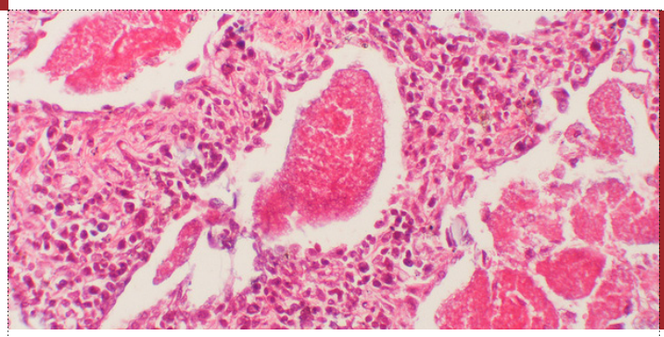

Pneumonia in the Immunosuppressed – a medical emergency!
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A Full Septic Screen

It is important to remember that an unwell, immunocompromised patient may have more than one infective process involving more than one organ system. It is therefore mandatory that cultures are obtained from as many sites as feasible, including from indwelling venous access devices.

Investigation	Comments
MSU/CSU	Even if no urinary symptoms
Throat swabs	Send to microbiology and virology. Ask for H1N1 and influenzae according to local policy.
Nasopharyngeal aspirate	Useful if a patient is corzyal, looks for common respiratory viruses such as parainfluenzae, RSV and adenovirus
Blood cultures	Take peripheral and central cultures observing strict aseptic techniques. Remember to ask for Fungal cultures in addition to bacterial. In HIV patients with low CD4 counts, separate blood cultures should be sent for non-tuberculous mycobacterium (NTM) in special bottles.
Swabs (*MRSA/line sites etc.)*	Look for discharge around any indwelling lines or catheters. Patients may be debilitated and have pressure damage, look!
Sputum sample	Send for MC+S, AAFB and mycology. Sputum production is often noticeably absent in patients with pneumonia and neutropaenia. Induced sputum can be helpful but if not always necessary, ask your ward physiotherapist.
Stool sample	If diarrhoea is a presenting feature

Table 2

Top Tip

Clearly label all your samples as being from a patient who is immunosuppressed and septic. If possible also document the immunosuppression they are taking as it guides the laboratory tests performed.

The Chest Radiograph (CXR)

This is a key investigation in all immunocompromised patients who present unwell. The CXR may show non-specific changes, diffuse shadowing/ infiltrates or nodular shadowing. A normal CXR DOES NOT exclude pulmonary infection in the immunosuppressed and the presence of a normal CXR may prompt further more detailed investigations (see below).

Although CXR appearances may be non-specific, certain infections have "classical" signs which may guide further investigations/treatment (table 3). It should be remembered that whilst infiltrates on a CXR should be treated as infection, there are other causes in the immunocompromised and these should be considered if a patient fails to respond to antimicrobial treatment (Table 4).

Respiratory Infection	Typical Radiological Appearances
PCP	CXR demonstrates alveolar infiltrates bilaterally spreading from the hilar, "Bats wing" pattern One third completely normal
Cytomegalovirus	Bilateral subtle diffuse infiltrates
Respiratory syncytial virus	Bilateral interstitial infiltrates
Invasive pulmonary aspergillosis	Peripheral nodules (CT scan more characteristic with a ground glass rim surrounding pulmonary nodules creating a "halo" effect
Nocardia	Typically produces cavitating nodules or masses Less common: - Diffuse infiltrates Pleural effusions

Table 3

PNEUMONIA IN THE IMMUNOSUPPRESSED – A MEDICAL EMERGENCY!

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None infectious causes of pulmonary infiltrates on CXR

- Drug induced lung disease eg. azathioprine, bleomycin, methotrexate
- Pulmonary oedema
- Diffuse alveolar haemorrhage
- ARDS – multiple causes including sepsis, drugs and aspiration
- Organising pneumonia
- Transfusion related lung injury
- Respiratory complications of the underlying illness – lymphangitis carcinomatosis, leukaemic infiltrates, leucostasis
- Diffuse alveolar damage
- Pulmonary embolism ± superadded infection

Table 4

Arterial blood gases (ABG's)

ABG sampling will enable accurate assessment of a patient's hypoxaemia, will guide oxygen therapy and will identify those patients who have developed respiratory failure and might require respiratory support in the form of non-invasive or invasive ventilation. Remember to confirm the platelet count before sampling if the clinical situation allows.

CD4 count

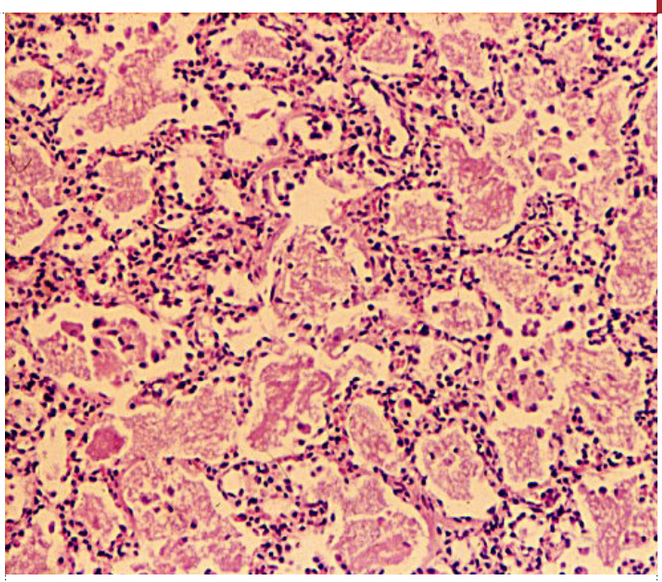
In patients with HIV, or where you think undiagnosed HIV is very likely, check a CD4 count. The lower the CD4 T cellcount the higher the risk of opportunistic infection. A CD4 count <2009 cells/µl should alert you to the possibility of pneumonia caused by organisms like P. Aueruginosa, S. Aureus and Pneumocystis jirovecii[6,7].

Early Management

Although initial investigations may not yield a diagnosis, because mortality is very high in this patient group it is imperative to start treatment immediately, whilst seeking advice from senior colleagues and other specialties about further targeted investigations and management.

Antibiotic therapy

In patients where there is a high suspicion of neutropaenia broad spectrum antibiotic treatment should be commenced without waiting for results of blood tests or other investigations. There is a direct correlation between delay in starting antibiotic therapy and increased mortality, highlighted by the ongoing Surviving Sepsis Campaign[8], and good practice should be to aim for less than an hour between presentation and administration of the first dose of antibiotics. Prescribe antibiotics according to your local guidelines and make sure they are given promptly. Don't be put of by an apparently normal CXR or negative cultures as source for sepsis will never be identified in 20-50% of neutropaenic patients[6].



Correct hypoxia

Respiratory failure in the immunocompromised is potentially a very serious problem. Hypoxia may often be out of proportion to a patient's symptoms and should be corrected aggressively, even if a patient appears comfortable. Aim to titrate oxygen to maintain saturations over 95% and remember that an increasing oxygen requirement is a sign of clinical deterioration even if saturations remain stable. In this situation seek senior help as early instigation of non-invasive ventilation may help to prevent the need for intubation. Intubation in this group usually confers a very poor prognosis with mortality rates approaching 100% in some series[6].

Remember it is good practice to prescribe your oxygen!

Supportive Care

Depending on the degree of immunosuppression present, these patients may need to be barrier nursed in a side room with appropriate use of masks, gloves and aprons. However, it is important to ensure that isolation does not compromise the high level of monitoring that this group require.

Careful attention to fluid balance in these patients is mandatory as they become dehydrated due to fever, diarrhoea and vomiting and reduced intake secondary to complications of their underlying disease such as chemotherapy-induce mucositis. Many patients will require intravenous fluids (which should be prescribed) and will need monitoring of their urine output and renal function. Urine output should be at least 0.5ml/kg/hr, and this is best monitored by insertion of a urinary catheter. However, this may not always be possible or desirable as catheterisation breaches mucous membranes and has the potential to introduce further infection.

Always check with a senior before undertaking any kind of invasive procedure in these patients if the platelet count is less than $50x10^9$/L. You may need to consider transfusion.

PNEUMONIA IN THE IMMUNOSUPPRESSED – A MEDICAL EMERGENCY!

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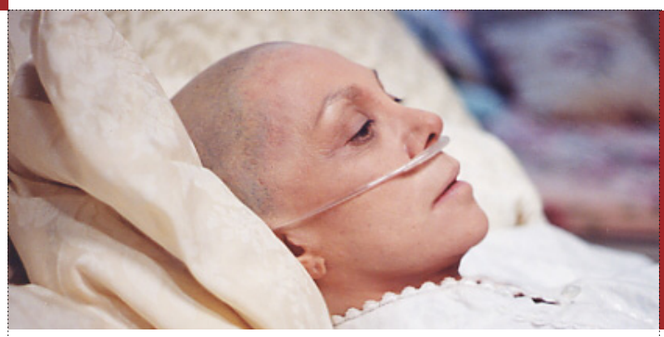

Pneumonia in the Immunosuppressed – a medical emergency!
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Review existing immunosuppressive regimens

Many patients will present on heavy immunosuppression or continued chemotherapy. The decision to continue chemotherapy is a difficult one and will often depend on the presence or absence of neutropaenia, the degree of neutropaenia and the stage and purpose of the underlying treatment. Ideally chemotherapy should be stopped but seek advice from the speciality involved.

Paradoxically patients with solid organ transplants may need increased doses of corticosteroids during intercurrent infection with the dose of their other immunosuppressive drugs being reduced. Always discuss patients with solid organ transplants and infection with a senior clinician or the transplant centre involved in their care.

View oral or intravenous corticosteroids with caution. Although causing potent immunosuppression stopping them suddenly can be just as dangerous. Always remember to ask for the duration of therapy and the reason. Stopping long term steroid therapy abruptly can precipitate an Addisonian Crisis due to adrenal suppression following prolonged exposure to exogenous glucocorticoid.

Further Investigations

Following initial investigation and management, the diagnosis may remain unclear in many of these patients. Senior advice may be required from a variety of specialties including Respiratory Medicine, Microbiology and Infectious Diseases, Haematology and Oncology, Radiology and HIV and Transplant Centres. A number of more detailed investigations may be necessary as described in brief below.

Bronchoscopy and Bronchoalveolar lavage (BAL)

Bronchoscopy is an ideal early investigation in patients who do not respond to initial conventional therapy. Bronchial washings and BAL samples provide a diagnosis in over two thirds of patients and bronchoscopy itself has a low complication rate and is normally well tolerated[6]. It is particularly good in diagnosing diffuse alveolar infections like pneumocystis. Over 50% of patients will undergo a change in their treatment as result of findings at bronchoscopy[9].

CT thorax

The role of CT scanning is not well defined and there are no specified criteria to guide use. Not everyone will need a CT scan, particularly if cultures or BAL provide a diagnosis. CT can be very useful in the group of patients with persistent fever and respiratory symptoms with a normal CXR. Up to 50% of these patients will have radiological abnormalities on CT images[6]. Appearances can be diagnostic but more often will demonstrate the extent and location of pathology without providing a definitive diagnosis. This may be helpful in guiding sampling at bronchoscopy. In some cases, a CT guided biopsy of peripheral lesions may be indicated.

Pleural aspiration

Ideally this should be ultrasound guided and undertaken in the event of continued deterioration despite maximal treatment. Send everything as standard and add on mycology to your microbiology sample.

Common Causes of Pneumonia in the Immunosuppressed - things to think about

Whilst the general principles for investigation and management of pneumonia in the immunocompromised are as detailed above, there are several specific presentations that are worth discussing in more detail.

Pneumocystis jirovecii pneumonia (PCP)

Most common in the HIV infected group, PCP presents with progressive exertional dyspnoea, dry cough and constitutional upset. It can produce little in the way of clinical signs and forms a diffuse infiltrate on imaging. In patients who are not severely unwell treatment should not be started for PCP without a definitive diagnosis and this can be obtained with bronchoscopy and bronchoalveolar lavage. However in those patients presenting with severe disease/respiratory failure, treatment should be started immediately and confirmation sought using BAL as soon as is clinically feasible. BAL will, however, remain positive for at least a week after starting empirical treatment so bronchoscopy can be delayed until the patient is more stable[6].

Co-trimoxazole is first line treatment for PCP and long courses are often necessary although side effects are common. Alternative treatments include atovaquone, pentamidine and clindamycin/primaquine. Patients with severe disease/respiratory failure should also be treated with high dose oral corticosteroids.

PNEUMONIA IN THE IMMUNOSUPPRESSED – A MEDICAL EMERGENCY!

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Having completed treatment for PCP patients are normally then commenced on either co-trimoxazole or nebulised pentamidine prophylaxis until their immunocompromised state is reversed.

Aspergillus

Aspergillus infection is a major problem in this patient group and accounts for most infective deaths in the allogenic bone marrow transplant group[6]. It presents non-specifically and progresses rapidly with a characteristic "Halo" sign being seen on CT thorax. Treatment should be instigated rapidly and involves reducing immunosuppression and treatment with antifungals such as intravenous caspofungin, intravenous amphotericin and oral voriconazole. Even with treatment the condition may relapse if the patient experiences further neutropaenia.

Other fungal infections

Candida, Cryptococcus neoformans and Mucor spp. can all cause fungal pneumonia. They are all relatively uncommon and can be very aggressive. Candida pneumonia reflects severe disease with nodules and consolidation present on imaging and carries high mortality. Cryptococcus can present acutely or insidiously and requires prolonged treatment of up to 12 months (Table 5).

Cytomegalovirus (CMV)

Infection is often due to reactivation but can be due to primary infection due to sero positive blood or organ donation. It presents with flu like symptoms with progressive hypoxia which can lead to respiratory failure. CXR demonstrates bilateral diffuse infiltrate and treatment with iv ganciclovir should be started early. Even with treatment there is up to 85% mortality.

Other respiratory viruses

These include respiratory syncytial virus (RSV), influenza, parainfluenza and adenovirus. These typically present with coryzal symptoms and fever and may go on to cause bilateral pneumonitis which carries high mortality rates. Treatment options are limited but there may be some benefit from early nebulised ribavirin.

Bacterial	Viral	Fungal
S.Aureus (inc MRSA)	Paraninfluenzae	*Pneumocystis jirovecci*
H.Influenzae	CMV	*Aspergillus*
S. Pneumoniae	Influenza including H1N1	*Mucormycosis*
Pseudomonas spp. and other gram –ive organisms	RSV	*Cryptococcus neoformans*
Nocardia	Adenovirus	
	Herpes Simplex	

Table 5

What to do if things aren't working

If a patient does not respond to initial management, senior advice should be sought, other investigations may be required and other diagnoses should be considered.

Look at your antibiotics

You need to make sure your antibiotic regimen has good gram positive and gram negative cover. This will differ between centres and you will need to check your hospital policy. Common regimens include piperacillin/tazobactam and gentamicin, and vancomycin and meropenem.

Check your results

Treatment for certain infections, for example PCP or CMV, will only be administered if a definitive diagnosis has been established or there is a very high index of clinical suspicion with continued clinical deterioration. Remember to chase your cultures and act accordingly.

Think about antifungals

Antifungal agents are useful in individuals where cultures have proved positive or imaging is consistent with a fungal pneumonia. They can also be introduced in patients who fail to respond to first or second line antibiotic therapy and have persistent fever/failure to thrive. Caspofungin is a good choice of antifungal agent for this group as it has been shown to have the lowest toxicity rates[10].

Reconsider your diagnosis

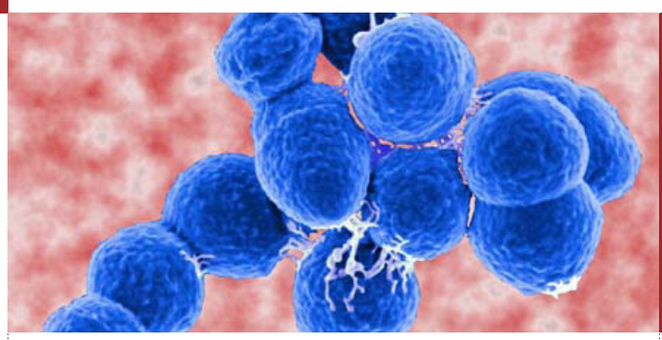
If patients aren't responding to antibiotic therapy and have persistent infiltrates on their CXR it may be worth reconsidering the diagnosis of pneumonia. In healthy and immunosuppressed individuals there are multiple other causes of pulmonary infiltrates some of which are listed in the advice box below table three. Infection may co-exist with any of these infiltrate causing conditions and some infecting organisms will have immunomodulatory properties and predispose to further infection. For example infection with CMV predisposes infected individuals to pneumonia caused by both PCP and aspergillus[6].

Case Study Revisited

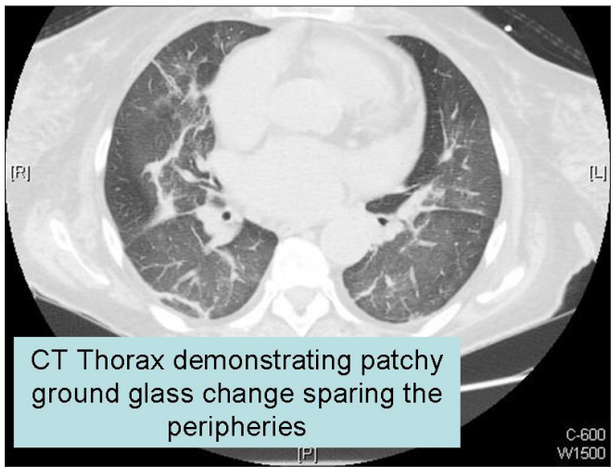
The patient underwent a high resolution CT (HRCT) (picture 2) of the thorax which demonstrated changes consistent with a non-specific pneumonitis. In view of her worsening hypoxia a bronchoscopy was undertaken, with BAL samples proving positive for pneumocystis jirovecii (PCP) (Pictures 3 and 4). She was initially treated with co-trimoxazole, which was changed to clindamycin and primaquine because of concerns about worsening neutropaenia. She recovered well and was started on prophylaxis to prevent recurrent episodes (Picture 5). The initial infection with PCP could perhaps have been avoided by prescribing prophylaxis in the first instance.

PNEUMONIA IN THE IMMUNOSUPPRESSED – A MEDICAL EMERGENCY!

G Hayes and N Withers

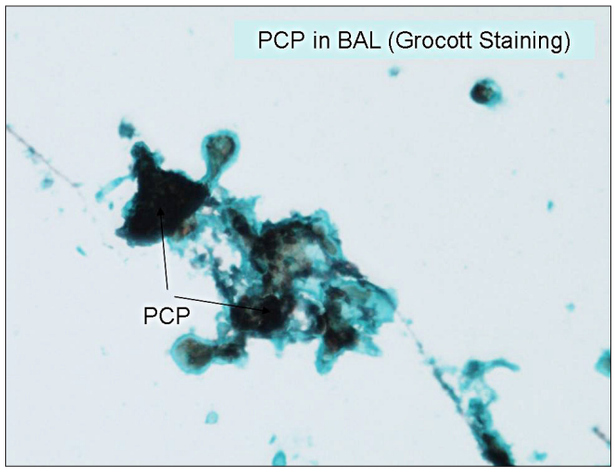


Pneumonia in the Immunosuppressed – a medical emergency!
Patient Management.

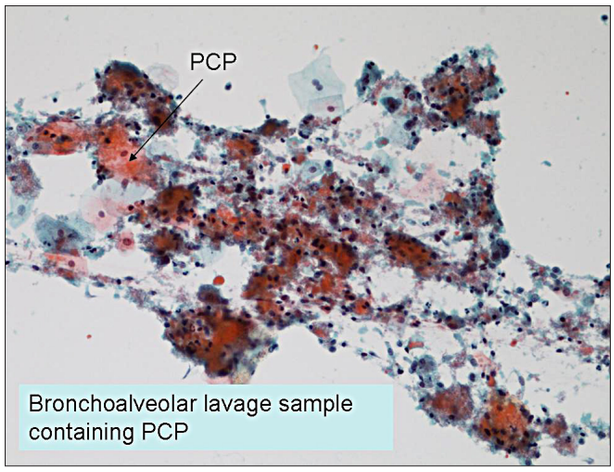


CT Thorax demonstrating patchy ground glass change sparing the peripheries

Picture 2

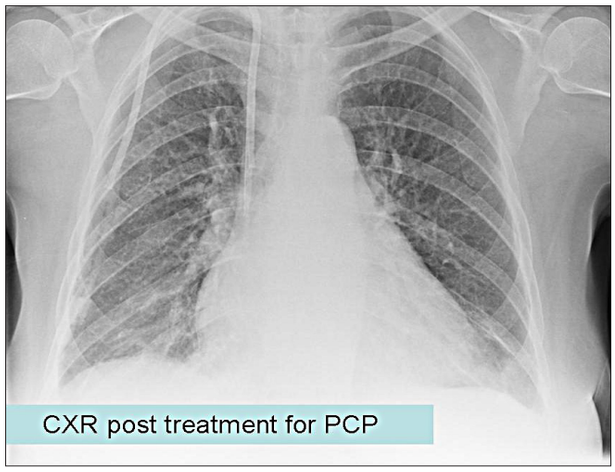


Picture 4



Bronchoalveolar lavage sample containing PCP

Picture 3



CXR post treatment for PCP

Picture 5

PNEUMONIA IN THE IMMUNOSUPPRESSED – A MEDICAL EMERGENCY!

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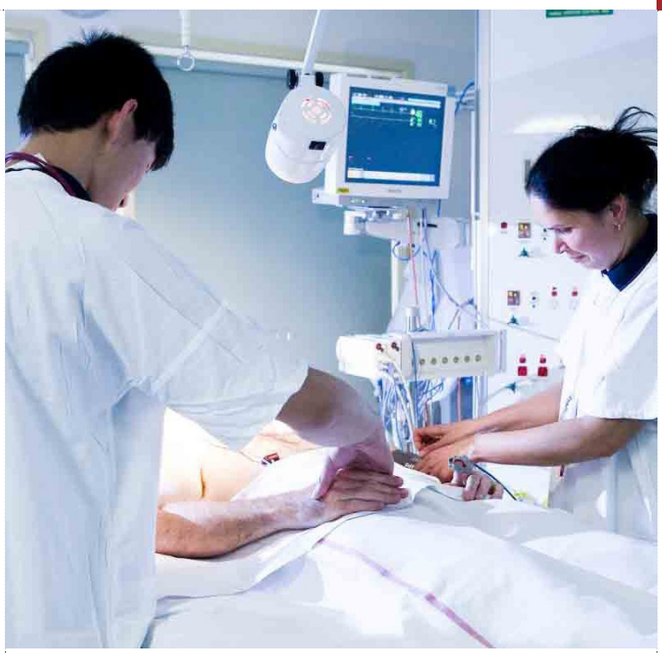
Key learning points

1. Remember immunocompromised patients are vulnerable even if they appear well – assess early
2. Start antibiotics within the first hour of admission following local guidelines
3. Don't be put of by normal CXRs
4. Low saturations warrant an ABG – don't underestimate the degree of hypoxia
5. Reassess often and seek senior support – these patients can deteriorate fast.



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PULMONARY VASCULAR DISEASES

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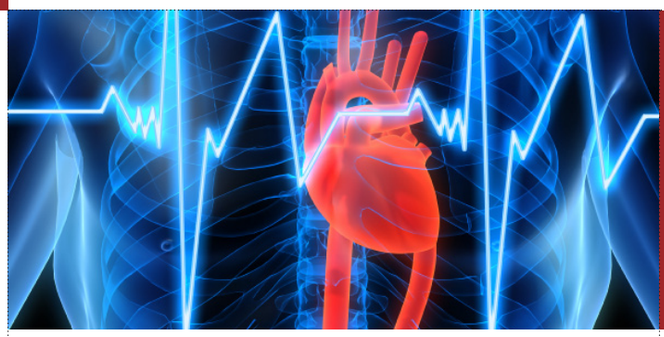

Pulmonary Vascular Diseases.
Patient Management.

Introduction

The normal pulmonary circulation is a low-resistance, high-flow circulation that is able to accommodate large changes in cardiac output. It may become disordered in many different disease situations. Pulmonary vascular disease can be divided into pulmonary thromboembolic disease, pulmonary hypertension, pulmonary vasculitis and haemorrhage. In this article we concentrate principally on the common problem of pulmonary thromboembolic disease. The final section deals briefly with pulmonary vasculitides which may occasionally present on the acute general medical take.

Pulmonary Venous Thromboembolism (VTE) Pulmonary Thromboembolic disease

Prevalence and Prevention

It is estimated in the UK 25,000[1] and in the USA 50,000[2] people die each year from pulmonary emboli (PE). There has been an overall decline in PE mortality over the last 25 years of by approximately 30%. This is attributed to better risk factor modification, thromboprophylaxis for deep venous thrombosis (DVT), inpatient mobilisation, management and treatment of DVT/PE [6].

"Prevention of Venous Thromboembolism (VTE) in Hospitalised Patients" was published by the Department of Health, UK in 2010. This is part of the National VTE Prevention Programme for the NHS in England. It required all hospitalised patients be assessed for the risk of VTE within 24 hours of admission. Mandatory VTE risk assessment data collection started from June 2010 and must be submitted by all hospitals on a monthly basis [3]. By taking such steps for primary prevention it is hoped to further reduce the incidence of VTE

Risk Factors

Increase risk of developing Thromboembolic disease relates to the principles of Virchow's triad of decrease blood flow (stasis), hypercoagulability and injury to the vascular endothelium (Figure 1). This risk can be further divided into two groups: inherited or acquired (Table 1).

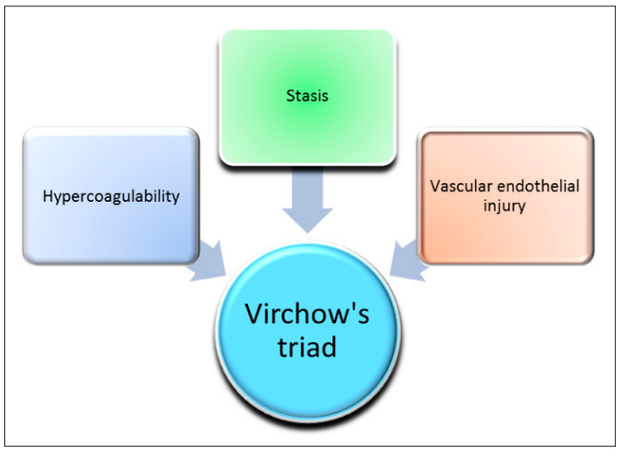

Figure 1. Virchow's Triad

Inherited Risk Factors	Acquired Risk Factors
• Antithrombin deficiency • Protein C deficiency • Protein S deficiency • Factor V Leiden • Prothrombin Gene mutation • Elevated Factor VIII levels • Hyperhomocysteinaemia	• Malignancy • Recent surgery • Immobilization • Pregnancy related – pre-eclampsia, late in pregnancy, caesarean section • Cardiovascular – congestive cardiac disease etc • Proteinuria

Table 1: Inherited and acquired risk factors for venous thromboembolism

PULMONARY VASCULAR DISEASES

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Clinical Features

The history of presentation can vary greatly depending on the age of the patient, severity of the disease and the underlying physical fitness of the patient - a young fit person may tolerate the physiological insult and be less symptomatic than someone who is older or has multiple co-morbidities. Classic presentations of pulmonary thromboembolism include:

- Pleuritic chest pain and haemoptysis (pulmonary infarction)
- Acute dyspnoea
- Exertional syncope due to poor cardiac reserve
- Circulatory collapse from massive PE in a previously well patient.

Clinical signs include:

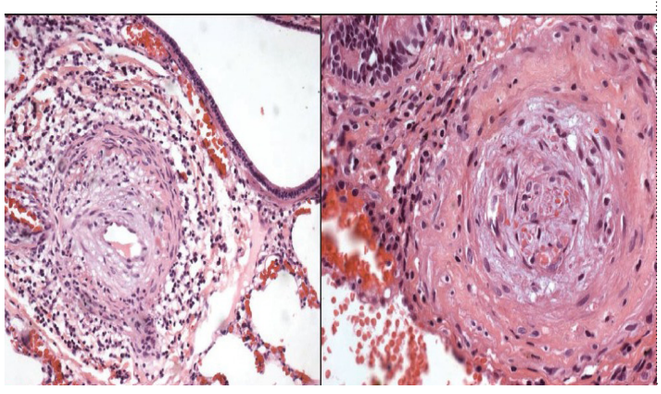
- Tachycardia
- Tachypnoea
- Reduced chest expansion/movement
- Pleural rub
- Hypoxia
- Signs of right heart strain/failure – raised jugular venous pressure, low blood pressure, right ventricular heave and loud P2 on auscultation of the heart.

Pre-test probability

History and clinical assessment along with certain basic investigations can be used to stratify an individual's risk of having had a PE. Various scoring systems have been devised and validated to assess the clinical probability of PE diagnosis. These include the Wells score [4] (Table 2) and the Revised Geneva score [5] (Table 3). Each hospital will have its own guideline and preferred scoring system so it is important to familiarise with the local policy.

Risk Factors	Score
• Clinical signs and symptoms compatible with DVT	3
• PE is the most likely diagnosis	3
• Surgery or bedridden for more than 3 days for the past 4 weeks	1.5
• Previous DVT or PE	1.5
• Heart rate >100/min	1.5
• Active cancer (ongoing treatment or within the previous 6 months, or for palliation only)	1.5
Clinical Probability of PE	
≤ 4.5	Low probability
4.5 – 6	Moderate probability
> 6	High probability

Table 2. Wells Score [4]



Risk Factors	Score
• Age > 65	1
• Previous DVT or PE	3
• Surgery (general anaesthesia) or fracture (lower limb) within 1 month	2
• Active malignant condition or cured < 1 year	2
Symptoms	
• Unilateral lower limb pain	3
• Haemoptysis	2
Clinical Signs	
• Heart rate	
❖ 75 – 94 bts/min	3
❖ ≥ 95 bts/min	5
• pain on lower limb deep venous palpation and unilateral lower limb oedema	4
Clinical probability	
• Low	0 - 3
• Intermediate	4 - 10
• High	≥ 11

Table 3. Revised Geneva score [5]

Investigations

Electrocardiography

The commonest ECG finding in PE is sinus tachycardia. Other changes to look out for include signs of right ventricular strain e.g. right axis deviation, dominant R wave in V1, right bundle branch block and T wave inversion in V1-V4.

Arterial Blood Gas

This will help to support the diagnosis and may show a respiratory alkalosis, hypoxia with a raised A-a gradient. In young healthy individuals however it may be normal.

D-dimer

D-dimer is a product of fibrin degradation (fibrinolysis) and its production can occur as a result of many different clinical situations e.g. sepsis, malignancy, pregnancy, trauma etc. It should only be used with a clinical pre-test probability assessment tool. A negative D-dimer with a low clinical probability score has >90% negative predictive value excluding PE [4].

Echocardiography

Echocardiography may show right ventricular dilatation / hypokinesis, and tricuspid valve regurgitation if there is significant pulmonary thromboembolism. Patients with right ventricular dysfunction and acute PE have a higher mortality compared to those with preserved right ventricular function.

PULMONARY VASCULAR DISEASES

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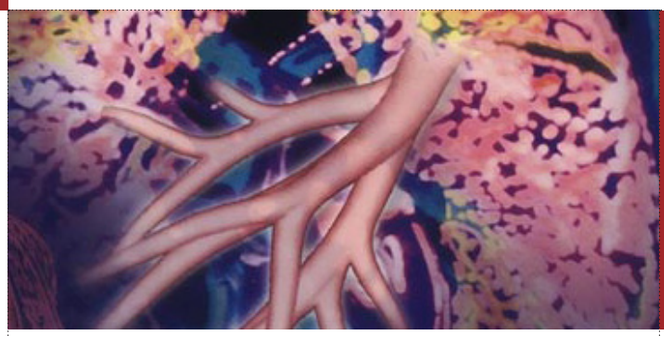

Pulmonary Vascular Diseases.
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Diagnostic Imaging

• Chest X-Ray changes are often non-specific. Appearances may vary from being normal to showing segmental collapse, pleural effusion, and pulmonary infiltrates. It may even point to a possible cause of the PE such as malignancy.

• CT pulmonary angiography (CTPA) is now the investigation of choice in diagnosing PE. It is quick and has a high sensitivity (>86%) [6]. It is particularly useful for detecting central and medium vessel PE. Compared to other imaging modalities it allows visualization of the embolus as filling defects, and other causes for the patient's symptoms such as pneumonia, pneumothorax etc. Signs of right ventricular dysfunction can also be demonstrated depending on the clot burden. The interobserver agreement for CTPA in the diagnosis of PE is also much better than V/Q scanning. New generation multidetector (>32 slice) CT scanner and newer imaging software increases the detection rate for PE.

• Ventilation/Perfusion Scan (V/Q scan) was for many years the investigation of choice for pulmonary thromboembolic disease but has largely been superseded by CT pulmonary angiography. However it still has a role in patients who cannot undergo CTPA due to contraindications such as significant renal disease or contrast allergy. A low V/Q mismatch (normal scan) excludes PE. Interpretation of a V/Q scan has to be done in correlation of the patient's clinical history.

The PIOPED II trial showed that more patients had a confirmed PE on CTPA (19.2%) compared to VQ scan (14%). However in chronic thromboembolic disease, a VQ scan is much more sensitive than CTPA in candidates possibly undergoing pulmonary endarterectomy [12].

Treatment

Anticoagulation

All patients with acute thromboembolic disease will need to be treated with anticoagulation.

• Heparin / Low molecular weight heparin (LMWH): This used to be intravenous (i.v.) heparin initially which has largely been replaced by LMWH due to ease of administration (once per day) and no requirement for monitoring. Patients suspected of thromboembolism should be started on this treatment prior to the confirmation of diagnosis. Once diagnosis is confirmed, this needs to continue for a total of at least 5 days overlapping with the use of oral anticoagulants.

• Vitamin K antagonist. It takes several days for the warfarin to be effective and there is a risk of thrombosis (transient drop in Protein C level) in the initial treatment period which is why it is given with Heparin/ LMWH until the INR is in the therapeutic level (2 - 3). For those intolerant of warfarin, phenindione can be used as an alternative.

• Thrombolysis: In cases of massive pulmonary embolism with haemodynamic compromise this treatment should be considered. Alteplase (r-TPA) is the agent of choice followed by i.v. heparin infusion. Evidence for using this in cases with massive PE with right ventricular dilatation but no haemodynamic compromise in less clear.

Special Situations

• Inferior Vena Cava Filter

For patients in whom anticoagulation treatment is contraindicated and who are at risk of further PE, an inferior vena cava filter can be used to mechanically prevent embolization from lower limb DVT to the pulmonary circulation.

• Malignancy associated PE.

Patients with underlying cancer with VTE disease will require long term anticoagulation since the mortality is greater compared to those without PE / DVT. The CLOT study compared the use of LMWH (dalteparin) vs. warfarin and demonstrated that patients receiving LMWH had less recurrent VTE (9% vs. 17%) [7]. LMWH long term is now the treatment of choice for cancer patients with VTE.

• Pregnancy

Investigation of suspected PE in pregnancy carries its own special problems. The Royal College of Obstetrics and Gynaecology has produced a guideline [7] addressing this area. This patient group is more than ten times at risk of VTE especially during the puerperium.

D-Dimer should not be used to diagnose PE but can be used to exclude it.

The average foetal radiation dose of CTPA is less than 10% of a VQ scan which makes it a relatively safe to the foetus. However it does carry a 13.6% lifetime risk of developing breast cancer to the patient [11].

PULMONARY VASCULAR DISEASES

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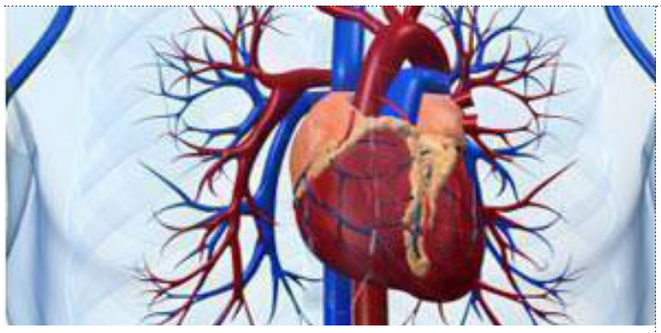

LMWH are more effective and associated with lower mortality than IV unfractionated heparin in pregnancy. Furthermore it also does not cross the placenta which is one of the problems associated with the use of warfarin. A twice daily regimen of LMWH is recommended over the once daily dose.

Summary

PE is a diagnosis that can be treated and managed well with the aid of a clinical probability scoring system. If it is used effectively then exposure to unnecessary investigation and radiation can be reduced. The incidence of VTE is falling due to better patient care and the use of prophylactic measures for VTE prevention.

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Questions

Case 1

A 73 year old man with stage 4 squamous cell lung carcinoma was admitted with sudden onset of shortness of breath and hypoxia. He underwent CT pulmonary angiography which confirmed a diagnosis of pulmonary emboli.

Which of the following will be the maintenance therapy of choice for his thromboembolic disease?

a. Aspirin
b. Warfarin
c. Sub-cutaneous low molecular weight heparin
d. Clopidogrel
e. No treatment

Case 2

An 83 year old lady had an elective left total hip replacement 2 weeks ago and was recovering well at home. She then developed a sudden onset of left sided pleuritic chest pain and became very dyspnoeic.

You are the SHO on call on the emergency unit. What would be investigation of choice to confirm her diagnosis?

a. D-dimer
b. CT pulmonary angiography
c. Venous doppler ultrasound of her lower limbs
d. Trans-thoracic echocardiography
e. Troponin

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Case 3

A 30 year old primagravida (gestation 32 weeks) had been complaining of swollen legs for several weeks. She developed acute left sided chest pain and was tachycardic when seen in the Accident & Emergency department. Her heart rate was 120 bpm, respiratory rate 24/min and oxygen saturations 92% on air. You suspected that she has had a PE and arranged for a CTPA.

What is her risk of developing breast cancer from the CTPA?

a. 7%
b. 13%
c. 25%
d. 35%
e.42%

Case 4

A 72 year old lady with a non-Hodgkin's lymphoma has just had her chemotherapy 1 day ago. She suddenly developed acute onset breathlessness and became very clammy. You are the F1 on call and on arrival her vital signs are as follows: BP 80/40, pulse rate 120 bpm, respiratory rate 28/min and oxygen saturations 88% on air. Her ECG (Image 1) and CTPA (Images 2 and 3) are as shown below.

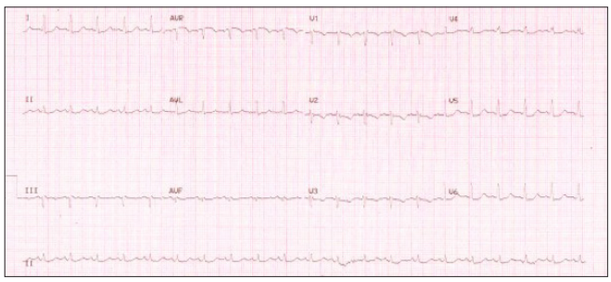

Image 1

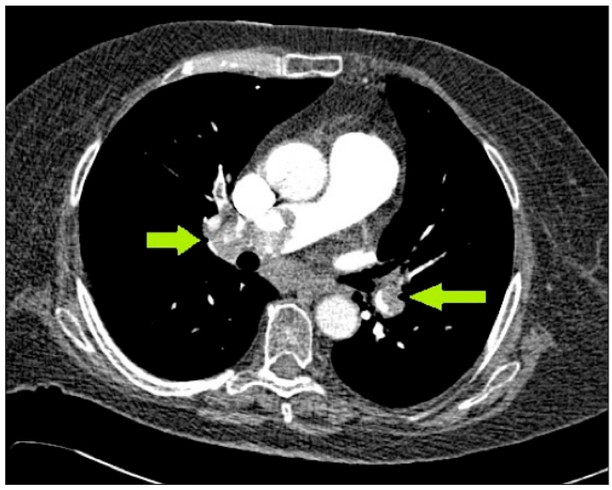

Image 2

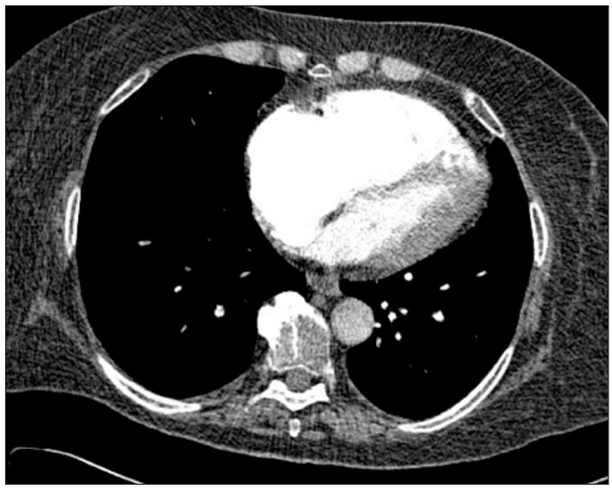

Image 3

PULMONARY VASCULAR DISEASES

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What will be the treatment of choice in this lady?

a. warfarin
b. sub-cutaneous low molecular weight heparin
c. i.v. heparin
d. Thrombolysis followed by anticoagulation
e. Aspirin and clopidogrel

Case 5

A 23 year old bus driver who smokes 5 cigarettes a day had been unwell for 5 days with flu-like illness and coughing up green coloured phlegm. He suddenly woke up with a right sided chest pain and coughed up some fresh blood in his sputum. On arrival at the Accident & Emergency department he was triaged and his heart rate was 110 bpm, blood pressure 110/70, respiratory rate 28/min, oxygen saturation 98% on air and he was apyrexial. ECG showed sinus tachycardia and his chest x-ray was normal. He had no lower limb swelling and no risk factors for VTE.

Based on the Wells score and the information above, select the answer which gives the most appropriate next course of action:

a. Request a d-Dimer and if it is raised arrange for a CTPA.
b. Discharge patient on analgesia and antibiotics
c. Arrange an echocardiogram as an out-patient
d. Start patient on LMWH
e. Arrange for out-patient bronchoscopy

Answers

Case 1. C. Sub-cutaneous low molecular weight heparin.

The Clots trial demonstrated that patients receiving LMWH had less recurrent VTE (9% vs. 17%) compared to warfarin

Case 2. B. CT pulmonary angiography.

This lady has a high risk factor of developing PE. Her Wells score is 7.5 assuming she was bed bound for several days. CTPA would be the diagnostic investigation of choice.

Case 3. B 13%.

CTPA in a pregnant woman carries a 13.6% lifetime risk of developing breast cancer to the patient [11].

Case 4. D Thrombolysis followed by anticoagulation.

The patient was become unstable would need fluid resuscitation to help maintain her blood pressure followed by thrombolysis and anticoagulation to improve her survival.

Case 5. A. Request a d-Dimer and if it is raised arrange for a CTPA.

His Well's score is low and it is likely his symptoms are secondary to an infection.

Pulmonary Vasculitis

This group of diseases is quite rare and thus the main challenge is recognition of the possible diagnosis in a patient. Clinical presentation can vary from weight loss, low grade fever, breathlessness, hypoxia, haemoptysis, sinus disease, haemoptysis, chest X-ray abnormalities to just 'a simple wheeze'.

Vasculitis implies inflammation in the vascular walls that can progress to necrosis. The end result can be infarction, necrosis or even end organ damage. Diagnosis should be suspected in diffuse alveolar haemorrhage (Figure 4) with or without haemoptysis and a fall of haemoglobin.

Table 1 shows the current classification of vasculitides. The two most common vasculitides affecting the lungs (Churg Strauss and Wegener's) are described below.

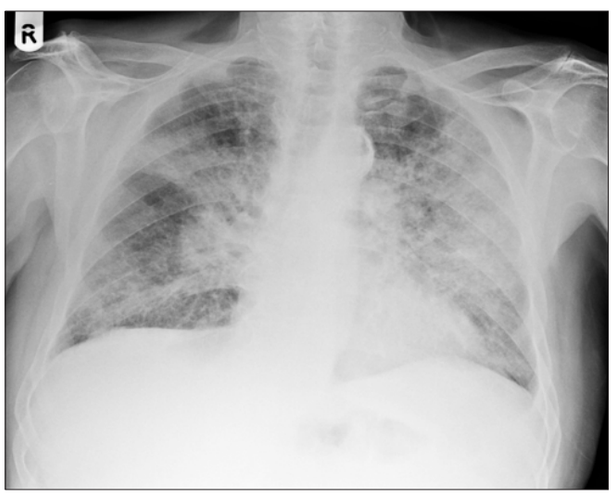

Image 4. Pulmonary haemorrhage

PULMONARY VASCULAR DISEASES

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Primary Vasculitis	Lung involvement	ANCA
Largest Vessel (aorta and major branches) ▪ Giant cell arteritis ▪ Takayasu's arteritis ▪ Aortitis in Cogan's syndrome ▪ Aortitis in spondyloarthropathies ▪ Isolated aortitis	 Rare Frequent	 Negative Negative
Medium-sized arteries ▪ Kawasaki's arteritis ▪ Polyarthritis nodosa	 No Rare	 Negative
Small and medium sized arteries ▪ ANCA associated arteritis ▪ Wegener's granulomatosis ▪ Microscopic polyangiitis ▪ Churg-Strauss syndrome ▪ Primary angiitis of the central nervous system	 Frequent Frequent Frequent	 c-ANCA in 75% p-ANCA in 15% c/p-ANCA p-ANCA 70%
Small arteries ▪ Henoch-Schönlein purpura ▪ Vasculitis associated with Rheumatoid arthritis, Sjögren's syndrome, lupus ▪ Cryoglobulaenemic vasculitis ▪ Pulmonary-renal (e.g. Goodpastures' syndrome) ▪ Drug induced Vasculitis	 No No	
Arteries and veins of different sizes ▪ Bechet's ▪ Relapsing polychondritis		

Table 1. Classification of Vasculitis (American College of Rheumatology)

Churg-Strauss Syndrome

In Churg-Strauss Syndrome, the medium and small vessel inflammation occurs, associated with pulmonary eosinophilia and eosinophilic pneumonia. This condition tends to affect middle aged adults with a slight male predominance of 2:1. Table 2 shows the diagnostic criteria for Churg Strauss - a diagnosis can be made when at least 4 out of 6 criteria are met.

History of asthma, maturity onset, associated with nasal polyps and rhinitis

Peripheral blood eosinophilia >10%

Vasculitic neuropathy (e.g. mononeuritis multiplex)

Pulmonary infiltrates

History of sinus disease

Table 2. Diagnosis of Churg-Strauss Syndrome (American College of Rheumatology Criteria, 1990)

A typical pattern involves 3 phases starting with asthma, followed by blood and peripheral tissue eosinophilia ending with systemic vasculitis.

- Common to develop pulmonary infiltrates on chest x-ray.
- p-ANCA and anti-MPO can be positive in up to 2/3 of patients
- Blood eosinophilia correlates better to disease activity.
- Diagnosis requires the combination of fulfilling the clinical criteria and pathological confirmation. However a negative biopsy does not necessarily excludes it.
- Treatment in pulmonary disease is with immunosuppression with oral corticosteroids (high dose initially) the slowly tapering it down. Patients may require i.v. methylprednisolone. Cyclophosphamide can be used in more severe organ involvement. There is of no benefit in using plasma exchange in Churg-Strauss syndrome.
- Prognosis is good in isolated pulmonary disease. Cardiac involvement occurs in more severe disease and is the main cause of death.

Wegener's granulomatosis

Classically this consists of a triad of lower, upper respiratory tract and renal vasculitis of the small and medium sized vessels. It is common for the patient to develop fever and weight loss. There is equal male to female ratio. Mainly affects 40-55 year age group.

- First presenting sign tends to be the upper airways (90%) with symptoms of nasal congestions and epistaxis. Nasal perforation can occur and some patients develop saddle nose, otitis media and subglottic stenosis.
- Lower respiratory tract involvement occurs in 65-85%. This can cause haemoptysis, cough, dyspnoea and pleuritic chest pain. A third of patients with lung involvement are asymptomatic.
- Kidney involvement occurs in over 70% of patients

Investigation

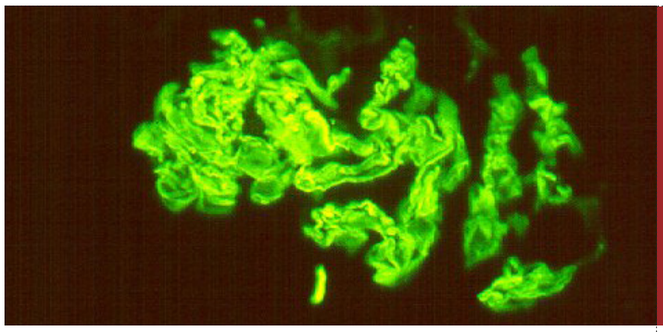
- Radiological imaging – Chest x-ray/ high resolution CT (HRCT) may show pulmonary nodules (can cavitate), pulmonary infiltrates and pleural effusion.
- 90% c-ANCA positive in extensive Wegener's and 75% in limited disease. P-ANCA can also be positive in 5-10%. ANCA measurement can guide when to start treatment. However high ANCA without clinical symptoms may not be a reflection of active disease.
- Pulmonary function tests – kCO may be raised in pulmonary haemorrhage.
- Nasal and respiratory tract biopsies may show granulomata and evidence of vasculitis.
- Renal biopsies would typically show focal segmental or diffuse necrotizing glomerulonephritis.

Treatment

- It is important to involve the renal team as part of the management plan.
- Treatment starts with high dose corticosteroids in combination with cyclophosphamide(depending on the severity of the disease)
- Prophylactic cotrimoxazole (960mg three times per week) is often used to prevent the risk of developing pneumocyctis jiroveci.
- Other agents have been used as well e.g. methotrexate, azathioprine, i.v. immunoglobulin and rituximab.
- Plasma exchange is effective in treating life threatening Wegener's granulomatosis.(e.g. massive pulmonary haemorrhage and rapidly progressing renal failure)

PULMONARY VASCULAR DISEASES

H Lockman and N Withers



Pulmonary Vascular Diseases.
Patient Management.

Goodpasture's syndrome

This autoimmune condition was first described in 1919 by an American pathologist Dr Ernest Goodpasture (1886-1960) and is part of the pulmonary renal syndrome characterised by glomerulonephritis and diffuse alveolar haemorrhage with circulating anti-glomerular basement membrane (anti-GBM) antibodies. Peak incidence is in the 20-30 age group with a male predominance (4:1) and can occur after a viral upper respiratory tract infection. Smokers are more likely to develop pulmonary haemorrhage alone or with renal involvement. There is a higher prevalence in those with HLA DR2 (60-70%) [2]

Patients may have a wide variation of clinical complaints including cough, breathlessness, lethargy, haemoptysis, chest pain / tightness, pyrexia and arthralgia. Finger clubbing can occur in up to 25% [6], inspiratory crackles are common and cyanosis in significant pulmonary haemorrhage.

Investigation

- Full blood count – iron deficiency anaemia
- Erythrocyte sedimentation rate (ESR) – commonly elevated in vasculitis but normal in anti-GBM disease.
- Renal biochemistry – renal impairment
- Urine dipstick – positive for blood (microscopic haematuria), red cell casts and proteinuria. Macroscopic haematuria may occur.
- Chest radiology (CXR/ CT) – diffuse pulmonary infiltrates with upper zone sparing. Some may develop ground-glass appearance due to pulmonary fibrosis.
- Pulmonary function test – restrictive lung defect (FEV1:FVC% > 70%) with raised kCO in presence of pulmonary haemorrhage.

Diagnosis

- Presence of circulating anti-GBM antibodies
- Renal biopsy – is the preferred confirmatory investigation in the presence of circulating anti-GBM antibodies. Features of proliferating or necrotizing glomerulonephritis with cellular crescents which may progress to glomerulosclerosis, interstitial fibrosis and tubular atrophy. Immunofluorescence staining would confirm the presence of IgG and complement (C3) along the glomerular basement membrane.
- Lung biopsy – could be done via transbronchial biopsy or open lung biopsy. Extensive haemorrhage with haemosiderin-laden macrophages and diffuse alveolar damage may be found. Immunofluorescence staining is difficult to perform on lung tissue

Treatment

- Plasma exchange may improve speed or recovery
- Immunosuppression with high dose steroids
- Haemodialysis in significant renal impairment

Prognosis

- Uncommon to relapse once the condition is controlled. Cases with rapidly diffuse pulmonary haemorrhage and renal failure are usually fatal if untreated.

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PULMONARY VASCULITIS

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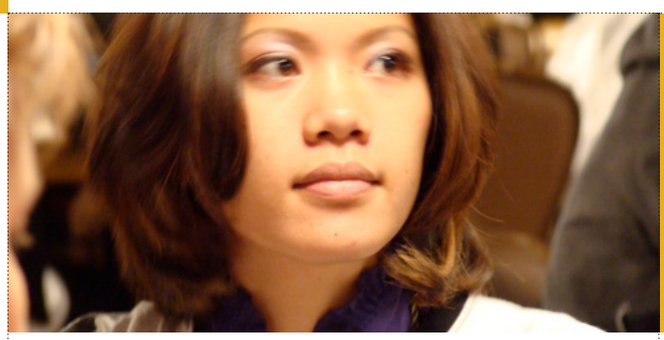

Pulmonary vasculitis.
Good Clinical Care.

Abstract

Pulmonary vasculitis is rare but carries high risk of morbidity and mortality if not diagnosed and treated early. Its main symptoms of cough, haemoptysis and general malaise are not specific and are often attributed to more common diseases such as pneumonia. In this article we discuss a representative case and provide a general review of this condition.

Case History

A 34 year old lady of Asian sub-continent decent presented to an emergency department with a 2 weeks' history of pyrexia, cough and haemoptysis. Her chest radiograph (CXR) showed left upper zone consolidation (figure1). Her illness was treated as pneumonia with amoxicillin and clarithromycin antibiotics. She was also investigated for pulmonary tuberculosis (T.B.) by 3 consecutive morning sputum sampling for acid fast bacilli (AFB) and mycobacterial culture and sensitivity. She was discharged from hospital after few days when she felt better.

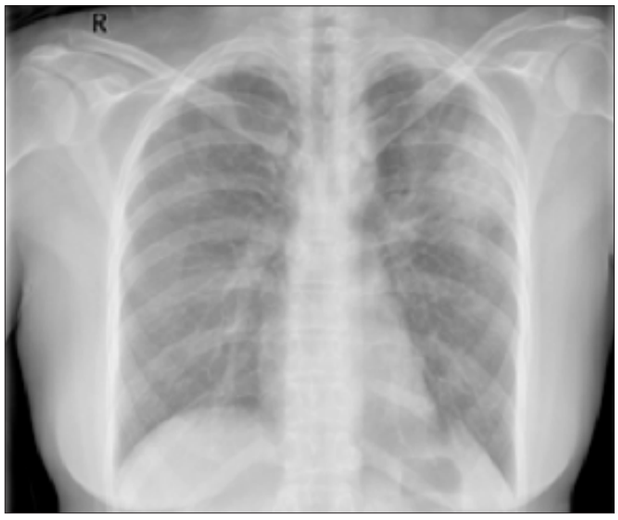

Figure1: CXR on first admission revealing left upper zone consolidation.

The patient represented 10 days later with worsening haemoptysis and shortness of breath. This was thought to be due to deterioration of her pneumonia or an underlying pulmonary TB. Her repeated CXR showed persistent left upper zonal shadowing and appearance of new right lung changes (figure 2). The blood tests results are shown in table 1. A urine dipstick showed a high number of red blood cells. The renal function was normal. Urgent bronchoalveolar lavage to look for cause was arranged but not conducted because the patient was too unwell to undergo bronchoscopy.

Within 24 hours of the second admission, the patient developed marked chest tightness, continuous haemoptysis and hypoxia (oxygen partial pressure (PaO_2) =7.5 kPa. Urgent computerised tomography (CT) of chest revealed bilateral pulmonary consolidation, ground glass and alveolar space filling pattern (figure 3). A significant drop in the haemoglobin level (9.5gm/dl at first admission to 5gm/dl in second admission) was observed when she became haemodynamically unstable and transferred urgently to the Intensive Care unit. In addition to fluid resuscitation she was intubated and commenced on ventilatory support. She received blood transfusion for anaemia. Despite high flow oxygen treatment (fraction oxygen flow (FiO_2) of 0.98) and maximum ventilator support her PaO_2 remained critically low at 7.9 kPa.

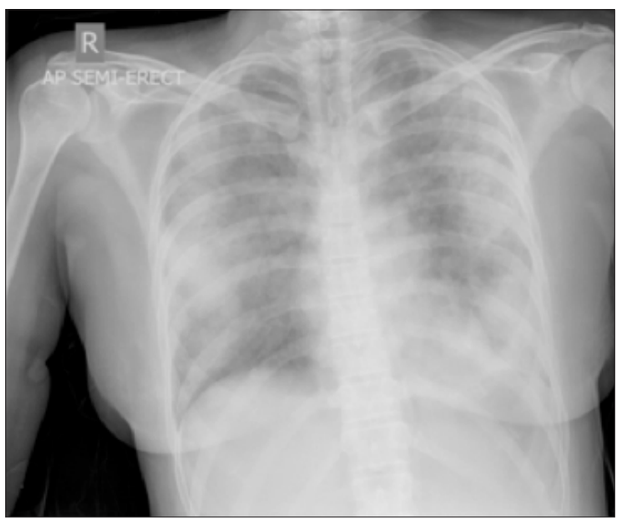

Figure 2: CXR during second admission revealing bilateral pulmonary shadowing.

PULMONARY VASCULITIS

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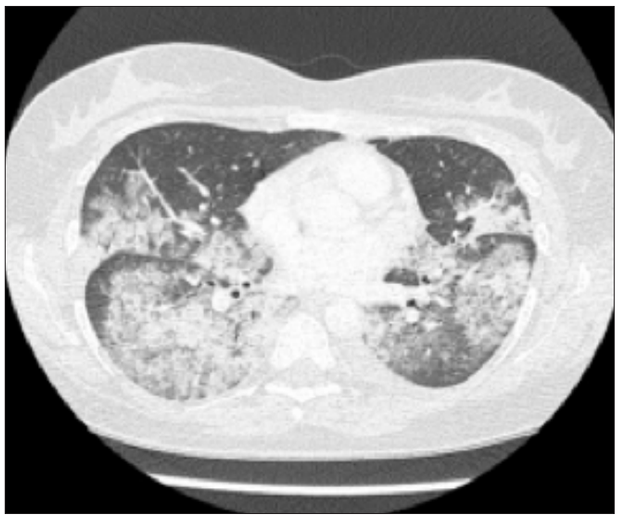


Figure 3: CT scan of thorax, revealing bilateral alveolar opacification pattern due to alveolar haemorrhage.

The presence of positive protein and red blood cells on urine analysis, rapid haemoglobin level drop, and changed pulmonary shadowing were suggestive of alveolar haemorrhage due to pulmonary vasculitis. Urgent anti-neutrophil cytoplasmic antibody (ANCA) screen showed positive cytoplasmic ANCA (c-ANCA) and raised proteinase 3 (PR3) auto-antibodies.

	1st admission	2nd admission	Normal range
WBC	**15** x10^9/l	**24** x10^9/l	4.0-11
Haemoglobin	**9.1** gm/dl	**5.0** gm/dl	11.5-16
Platelet	325 x10^9/l	**500** x10^9/l	150-400
CRP	**140** mg/l	**359** mg/l	0-10
Urea	5.4 mmol/l	6.0 mmol/l	2.5-7.5
Creatinine	65 umol/l	75 umol/l	50-110
Sodium	142 mmol/l	140 mmol/l	133-147
Potassium	3.8 mmol/l	3.5 mmol/l	3.5-5.0
ANCA	-	+ve **c-ANCA**	
Proteinase 3	-	**35** units	<15

Table 1: blood tests results. Abnormal results are highlighted in bold.

A management dilemma arose at this point, in which pulmonary TB was not definitely excluded but vasculitis treatment will require substantial immune-suppression. An enzyme-linked immunosorbent spot (ELISPOT or ' T-spot') assay to test for TB was negative as well as sputum testing for AFB. Following very careful consideration and discussions with the microbiologist, the TB specialist, and the vasculitis specialist it was agreed to commence the patient on high dose intravenous steroids and pulsed cyclophosphamide. In the early phase of this treatment, the patient required extra corporeal mechanical oxygenation (ECMO) support for 48 hours when she rapidly improved and weaned off ventilation. When she was more stable, a renal biopsy was conducted, confirming the presence of crescentic glomerulonephritis. The patient's condition gradually improved until she was discharged home 14 days after second admission. She continued on oral prednisolone and pulsed outpatient cyclophosphamide intravenous infusions. Her CXR normalized, as well as inflammatory markers and vasculitis screen.

Introduction

Vasculitis is a disease process involving inflammation of the blood vessel wall. It can involve any type of vessels and can affect virtually any organ. The pulmonary vasculitides are a heterogeneous group of conditions that often occur as a component of systemic vasculitic diseases. Most frequently, pulmonary vasculitis is observed in vasculitic syndromes that preferentially affect small vessels (arterioles, venules, and capillaries). Systemic lupus erythematosis (SLE) is another important differential diagnosis.

The main small vessel vasculitides are:

· Wegener's granulomatosis (WG)

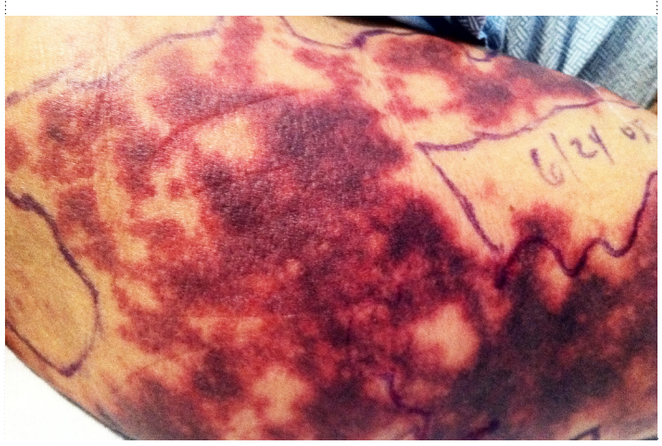
· Microscopic polyangiitis (MPA)

· Churg-Strauss syndrome (CSS)

· Henoch-Schönlein purpura

· Antiglomerular basement membrane (anti-GBM) disease

· Cryoglobulinaemic vasculitis



PULMONARY VASCULITIS

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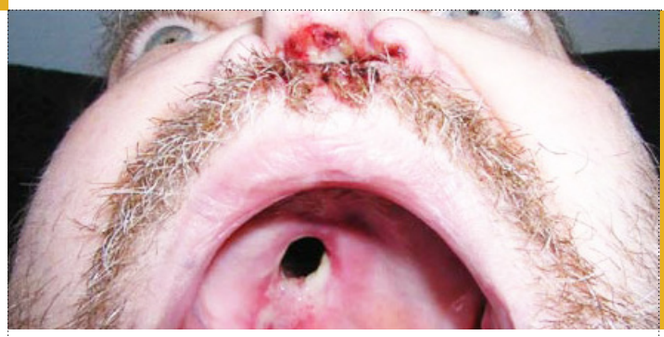

Pulmonary vasculitis.
Good Clinical Care.

Pathophysiology

WG is a complex disorder where a specific immune response against an initiating inflammatory event results in tissue injury. Part of this response is the production of high titre autoantibodies known as anti-neutrophil cytoplasmic antibodies (ANCA) which is one of the hallmarks of WG and related forms of vasculitis. ANCA are directed against antigens present within the primary granules of neutrophils and monocytes.

The most commonly identified and evaluated antigens in WG are the following two proteins:

· Proteinase 3 (PR3), observed in 70 to 80% of patients.

· Myeloperoxidase (MPO), found in approximately 10% of patients

ANCA directed against these antigens are known as PR3-ANCA and MPO-ANCA respectively. The events leading to initiation of WG are obscure. Infectious, genetic and environmental risk factors have been postulated.

Clinical Features

WG frequently affects the lungs. This is more commonly seen as part of a more generalised disease. Many organs of the body can be affected (systemic vasculitis), but usually involvement of the kidneys, the lungs (pulmonary vasculitis), and upper respiratory tract (nasal cavity and sinuses) is seen. This classic triad is frequently not present at initial presentation. Constitutional symptoms and ocular, skin, musculoskeletal, and central and peripheral nervous system disease are also relatively common.

Diffuse alveolar haemorrhage (DAH) is a clinical syndrome that usually results from primary small-vessel vasculitis in the lungs. The onset of alveolar haemorrhage is usually abrupt but some may have a more insidious presentation. Cough, haemoptysis, fever, and breathlessness are common initial symptoms. Some patients, however, present with acute severe respiratory distress requiring mechanical ventilation.

Haemoptysis may be absent at presentation in up to 33% of patients with DAH from any cause. In this setting, new alveolar infiltrates (either localized or diffuse), a falling haemoglobin level, and the finding of increasingly haemorrhagic fluid on sequential bronchoalveolar lavage favor the diagnosis of WG.

History taking in vasculitis

Vasculitis seldom affects the lungs alone as it is a systemic condition. Therefore a comprehensive history and full review of systems is necessary. The following should also be specifically enquired about.

- Constitutional symptoms
- Nasal/sinus symptoms: nasal congestion, recurrent epistaxis, sinus pain, tearing
- Pulmonary: chronic cough, haemoptysis, shortness of breath, stridor, wheezing, chest pain
- Musculoskeletal: joint pain or swelling, myalgia, calf pain
- Renal: haematuria, hypertension

Investigations

A high index of clinical suspicion in any patient with haemoptysis is essential. An ANCA (figure 4 and 5) and urine dipstick is mandatory with this presentation. A urine dipstick is a very sensitive and simple test as microscopic haematuria is very common in these patients.

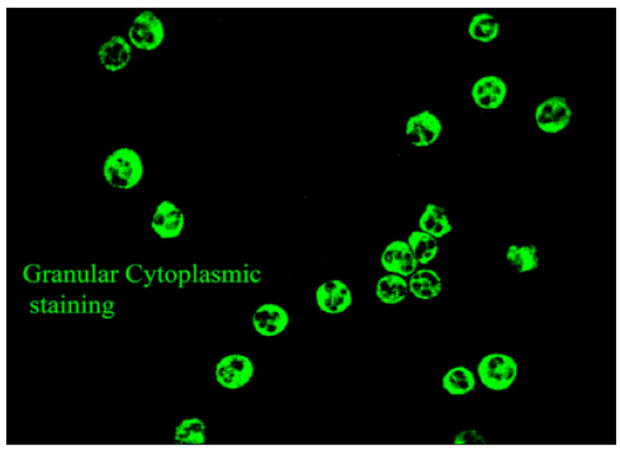

Figure 4 – Staining of proteinase 3 (PR3) results in a cytoplasmic cANCA pattern

PULMONARY VASCULITIS

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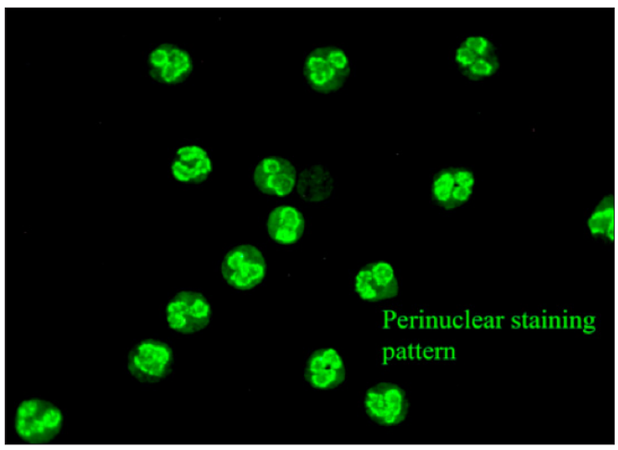


Figure 5 - Staining of myeloperioxidase (MPO) results in a perinuclear pANCA pattern

Other tests to consider in Pulmonary Haemorrhage

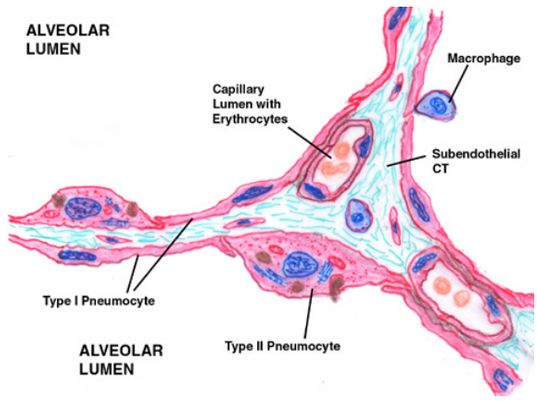
· Anti-glomerular basement membrane antibodies (anti-GBM) — the presence of these antibodies in the serum is diagnostic for anti-GBM antibody disease, which is called Goodpasture's syndrome when accompanied by alveolar hemorrhage.

· The presence of hypocomplementaemia, antinuclear antibodies, and anti-DNA antibodies is consistent with the diagnosis of systemic lupus erythematosus

· Antiphospholipid antibodies — the presence of IgG and IgM anticardiolipin antibodies, IgG and IgM anti-ß2-glycoprotein I, and/or a lupus anticoagulant is consistent with the antiphospholipid syndrome.

· Antistreptococcal antibodies and blood cultures — Antibodies directed against streptococcal antigens, or the documentation of positive blood cultures can suggest a diagnosis of post-streptococcal glomerulonephritis or other infection.

Although chest radiography is often the first imaging study performed in patients, CT gives a more accurate assessment of thoracic involvement. The findings are generally nonspecific. The presence of multiple cavitating nodules usually raises the suspicion of pulmonary vasculitis. Diffuse ground glass opacification due to underlying diffuse pulmonary haemorrhage is also observed in the acute phase of the disease. The finding of mediastinal adenopathy is not common and is more suggestive of infection or malignancy.



If conducted, lung function often shows rise in the pulmonary gas transfer indices due to increased carbon monoxide uptake at alveolar level because of bleeding.

Bronchoscopy is used primarily to look for infection and haemorrhage. Bronchoalveolar lavage can reveal haemosiderin laden macrophages because of alveolar haemorrhage.

Although a confident diagnosis may occasionally be made without tissue sampling, diagnostic biopsy remains the cornerstone of diagnosis. Diagnostic tissue may infrequently be obtained from easily accessible sites, such as skin or upper airway lesions.

Percutaneous renal biopsy is commonly performed during the evaluation of an acute glomerulonephritis. It is important that in addition to conventional histopathology, immunofluorescence studies are performed. In WG the characteristic finding is of a focal, segmental necrotizing glomerulonephritis without immune deposits (pauci-immune). A crescentic pattern is also commonly seen.

The presence of other characteristic immunofluorescence patterns, such as IgA deposition in Henoch-Schönlein purpura, linear IgG deposition in Goodpasture's syndrome, and irregular immunoglobulin and complement deposition in SLE, help to provide a specific diagnosis in patients presenting with pulmonary haemorrhage.

Treatment

The presence of symptoms that constitute immediate threats to either the function of vital organs or to survival require urgent treatment with both a cytotoxic agent and high doses of glucocorticoids. Cyclophosphamide is usually the drug of choice for and is given for 3-6 months. This is followed by azathioprine for an additional 18 months.

Prognosis

Up to 40% of patients suffer from relapses, but the majority respond well to treatment. Localised complications of WG such as rhino-sinus disease and tracheal stenosis may require specific interventions such as surgery. Relapses can be long and troublesome.

PULMONARY VASCULITIS

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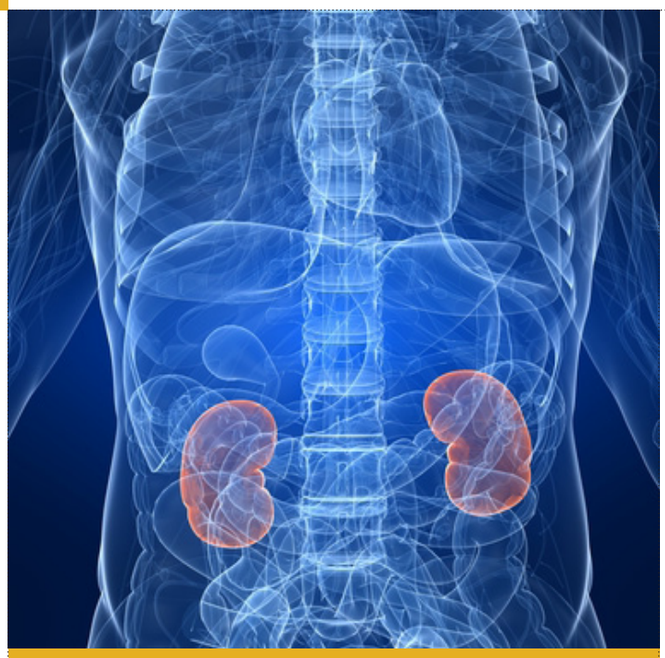

Pulmonary vasculitis.
Good Clinical Care.

Long-term complications are very common. These include chronic renal failure, hearing loss and corticosteroid related side effects. In general rising or falling ANCA titres can indicate relapse or remission respectively. However, adjusting a patient's medication based on ANCA titres alone cannot be justified. Therefore a rise in titre would prompt the clinician to evaluate the patient carefully for any signs of active disease.

Summary

Pulmonary vasculitis is a rare but serious condition associated with high morbidity and mortality if not diagnosed and treated early. Pulmonary vasculitis presentation is often not specific and patients' symptoms are frequently attributed to other more common conditions. A high clinical suspicion index, especially in patients presenting with haemoptysis, pulmonary shadowing and anaemia is necessary and should prompt urgent investigations to establish the diagnosis. Once diagnosis is established, remission can be achieved through carefully monitored treatment with high dose corticosteroids and cytotoxic agents. However, disease relapse is common, and careful follow up in designated vasculitis clinics is required to look for early signs of recurrence as well as to monitor treatment and minimise side effects.

Learning Points

• The diagnosis and management of a systemic vasculitis is amongst the most demanding challenges in clinical medicine.

• A simple yet very sensitive test for vasculitis is a urine dipstick showing the presence of elevated numbers of red cells.

• Moderate to high titre ANCAs are specific for the diagnosis and a rising titre should prompt the clinician to look for signs of disease activity as this can herald a relapse.

• A tissue biopsy from an affected organ is the gold standard for diagnosis but is not always possible before starting treatment.

• The disorders themselves are rare and their signs and symptoms are nonspecific and overlap with infections, connective tissue diseases, and malignancies.

• The presentation of any given disease is highly variable; only rarely does a patient present with all of the "classical" findings.

• Delays in diagnosis are common and result in excess morbidity and mortality.

• The diagnosis of vasculitis relies on the astute clinician recognizing combinations of particular clinical, laboratory, radiologic, and pathologic features

Suggested Further Reading

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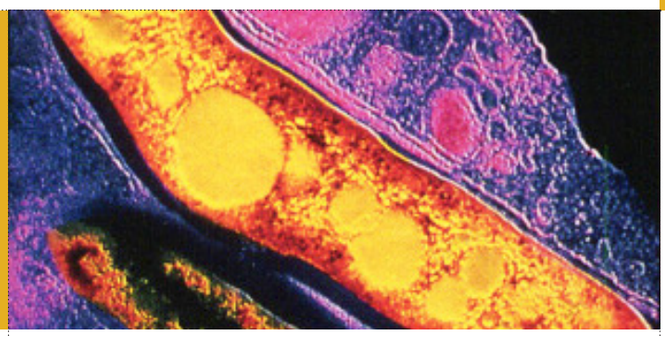
TUBERCULOSIS

V White



Tuberculosis.
Good Clinical Care.

Case history

A 26 year old woman presents to her GP on several occasions over a 3 month period with a dry cough and non-specific chest pains. She is given two courses of antibiotics, but has no improvement. Her GP sends for a CXR and the duty radiologist asks the medical team to review the patient. You review her on the AAU.

She has had a chronic cough for 3 months; initially it was non-productive, but over the last month she has been coughing up small amounts of 'rust-coloured' sputum, but no frank haemoptysis. She does not describe shortness of breath, but does say that she tends to walk more slowly to try to maintain her breathing. She has had a couple of night sweats and has lost about 4Kg in weight, but no daytime fevers.

The patient was born in the UK and is of Indian heritage; she has visited India on several occasions but never lived there for any significant length of time. She has had a BCG vaccination and stopped smoking 1 year ago. She does not take any recreational drugs and drinks 3-4 units of alcohol per week; she lives by herself. She works as a PA in a shipping company and shares an office with 15 others employees.

Her only past medical illness is an appendicectomy aged 7 years. Her mother has ceoliac disease. None of her family have had TB.

On examination she looks relatively well with no lymphadenopathy; her chest is clear and abdominal examination unremarkable. CXR is shown in figure 1. Subsequent sputum samples are smear positive for acid-fast bacilli (AFB) and she is referred to the tuberculosis clinic. Her subsequent blood tests show a normal FBC, but an ESR of 55; normal renal and liver function.

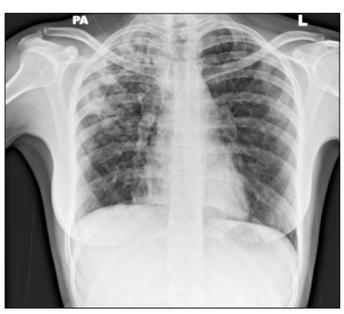


Figure 1: Note the shadowing in the right upper lobe

Introduction

Over 9,000 patients are treated in the UK each year for tuberculosis (14,100,000) of which approximately 40% live in Greater London (47,100,000) (1). About 60% have pulmonary tuberculosis, as does our patient here. The rest have extra pulmonary disease, half of which will be in the lymph nodes and the rest can occur in any other part of the body such as pericardium, kidneys, brain, spine and bones.

Tuberculosis is an infectious disease, although, in general, only patients with smear positive pulmonary disease are considered infectious to others. It is also a notifiable disease and it is a statutory requirement for the diagnosing clinician to report all cases of tuberculosis to the local Control of Communicable Disease consultant, CCDC, and requires contact tracing (2).

Aetiology

Tuberculosis is caused by the bacteria Mycobacterium Tuberculosis (MTB), one of the Mycobacteria species. It is an acid-fast aerobic bacilli which tends to grow very slowly. Infection is normally by person to person from air-borne droplet infection of respiratory secretions (3).

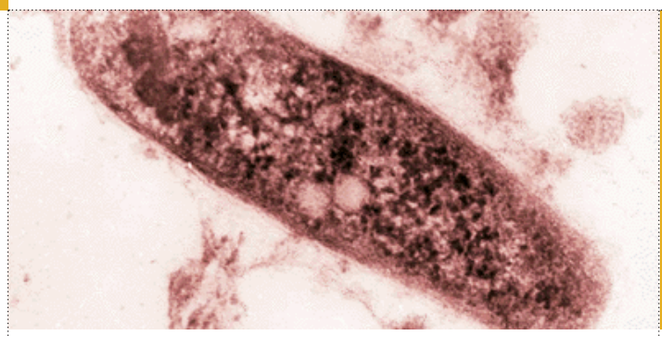
Other members of the Mycobacteria family can also cause disease and are known as the non-tuberculous mycobacterium (NTN) (also environmental mycobacterium or atypical mycobacterium), e.g. M avium, M kansassi, M malmoensae. They tend to cause active disease in patients with underlying lung disease such as COPD or bronchiectasis, or in those who are immunocompromised (4). Some patients may produce sputum which is smear positive for AFB and are started on treatment for MTB, but in culture subsequently grows an atypical mycobacterium. This often changes the medication that they receive as well as the length of treatment.

Multi-drug Resistant Tuberculosis is described as infection with an isolate of Mycobacterium Tuberculosis with in vitro resistance to both isoniazid and rifampicin. In the UK, it makes up 1-2% of all cases of TB. It tends to be caused by inadequate treatment of fully sensitive disease which allows the organism to mutate and develop drug resistance (acquired MDR TB) although person to person transmission also occurs (primary MDR TB).

XDR TB (Extensively drug-resistant tuberculosis) is in vitro resistance to isoniazid and rifampicin as well as one of the injectable second line drugs (e.g. amikacin) and any of the fluroquinolones (1).

TUBERCULOSIS

V White



Tuberculosis.
Good Clinical Care.

TB Jargon table

Active disease v. Infection

- Active disease: symptomatic, pathological.
- Infection: infected with 'dormant' tuberculous bacterium - not unwell - 10% lifetime risk of developing active disease (10% per year in HIV).

Smear positive v. Smear negative

- Smear positive or 'open' TB: TB where AFBs are seen on light microscopy of sputum or pus; Patient considered infectious
- Smear negative or 'closed' TB: TB where no AFBs seen on microscopy, but may later grown in laboratory (culture positive); Not generally considered infectious, but infection control measures should still be considered

Pathology

Tuberculosis is a slow, progressive chronic infection, which produces an inflammatory response that leads to the formation of caseating granuloma. Primary infection tends to be in the lung, with blood-borne or lymphatic spread to other organs (3).

Pulmonary TB tends to manifests as consolidation and cavities, and heals with calcification.

Non-pulmonary sites include:

- Pleurisy (pleural space) - presents with pleural effusion
- Lymph node - 90% of cases affect cervical lymph nodes; nodes develop central caseation
- Bone – osteomyelitis, 'Pott's fracture' of the spine
- Brain – meningitis, tuberculoma
- Skin – rare; 'lupus vulgaris' – produces raised red lesions more common on face and head
- Genitourinary tract - kidneys, prostate, uterus: may effect any part of male or female GU tract; TB salpingitis is a cause of infertility
- Heart - TB pericarditis

Presentation of Tuberculosis

Important history and symptoms to consider:

- Cough
- Haemoptysis
- Fever and night sweats
- Weight loss

Also:

- Chest pain - associated with CXR abnormalities
- Socioeconomic deprivation
- Patient from an ethnic background with a high incidence of TB
- Patients with a history or iv drug and/or alcohol abuse
- Family or personal history of TB
- Immunocompromised secondary to HIV, therapeutic drugs or haematological malignancy
- Recent visit to high prevalence area such as Indian subcontinent, Africa

Beware the atypical presentation:

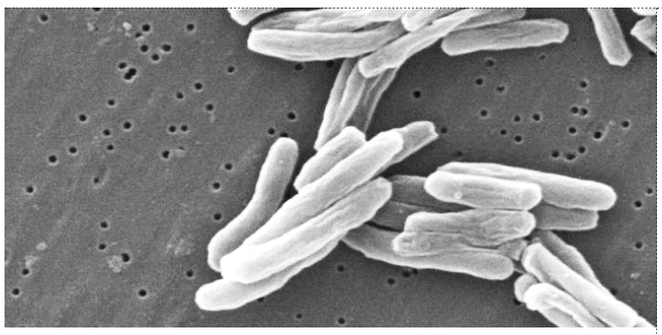
- Unexplained weight loss and anorexia.

Often assumed to have malignant disease

- Unexplained fevers and sweats
- Lymphadenopathy - may be hot and tender, simulating pyogenic infection
- Recurrent chest infection
- Clinical and radiological confusion with lung cancer
- Back pain (falsely thought to be degenerative)
- Joint disease assumed to be pyogenic or inflammatory.
- Non-healing ulcers or sinuses
- Recurrent abdominal pain or ascites
- Recurrent dysuria, associated with 'sterile' pyuria
- Symptoms of TB meningitis attributed to 'tension headache' or depression

TUBERCULOSIS

V White



Establishing a diagnosis

The importance of a thorough clinical history and examination should never be underestimated, particularly enquiry about systemic symptoms e.g. fever, weight loss, in potential non-pulmonary disease.

In pulmonary tuberculosis, as with the above patient, a CXR and sputum for AFB staining and culture (x3) are essential. If the patient is not productive of sputum a bronchoscopy should be organised. In non-pulmonary disease, samples, where ever possible, should be taken and sent for both histology/cytology and microbiology for AFB (if you don't ask, it won't get tested!) e.g. pus, resected sample e.g. biopsy of bone, skin, lymph node etc (must be sent to lab in normal saline). Ensure you remind your surgical colleagues exactly what you want your specimens sent for. EMUs are only helpful in disseminated TB or TB in the GU tract i.e. kidneys, bladder. Do not send them off routinely – they don't help make the diagnosis and may not be processed by the laboratory. Remember that any sample sent for analysis to microbiology does not automatically get tested for tuberculosis and this needs to be specifically requested (2,3).

Appropriate imaging should always include an CXR, but for non-pulmonary disease may be ultrasound (lymph nodes TB), CT scan (pleural, abdominal) or MRI (cerebral and spinal TB).

Bloods tests. FBC: may be anaemic due to bone marrow involvement, inflammatory markers are usually high, but not always; baseline U+E and LFTs: patients with renal failure may need their doses of medication adjusted and several of the drugs cause hepatotoxicity. Most services also measure bone profile and vitamin D levels as there is an association between TB and low Vit D levels. HIV testing should be offered to all patients.

Mantoux tests or Interferon gamma releasing assays (IGRAs), that is the Quantiferon Gold or T-spot test, should not be routinely done in clear cut cases of tuberculosis – that's a waste of money. Useful in looking for latent disease in contacts and in cases where the diagnosis is unclear, but can have false negatives in the immunosuppressed, malnutrition and the elderly (as well as false positives in other patients) which can be misleading, so interpret with caution in cases where there is diagnostic uncertainty.

The Mantoux test

The Mantoux test is an intradermal injection of tuberculin, otherwise known as PPD – Purified protein derivative (PPD prepared from a heat-killed reference strain of M. tuberculosis). A small bleb of the diluted material is injected on a patient's forearm. The test is 'read' 48-72 hours later – the induration made by the test is measured in millimetres. A measurement over 10 mm and above is felt to be significant in patients with no history of BCG or 15mm and above with patients with a BCG history. False positives can occur with BCG vaccination and NTN infection. False negatives can occur if the test is not properly performed, in HIV co-infection, severe active TB, malignancies and other illnesses that may cause immunosuppresion (3).

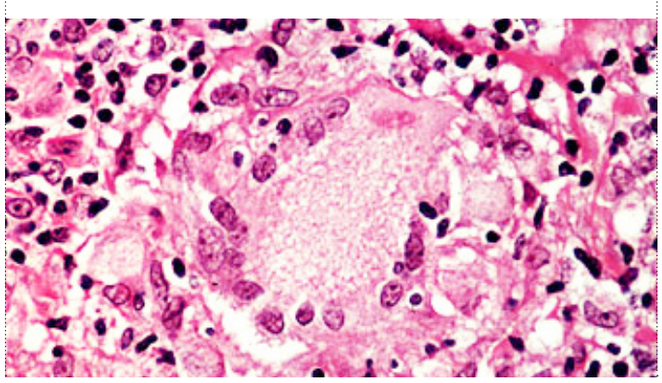
Infection control and contact tracing

Tuberculosis is a public health issue. One of the challenges of treating patients with the disease is maintaining their medical confidentiality whilst ensuring others are protected and screened.

Our patient is smear positive, but lives alone. If she lived in a large household, particularly where young children lived, you might consider admitting her to hospital to start treatment in order to protect those at home from further infection. Any patient admitted to hospital with potentially infectious TB should be barrier nursed in a side room.

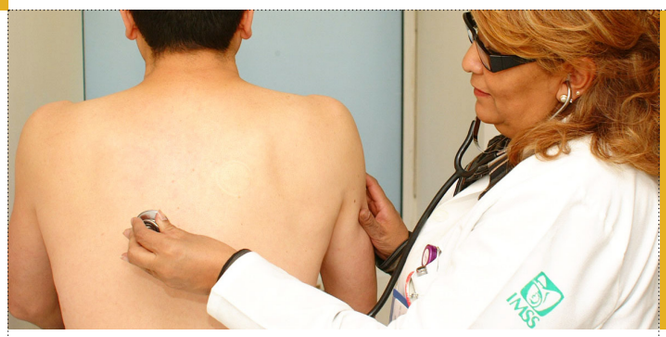
For patients who live with others, household contacts should be offered screening in the contact clinic, which are run by TB specialist nurses. Our patient works in an office which she shares with a large number of other people. All of them should be offered screening.

Asymptomatic contacts are offered a Mantoux test or IGRA test. If these are negative, the contacts are discharged and reassured. If positive, they are booked into a medical clinic, where they are likely to have a CXR, medical history and examination and blood tests if appropriate. If there is no evidence of active TB and they are under 35 years of age, they will be offered chemoprophylaxis. If over 35 they will be reassured, informed about TB symptoms and discharged. Any contact suspected of having active TB will be managed appropriately (2, 3).



TUBERCULOSIS

V White



Tuberculosis.
Good Clinical Care.

Treatment of Tuberculosis - should be supervised by a hospital physician with a special interest in the disease, regardless of the site of disease (2).

Six month drug regime for pulmonary and non-pulmonary disease, except TB meningitis (one year) – adult doses >50kg:

Isoniazid	300mg od	six months	(before food)
Rifampicin	600mg od	six months	(before food)
Pyrazinamide	2g od	two months	(after food)
Ethambutol	15mg/kg od	two months	

Table 1

Regimens using isoniazid should include pyridoxine (Vitamin B6). Pyrazinamide and Ethambutol should not be stopped until the results of the culture and drug sensitivities of the organism are seen. If in doubt, continue four drugs and seek expert advice (2, 3, 5).

Side Effect Profiles

Isoniazid
Nausea and vomiting, hepatitis, peripheral neuritis - therefore tends to be prescribed with Vit. B6, SLE-like syndrome, optic neuritis

Rifampicin
GI disturbance, hepatitis, orange-red bodily secretions, interacts with oral contraceptive pill (OCP)

Pyrazinamide
Hepatitis, nausea and vomiting, rash, arthralgia

Ethambutol
Optic neuritis, red/green colour blindness, peripheral neuritis (dose reduction in renal failure)

Therapy monitoring should include monitoring LFTs, particularly in the first few weeks of treatment. Most clinics check two weeks into treatment and patients with known liver disease should be monitored more closely. Patients should be warned about visual changes and the warning recorded in the notes. Visual assessment at beginning of treatment is mandatory, with a specialist ophthalmology review where appropriate.

Dispensing errors do occur. The commonest are administering rifampicin alone when Rifinah or Rimactazid (combined rifampicin/isoniazid preparations) are intended, and wrongly assuming that two Rifinah 150 tablets are equivalent to one Rifinah 300 tablet (the isoniazid dose differs). Many TB services now dispense their own medication and do not rely on primary care.

Follow-up

This patient was started on anti-tuberculous therapy with isoniazid, rifampicin, pyrazinamide and ethambutol. She had baseline Snellen chart and Ishihara colour blindness tests undertaken by the specialist TB nurses. Her baseline LFTs had already been taken and are repeated 2 weeks into treatment to ensure that she has not developed hepatotoxicity. She also had an HIV test which was negative. She was seen at 8 weeks with a marked improvement of her CXR. AFB culture was now available and showed that she had fully sensitive disease. Therefore the pyrazinamide and ethambutol where stopped and she continued with Rifinah 300 2 tablets od for a further 4 months. At that stage her CXR had returned to normal and the medication stopped. She was discharged from clinic, but warned to represent if her symptoms returned. She has approximately a 5% chance of a recurrence.

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TUBERCULOSIS

V White

Multiple Choice Questions

1. Tuberculosis, true or false?

a. Approximately 55% of cases of tuberculosis in the UK are pulmonary.
b. The abdomen is the second commonest site of disease.
c. Patients rarely die of tuberculosis in the UK.
d. Only cases of pulmonary TB need to be notified
e. In the UK, 1% of cases of TB are isoniazid resistant

2. Treatment for tuberculosis, true or false?

a. Raised liver enzymes are rare with current recommended TB treatment regimes
b. Isoniazid causes red/orange urine
c. Pyrazinamide cause arthralgia
d. Optic neuritis is a rare side effect of ethambutol
e. Rifampicin can cause a peripheral neuritis

3. Infection control, true or false?

a. All patients with smear positive pulmonary TB need admission to hospital.
b. Any patient suspected of having pulmonary TB and needing hospitalisation should be nursed in a side room.
c. Only household contacts of patients with smear positive pulmonary TB need to be offered screening.
d. Most contacts of a patient with smear positive disease will require full TB treatment
e. Chemoprophylaxis is with isoniazid 300mg od for 3 months

Answers

Answers: T, F, F, F, F

Around 55 % of cases of TB in the UK are pulmonary. Lymph nodes either in the neck, mediastinum or elsewhere are the second commonest site of disease. 300-400 patients continue to die each year of tuberculosis. All cases of M TB should be notified to the CCDC. Rates of isoniazid resistant TB are about 7% in the UK and MDR TB is 1-2%.

Answers: F, F, T, T, F

Isoniazid can cause a peripheral neuritis and should generally be given with pyridoxine (vitamin B6). Rifampicin causes red/orange bodily secretions and the patient should be warded about this before starting treatment as they can become alarmed by red coloured urine. Pyrazinamide can cause an arthragia, which resolves on stopping the drug as well as a florid rash and/or itching in some patients. All three of these drugs separately as well as in combination can cause a drug-induced hepatitis. A transient rise in liver enzymes is common in up to 20% of patients and toxicity requiring cessation of treatment, even temporarily, occurs in 1% of patients. The ophthalmic effects of ethambutol are dose related and at a dose of 15mg/kg the chances are less than 1%.

Answers: F, T, F, F, F

Most cases of uncomplicated TB can be treated as an outpatient. In the case of smear positive disease the patients only needs admitting to hospital if they are unwell, have complex social and medical problems that compound their treatment or the have young children at home. Any patient admitted to hospital with TB that could be infectious to other patients or staff needs to be nursed in a side room. Negative pressure rooms are reserved for those with MDR TB. Any close contacts of a smear positive case whether family, social or work based should be offered screening. Those who are under 35 years of age with evidence of latent disease should be offered chemoprophylaxis with either isoniazid 300mg for 6 months (adult dose) or isoniazid 300mg and rifimpicin 600mg od (>50kg) for 3 months.

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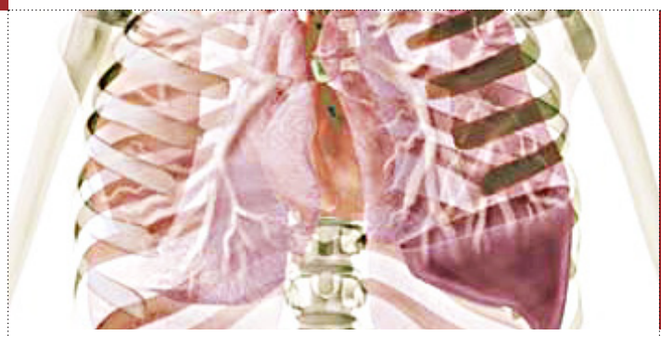
PLEURAL EFFUSION – A RARE BUT IMPORTANT CAUSE

M Connolly



Pleural Effusion – A rare but important cause. Patient Management.

Mr GD, a 77 year old male retired pharmacist, presented to the Ulster Hospital Dundonald with cough and breathlessness of approximately four months' duration. He had previously been well. He was a lifelong non-smoker and had never been exposed to asbestos or tuberculosis. He denied fever, sputum, haemoptysis or weight loss. He had previously been well from a respiratory point of view. His past medical history included hypertension and duodenal ulceration.

Vitals signs were all within normal limits. General examination showed no evidence of cachexia, cyanosis, anaemia or jaundice. He had no finger clubbing. There was no lymphadenopathy. Examination of the chest revealed reduced expansion, stony dullness and reduced air entry at the right base and midzone. Cardiovascular examination revealed normal heart sounds, no murmurs, normal JVP and bilateral non-pitting oedema to the mid calf level. This had been present for four months, and was felt to represent lymphoedema.

Of interest, the patient had a yellowish discolouration of all nails of the hands and feet. The nails were dystrophic, thickened and curved. This had been present for twelve months. He had attended a dermatologist who excluded fungal nail infection. Nail scrapings were negative on fungal culture.

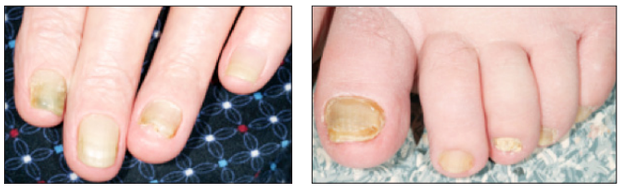


Fig 1: Finger and toe nails.

Admission bloods including full blood picture, renal function, liver function and bone profile revealed no abnormality except an anaemia, Hb 11.7g/dl, MCV 90, consistent with chronic disease. Thyroid function was also normal. Sputum cultures were negative.

A chest radiograph was performed (Fig 2) which showed a right sided pleural effusion. A CT scan of his chest, abdomen and pelvis confirmed a large right sided pleural effusion with no mass lesion seen.

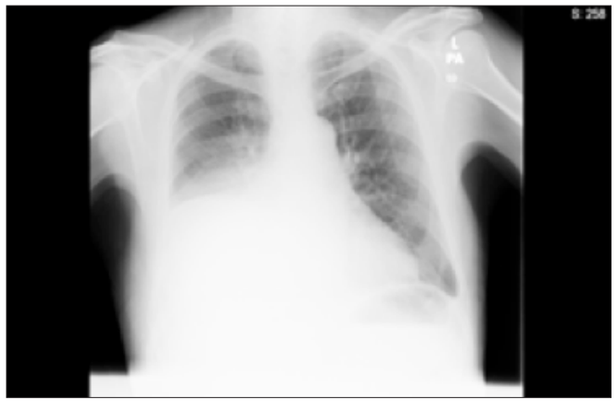


Fig 2: CXR showing large right sided pleural effusion.

An ultrasound of the chest was performed which showed a large volume of free fluid measuring 6.6cm (Fig 3).

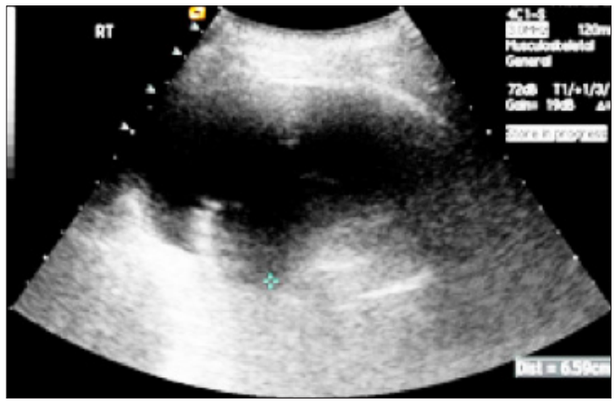


Fig 3: Ultrasound chest showing large pleural effusion.

PLEURAL EFFUSION – A RARE BUT IMPORTANT CAUSE

M Connolly

A theurapeutic pleurocentesis was performed, after ultrasound marking. 1,700mls of straw coloured liquid was aspirated. It was not chylous. Results showed an exudate:

Colour: Straw coloured
Ph 7.49
Total Protein: 39
Glucose: 6.3
LDH 84
Trig: 0.16
No growth / No AFB seen
Cytology –ve

In summary, history, examination and investigations excluded cardiac failure (normal left ventricular function on transthoracic echocardiogram in April 2010), liver failure, renal failure, malnutrition, malignancy, infection, tuberculosis or chylothorax as possible causes.

It was felt that as the patient fulfilled the triad of idiopathic pleural effusion, lymphoedema and yellow nails, that a diagnosis of 'Yellow nail syndrome' was the most likely cause.

Discussion

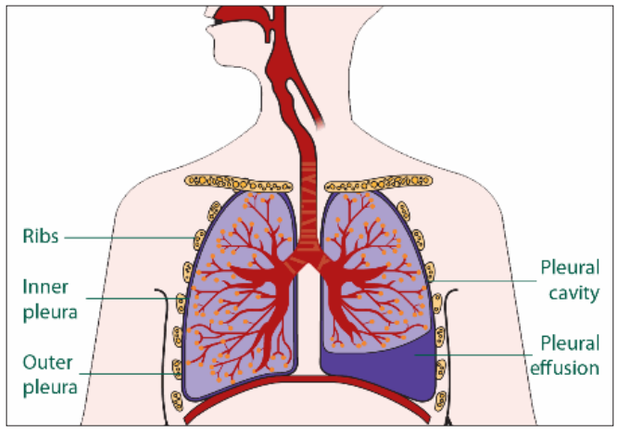
Although pleural effusion is a common presenting entity in medical practice, if common causes are excluded, discovering the diagnosis can be challenging. Yellow nail syndrome is a rare disorder, with approximately only 100 published cases[1]. It was first described in 1964 by Samman and White[2]. It comprises the triad of a dystrophic yellow discolouration of the nails, lymphoedema, and pleural effusions[3].

Although familial and sporadic cases have both been reported, a genetic basis for the disorder has been disputed[4]. The cause and pathogenesis of the nail changes and lymphoedema is also not clear[5,6]. It has been suggested that the basic abnormality is that of hypoplasia of the lymphatic vessels[7].

Nails are typically yellowish green, curved and thickened and slow growing. Onycholysis may occur. Lymphoedema is usually mild. Pleural fluid is usually exudative, and can recur rapidly after thoracocentesis[8]. Persistent pleural effusions may require chemical pleurodesis.

The disorder can be associated with bronchiectasis, chronic sinusitis, recurrent pneumonia, and immunodeficiency[1]. The present patient had no evidence of these.

Yellow nail syndrome is a clinical diagnosis, once other potential causes are excluded. There is no specific treatment. The condition is managed with thoracocentesis, or pleurodesis for recurrent effusions. Nails may be treated with Vitamin E [9] or Zinc [10], although evidence for this is scanty.



There is little mention of prognosis in the literature. However, several case reports demonstrate patients in their seventies[1]. A major complication is that of recurrent effusions. Occasionally, nail changes spontaneously resolve [3].

In summary, Yellow nail syndrome is a rare but important cause of pleural effusions in medical practice. Increasing awareness of this syndrome may avoid delay in diagnosis of an idiopathic pleural effusion.

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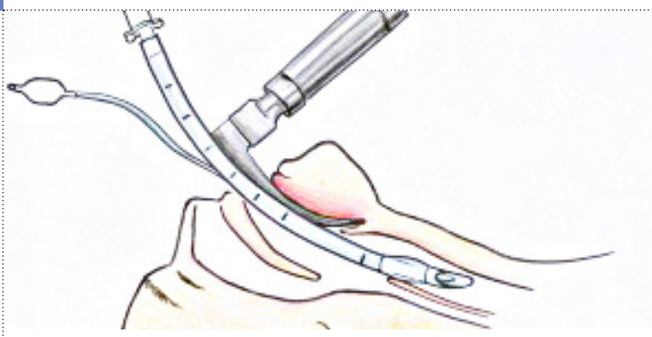
CHEMICAL PLEURODESIS - WHAT IS IT AND HOW TO DO IT

A Gondker, S Pathmanathan and JA Kastelik



Chemical Pleurodesis - What is it and how to do it. Practical Procedures.

Abstract

Bedside medical pleurodesis is a procedure that is performed to prevent re-occurrence of pleural fluid. Medical pleurodesis is usually performed in the context of patients with recurrent pleural effusion due to underlying malignancy. The procedure involves instillation of an agent such as Talc into the pleural space. The aim of the procedure is to prevent pleural fluid from recurring by artificial obliteration of the pleural space through creation of an adhesion between the parietal and visceral pleura. The common complications of pleurodesis include pain, fever and occasionally potentially fatal respiratory failure due to pneumonitis or adult respiratory distress syndrome. It is important that the procedure and its complications are carefully explained to the patient and documented in the medical notes. Currently medical bedside pleurodesis carries a success rate of approximately 80%. Alternative procedures that allow for pleurodesis to be performed, which carry much higher rate of success but are also more invasive, include medical thoracoscopy and video-assisted thoracoscopic surgery (VATS).

Case History

A 72-year-old patient diagnosed with an incurable lung cancer was admitted 10 days ago to the admission ward with breathlessness secondary to a large right-sided pleural effusion. The pleural effusion was drained and the patient was discharged. The patient is re-admitted now with worsening breathlessness. The chest radiograph confirms a recurrence of his right-sided pleural effusion. How would you manage the patient?

Discussion

This is a scenario that you may come across while on acute medical take. Malignant pleural effusion is a common presentation to respiratory or oncology teams on acute medical take. It is not uncommon, particularly in mesothelioma, breast and ovarian cancers for pleural fluid to recur despite the therapeutic drainage. The recurrence of an effusion can be very distressing for the patients and their families. This may cause particular distress in patients with advanced cancer when the focus of care aims towards palliation and control of the symptoms. Pleurodesis is commonly performed in patients with advanced cancer and recurrent pleural effusion. The pleura is a serous membrane that forms two layers; the parietal pleura, which covers the inner part of the chest wall and the diaphragm and the visceral pleura that covers lungs and adjoining structures[1].

The pleural space is the cavity that surrounds the lungs, which is formed between the parietal and visceral pleura. Pleural effusion is the abnormal accumulation of pleural fluid within the pleural cavity. The aim of pleurodesis is to prevent pleural fluid from re-occurring by artificial obliteration of the pleural space through creation of an adhesion between the parietal and visceral pleura.

What is Chemical Pleurodesis?

Chemical pleurodesis is a process whereby a sclerosing agent is introduced into the pleural space with the aim to seal the pleural space. This is achieved by causing an inflammatory process, which leads to fibrin formation causing the visceral and parietal pleura to stick together. By closing this space, the aim is to prevent the recurrence of fluid within the pleural space. The main indication for pleurodesis is to manage recurrent malignant pleural effusions with the aim of palliation of symptoms. Pleurodesis can also be indicated in the treatment of recurrent, or difficult to treat, pneumothorax. This is employed mainly for patients who are not suitable for surgery due to reasons such as the patient's preference, frailty or co-morbidities. The gold standard treatment for management of recurrent pneumothorax is video-assisted thoracoscopic surgery (VATS) pleurectomy and pleural abrasion or an open thoracotomy and pleurectomy. In exceptional cases, non-malignant effusions may be pleurodesed. This is mainly if patients are not fit for surgery, remain symptomatic and the underlying disease process cannot be controlled.

Pleurodesis can be broadly divided into medical and surgical procedures. Medical options include bedside pleurodesis (which is what this article will concentrate on) or medical thoracoscopy. Medical thoracoscopy is a minimally invasive procedure usually performed by a respiratory physician under a local anaesthetic. A rigid or flexible scope is introduced into a pleural space providing direct visualisation of the pleural space and allowing for introduction of talc and pleurodesis. Surgical pleurodesis is usually performed by a thoracic (or cardiothoracic) surgeon during VATS. VATS is an invasive procedure which requires a general anaesthetic and uses multiple ports for viewing and working instruments to access pleural space.

CHEMICAL PLEURODESIS - WHAT IS IT AND HOW TO DO IT

A Gondker, S Pathmanathan and JA Kastelik

Several considerations need to be taken into account when deciding which method to use. Ultimately it is the patient's preference and fitness, mainly with regards to general anaesthesia, that contributes to decision-making on the choice of the procedure. The British Thoracic Society (BTS) guidelines favour either bedside pleurodesis or medical thoracoscopy as the first line intervention for malignant effusions without the presence of trapped lung[1]. A recent Cochrane report reviewed two studies with a total of 112 patients and found that there was a greater success rate in patients with thorascopic pleurodesis (96%) as compared to bedside pleurodesis (81%) (RR 1.68 95% CI 1.35 - 2.10, NNTB 3 95%CI 2.02 - 4.36)[2]. Nevertheless, bedside pleurodesis remains the most commonly used method, mainly due to its convenience and, in many centres, lack of access to thoracoscopic services. At present access to medical thoracoscopy is variable throughout the UK with some regions only offering the procedure in tertiary centres. However if available, the higher success rates mean that it should be offered as a first line to patients fit to undergo the procedure.

What sclerosant is used?

There are two main agents used in pleurodesis, Talc and Bleomycin. Tetracycline had previously been a popular and widely used agent for pleurodesis, however as its production has now ceased it is no longer available. Talc (trilayered magnesium silicate sheet, $Mg_3Si_4O_{10}(OH)_2$) was the first agent used for pleurodesis, back in 1935. It is well tolerated and has a reasonable side-effect profile. Talc's main side effects include pleuritic chest pain and mild fever, although more severe complications have also been described namely acute respiratory failure secondary to either pneumonitis or adult respiratory distress syndrome1. Pleurodesis with Talc has been demonstrated to have success rates between 81 and 100%[1]. Talc has a higher success rate than Bleomycin and so, in the UK, is the preferred sclerosant. Therefore the rest of this article will focus on using Talc as the sclerosant of choice.

How is pleurodesis performed?

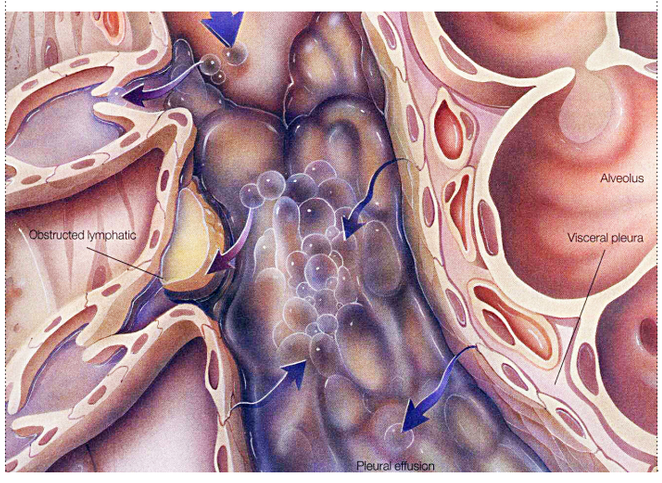
Before pleurodesis is carried out, it is important that the diagnosis of malignant pleural effusion is confirmed. Pleurodesis is not usually indicated in transudate pleural effusions or effusions secondary to infection. Therefore it may be necessary to perform a pleural aspiration to gain cytological confirmation of malignancy before considering the prospect of pleurodesis. For example, the patient in our vignette has a confirmed diagnosis of recurrent malignant pleural effusion on the background of advanced lung cancer. To perform bedside medical pleurodesis the patient should have an intercostal chest drain 10 - 14 F inserted ideally under ultrasound guidance (Figure 1)[1]. The fluid should be carefully drained using the intercostal chest drain. It may be appropriate to consider clamping the intercostal chest drain for 1 - 2 hours for every 1 - 1.5 litre of pleural fluid drained.

Guidance Pleurodesis Protocol - adapted from BTS guidelines[1]

- Consent from the patient for the procedure.
- Insert 10 - 14 F intercostal chest drain and rain the pleural fluid.
- Confirm lung re-expansion and fluid drainage on chest radiograph.
- Pre-medicate patient with anxiolytics or opioids 15 to 30 minutes prior to starting the procedure.
- Using a sterile technique instill Lidocaine 1% (3 mg/kg, maximum of 250 mg) via the intercostal chest drain; intra-pleurally.
- Instill pre-prepared Talc and Normal Saline mixture or mix 4 gram of graded sterile Talc with 50 ml of sterile Normal Saline in a syringe and inject intra-pleurally through the intercostal chest drain using aseptic technique.
- Flush the intercostal chest drain with sterile Normal Saline.
- Clamp the intercostal chest drain for one hour and then allow free drainage.
- Remove the intercostal chest drain.

Figure 1. Guidance pleurodesis protocol adapted from the British Thoracic Society (BTS) guidelines[1].

This may reduce the risk of developing of recognised and potentially fatal complication of re-expansion pulmonary oedema. The pleural fluid drainage should continue until the intercostal chest drain measured fluid output is approximately less than 150 ml in 24 hours. A chest radiograph and, if available, a bedside thoracic ultrasound examination will be required to confirm that the lung is fully expanded and the pleural fluid is removed. Once this is confirmed the patient could be considered for pleurodesis. Prior to pleurodesis, corticosteroids and NSAIDS, if possible, should be stopped as those agents can impair pleurodesis by inhibiting the inflammatory process. It is important that the appropriate equipment for pleurodesis is set up before the procedure takes place. The following list may be of assistance when setting up the trolley for the bedside medical pleurodesis:



CHEMICAL PLEURODESIS - WHAT IS IT AND HOW TO DO IT

A Gondker, S Pathmanathan and JA Kastelik

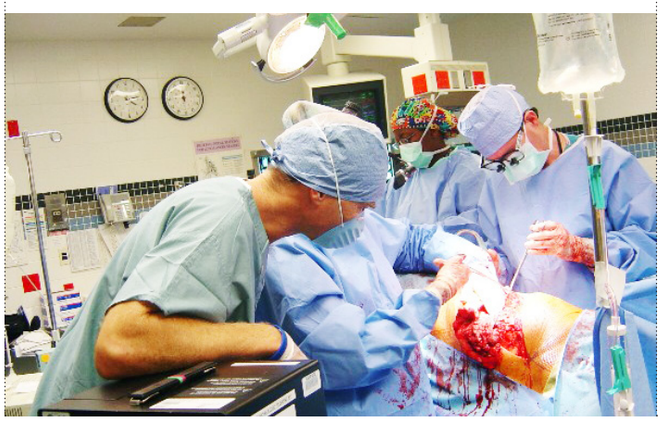
List:

- Procedure Trolley, sterile field
- Sterile dressing pack
- Sterile Gloves
- Sterile Wipes
- 50 ml syringe
- 2 x 20 ml syringe
- 1% Lidocaine
- 4 gram of sterile Talc
- Sterile pot
- Sterile Normal Saline

Written consent must be obtained before performing bedside medical pleurodesis. The nature of the procedure should be explained to the patient, as well as possible common complications such as pleuritic chest pain, fever and the more serious complications of pneumonitis and respiratory distress syndrome, which although rare when medical grade large particle talc is used, may occasionally be fatal. It is generally recomended that premedication should be considered to alleviate anxiety and pain. The premedication should be administered at approximately 15 to 30 minutes prior to the procedure and should include opiates such as Oromorph together with an anti-emetic agent e.g. Metoclopramide.

In addition, benzodiazepines such as Midazolam (1 to 2 mg) can be used if the patient is particularly anxious, but it must be remembered that these will not have the benefit of producing an analgesic effect. The patient should be positioned in a bed lying comfortably in a supine position at 45 degrees. It is important to ensure that the patient is carefully monitored during the procedure. The suggested observations should include respiratory rate, oxygen saturations, blood pressure and heart rate.

Once it is established that the premedication has started to have effect, using an aseptic technique, 1% Lidocaine should be administered intra-pleurally via the intercostal chest drain. The amount of Lidocaine delivered intra-pleurally should not exceed maximum dose as Lidocaine toxicity can lead to arrhythmias, drowsiness or respiratory failure. The maximum dose of Lidocaine that can be administered is 250 mg or 3 mg/kg. Thus for a patient weighing 70 kg a maximum of 21 ml of 1% Lidocaine can be administered. This should be followed by a 10 ml of sterile Normal Saline flush.



Then intra-pleural Talc administration can take place again using the intercostal chest drain. Most pharmacies provide the Talc ready diluted in a 50 ml syringe. If not already premixed, 4 gram of talc should be mixed, under sterile conditions, with 50 ml of sterile Normal Saline, thus forming a suspension.

The administration of Talc should be followed by another 10 ml flush of sterile Normal Saline through the intercostal chest drain to ensure that the Talc does not block the drain. The drain should then be clamped for 1 hour, before releasing to freely drain. In the past patients used to be rolled and rotated in bed, in an effort to 'spread' the Talc in the pleural cavity, however, there is no evidence to show that this is effective[1]. If anything it has been shown to be time consuming and uncomfortable for the patient. It is important that analgesia and anti-pyretics are prescribed for symptom control. The patient should have observations (respiratory rate, heart rate, blood pressure, oxygen saturations and temperature) monitored half-hourly for the first 2 hours, followed by 6 hourly observations thereafter.

Once the procedure is finished it is important to safely dispose of the equipment including any sharp objects. In addition, the procedure requires to be documented in the medical notes including the instructions for monitoring and after care as well as the management of any potential complications. The intercostal chest drain can be removed in the next 24 to 48 hours, provided the drain output is less than 250 ml in 24 hours. If the patient has an underlying diagnosis of malignant mesothelioma, they should be considered for prophylactic radiotherapy (21 Gy in three fractions) to the drain site, to prevent malignant seeding[1].

What if the pleurodesis fails?

In the initial phase it is difficult to predict whether the bedside medical pleurodesis was successful. For example, the overall success rate of bedside medical pleurodesis using Talc is around 80%[1]. Failure of pleurodesis is demonstrated by re-accumulation of the pleural fluid at any time after the procedure. If medical bedside pleurodesis fails, there are a number of options that could be considered to manage re-occurrence of pleural fluid. Firstly bedside medical pleurodesis can be repeated. This may be more appropriate for patients with poor performance status and/or co-morbidities. However if the patient is fit, then medical thoracoscopy with Talc poudrage should be considered due to the higher success rate of pleurodesis. Another option would be an insertion of a long term indwelling pleural catheter such as PleureX®.

This is inserted under a local anaesthetic. The indwelling pleural catheter has a one-way safety valve system that only allows for fluid to be drained out without a risk of aspirating air or fluid into the chest cavity. The indwelling catheter is attached to a container. The patient drains the pleural fluid at home, utilizing vacuum bottles. This allows the patient to be managed at home independently or with a help of a district nurse. The final option that can be considered is surgical management such as pleurectomy.

CHEMICAL PLEURODESIS - WHAT IS IT AND HOW TO DO IT

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Conclusions

Recurrent pleural effusion can affect many patients with advanced malignancy. The recurrence of pleural effusion may be very distressing for the patients. Medical bedside pleurodesis is a procedure that aims to prevent pleural fluid from re-occurring. It is a commonly performed procedure and so it is important that junior doctors are aware of the indications and complications of medical pleurodesis and have a clear understanding of how it is performed.

MCQ Questions

Question 1: Regarding pleurodesis, true or false?

a) Indications for pleurodesis include recurring pleural effusion in patients with lung cancer.
b) Insertion of an intercostal chest drain is required prior to performing medical bedside pleurodesis.
c) The dose of 1% Lidocaine that can be administered for pain relief via the intercostal chest drain should not exceed 3 mg/kg.
d) Chest radiograph is required prior to performing bed side medical pleurodesis.
e) Patients do not require sedation prior to pleurodesis.

Question 2: In the context of complications of pleurodesis, true or false?

a) Pleuritic chest pain and bradycardia are recognised complications of medical pleurodesis.
b) Formal consent is not required prior to performing medical bedside pleurodesis.
c) Medical pleurodesis with Talc does not cause pneumonitis.
d) Respiratory rate does not need to be measured during or after pleurodesis.
e) Following pleurodesis patients should be rolled and rotated in bed, in an effort to 'spread' the Talc in the pleural cavity.

MCQ Answers

Answers to question 1:

a) True. Indications for pleurodesis include recurrent pleural effusion in patients with advanced cancer such as lung cancer, breast cancer or mesothelioma.
b) True. Patients require insertion of an intercostal chest drain and pleural fluid drainage prior to performing medical bedside pleurodesis.
c) True. The dose of Lidocaine should not exceed 3 mg/kg as toxic doses can lead to arrhythmias, drowsiness or respiratory failure.
d) True. A chest radiograph is required prior to performing bedside medical pleurodesis to confirm that the lung is fully expanded and the pleural fluid is removed.
e) False. Premedication should be administered at approximately 15 to 30 minutes prior to performing medical bedside pleurodesis and may include opiates or benzodiazepines together with an anti-emetic agent.

Answers to question 2:

a) True. Recognised complications of pleurodesis include pleuritic chest pain, fever, bradycardia and the more serious side effects of pneumonitis and respiratory distress syndrome that may occasionally be fatal.
b) False. Prior to performing bedside medical pleurodesis written consent must be obtained and the nature of the procedure as well as the possible complications should be explained to the patient.
c) False. The more serious complications of Talc pleurodesis include pneumonitis and respiratory distress syndrome that may occasionally be fatal.
d) False. The patient should have observations (respiratory rate, heart rate, blood pressure, oxygen saturations and temperature) monitored during the pleurodesis and following the procedure half-hourly for the first 2 hours, followed by 6 hourly observations.
e) False. In the past patients used to be rolled and rotated in bed, in an effort to 'spread' the Talc in the pleural cavity, however, there is no evidence to show that this is effective.

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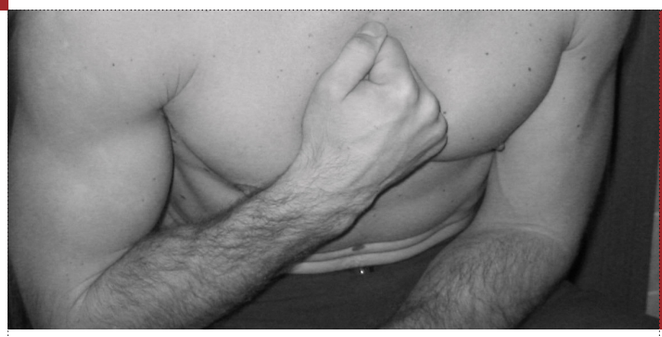
THE ACUTE RESPIRATORY DISTRESS SYNDROME IN AN ADULT PATIENT PRESENTING WITH SEPSIS

P El-Dalil, L Harding, P Ellahee and W Tunnicliffe



The Acute Respiratory Distress Syndrome in an adult patient presenting with Sepsis. Patient Management.

You are the Foundation Year doctor called to see Mr R, a 27 year old man who has presented to the Emergency Department with severe central chest pain. Mr R reports a week's history of fever, myalgia, and loss of appetite; his chest pain developed over the past 24 hours and has increased in severity over the past 2 hours. On examination Mr R was pyrexial (temperature 38.3°C), tachycardic (HR 126 bpm), tachypnoeic (RR 34) with a blood pressure of 64/40mmHg.

You consider Mr R to be developing possible septic shock; what should you do?

Initial steps:

Call for urgent senior help and follow an ABCD approach

- A: Airway patent; you apply high flow oxygen via a non-rebreath mask (15 L/min). You establish oxygen saturation monitoring.

- B: Mr R's respiratory rate is 34 breaths/minute, his chest movements are symmetrical and his trachea is central. Percussion is unremarkable and auscultation confirms breath sounds are vesicular and equal bilaterally, with some added crackles audible at the left base. You request an arterial blood gas analysis (pH 7.01, $PaCO_2$ 2.7 kPa, PaO_2 7.4 kPa, SBE -14.4, Lactate 6.1).

- C: You verify hypotension, assess peripheral circulation (warm) and check the capillary refill time (4 sec). You confirm that Mr R's neck veins are not overtly distended, and look for evidence of blood loss. You listen to his heart sounds and exclude any significant murmurs. You establish large bore intravenous access and take blood samples including blood cultures. You initiate fluid resuscitation and establish continuous ECG monitoring.

- D: GCS 15/15, no limb movement deficits and pupils are of normal size and reactivity. You perform a blood glucose estimation (5.6 mmol/l).

Subsequent management steps:

Your registrar agrees that Mr R is likely to have septic shock and that his chest signs suggest a respiratory cause. You administer broad-spectrum intravenous antibiotics, request an urgent chest x-ray (Figure 1) and a 12 lead ECG (unremarkable). A urinary catheter is inserted and the patient continues to be fluid resuscitated; consequently Mr R's clinical condition begins to stabilise.

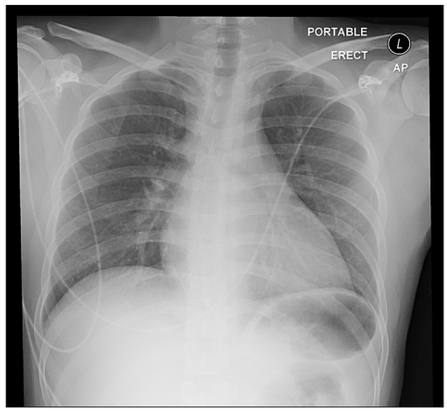


Figure 1

Mr R's chest x-ray does not demonstrate a clear respiratory cause, you therefore consider other possible causes including pulmonary embolism and thoracic aortic dissection. You arrange an urgent CT thoracic aortogram, which demonstrates a pericardial effusion, some ground glass opacity of the pulmonary parenchyma and enlarged hilar and sub-carinal lymph nodes.

The duty cardiologist performs a percutaneous pericardial drainage, which reveals frank pus in the pericardial space.

THE ACUTE RESPIRATORY DISTRESS SYNDROME IN AN ADULT PATIENT PRESENTING WITH SEPSIS

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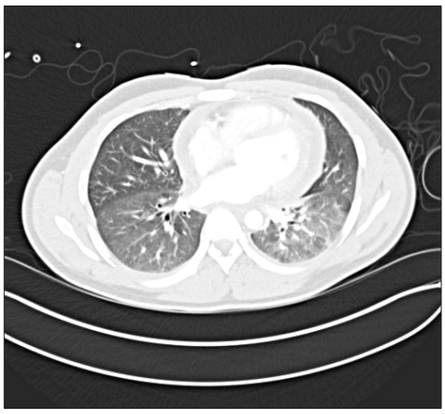


Figure 2

Mr R is admitted to the critical care unit for further management with a working diagnosis of acute septic pericarditis leading to septic shock and associated acute lung injury.

Events in the critical care unit:

Mr R's condition deteriorates further, with increasing tachycardia, tachypnoea, persistent hypotension and falling oxygen saturations despite CPAP. The decision is made to intubate Mr R, his chest X-ray is repeated (Figure 3) and a further arterial blood gas is taken (FiO_2 0.7, pH 7.26, $PaCO_2$ 8.9 kPa, PaO_2 7.4 kPa, SBE -7.7, Lactate 4.8).

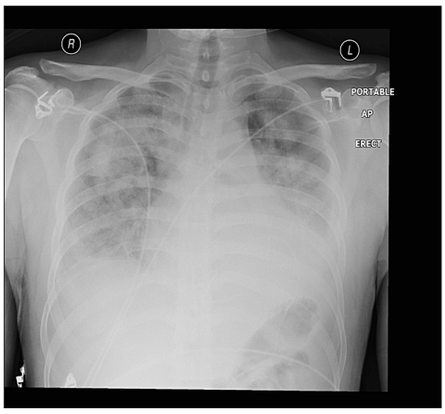


Figure 3

A diagnosis of septic shock complicated by Acute Respiratory Distress Syndrome (ARDS) is confirmed.

Acute Lung Injury and Acute Respiratory Distress Syndrome:

Acute lung injury is characterised by non-cardiogenic pulmonary oedema and respiratory failure in the critically ill patient; ARDS lies at the extreme end of this spectrum and is identified by more severe hypoxemia. Diagnostic criteria for ARDS are listed in Box 1.

Box 1 - Diagnostic criteria for ARDS	
1.	Acute onset following an appropriate precipitating condition
2.	PaO_2 to FiO_2 ratio ≤ 26.7 (kPa) or ≤ 200 (mmHg)
3.	New bilateral infiltrates on chest radiograph
4.	No clinical evidence of left-sided heart failure (PAWP ≤ 18 mmHg if measured)

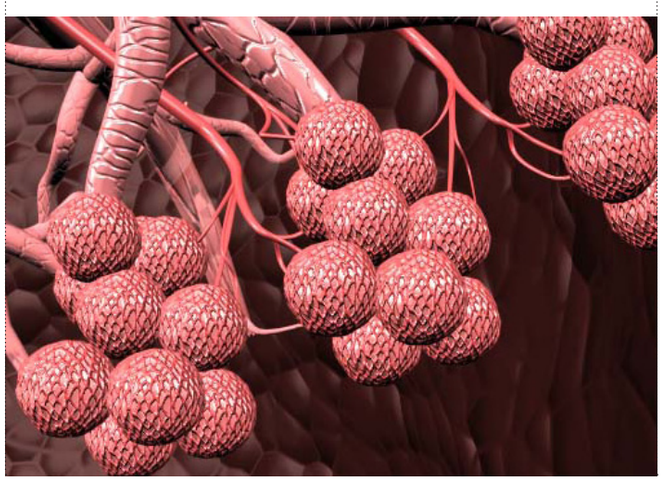
The incidence of ARDS is around 58.7 cases per 100,000 person-years and the in-hospital mortality rate is around 40%. There are multiple aetiologies, which can be categorised into systemic insults and primary lung pathologies (Box 2).

Box 2 - Aetiology of ARDS	
Direct pulmonary causes	**Indirect extra-pulmonary causes**
Pneumonia	Sepsis
Aspiration of gastric contents	Trauma
Pulmonary contusion	Multiple transfusions
Smoke inhalation	Acute pancreatitis
Near drowning	Burns

Pathophysiology

An inflammatory or infective insult results in the loss of integrity of the normal alveolar capillary membrane, causing alveolar flooding and a disruption in the production of surfactant[1]. This leads to alveolar collapse and reduced lung compliance, culminating in impaired ventilation. Furthermore it causes an increased ventilation-perfusion mismatch resulting in an intra-pulmonary shunt, evident by hypoxemia refractory to an increase in inspired oxygen[1]. Type I alveolar cells are damaged and type II cells proliferate; later, fibroblast infiltration and collagen proliferation lead in some cases to an accelerated fibrosing alveolitis, and micro vascular obliteration. The disease process does not affect the lung uniformly.

Interestingly in terms of outcome, refractory hypoxemia is the cause of death in only 20% of cases, whilst multiple organ failure accounts for up to 80% of deaths[1]. This is thought to be secondary to inflammatory mediators released by damaged lung tissues contributing to the systemic inflammatory response, progressing to multiple organ failure[4].



THE ACUTE RESPIRATORY DISTRESS SYNDROME IN AN ADULT PATIENT PRESENTING WITH SEPSIS

P El-Dalil, L Harding, P Ellahee and W Tunnicliffe

The Acute Respiratory Distress Syndrome in an adult patient presenting with Sepsis. Patient Management.

Management

The cornerstone of ARDS management is best supportive care combined with the use of invasive positive pressure ventilation (IPPV). There is no specific treatment for ALI/ARDS that has proven to be beneficial other than the adoption of a lung protective ventilatory strategy.

Ventilating the Injured Lung:

The aim of ventilation is to maintain adequate gas exchange whilst limiting ventilator associated or induced lung injury (VALI/VILI), (Box 3).

Box 3 - The principles of lung protective ventilation include:	
1.	Limiting the over-distension of the relatively compliant lung units during inspiration (reducing the potential for *volutrauma*).
2.	Limiting the cyclical collapse of unstable lung units at the end of expiration (reducing the potential for *atelectotrauma)*
3.	Limiting the transalveolar pressures (to reduce the potential for *barotrauma*)
4.	Limiting the fraction of inspired oxygen that the injured lung is exposed to; this may require the limiting of the target P_aO_2 (*permissive hypoxia*) to be achieved during mechanical ventilation reducing one potential element of *biotrauma.*
5.	Limiting the target rate of CO_2 clearance by allowing the patient's P_aCO_2 to rise (*permissive hypercarbia*) and as a consequence reducing the overall need and 'cost' of ventilation.

This is generally achieved through setting appropriate targets for oxygenation and carbon dioxide clearance, adopting a low tidal volume strategy, with the use of appropriate levels of PEEP, and limiting the mean airway pressure to no greater than 30 cmH_2O.

The use of low tidal volumes as a lung protective strategy is well supported by current evidence. The most important study was published by the ARDS network in 2000, which found a significant reduction in mortality in patients ventilated with low tidal volumes compared with those ventilated at higher tidal volumes[21].

Subsequent developments in the critical care unit:

Despite Mr R receiving optimal lung protective ventilation through a conventional ventilator, his clinical condition worsened still. His oxygenation became critical 48hrs into admission to critical care, with a PaO_2 of 5.8 kPa on 100% oxygen.

How could Mr R be managed?

• The adoption of a less conventional mode of ventilation via a conventional ventilator, such as Airway Pressure Release ventilation (APRV) or High Frequency Oscillatory Ventilation (HFOV).

• Referral for consideration of extracorporeal membrane oxygenation (ECMO) Airway Pressure Release Ventilation (APRV) produces tidal ventilation using a release of airway pressure from an elevated baseline to simulate expiration. The elevated baseline facilitates oxygenation, and the timed releases aid in carbon dioxide removal[26]. APRV allows the patient to breathe spontaneously throughout the ventilatory cycle and therefore reduces the requirement for sedation. There is currently no evidence supporting its use as a rescue mode of ventilation in severe ARDS[27].

High frequency oscillation is an alternative technique of ventilation in which small (sub dead-space) tidal volumes are delivered at high frequencies (3-15 Hz) with an oscillatory pump. High frequency oscillation theoretically meets the goals of a strategy of lung protective ventilation with extremely small tidal volumes (1-4 ml/kg) and constant lung recruitment. High frequency oscillation is being used more frequently in ARDS, but its use remains controversial. Currently multicentre randomised control trials are being undertaken in the UK and Canada to try to establish if HFOV can improve outcomes in ARDS.

Extracorporeal membrane oxygenation is a process by which venous blood is diverted via an external circuit and passed through the equivalent of a heart/lung machine, before being returned to the patient; this allows mechanical ventilation to be reduced, consequently reducing the risk of iatrogenic lung injury[1]. The CESAR trial demonstrated improved outcomes in patients referred to a centre with expertise in advanced respiratory support (including the use of ECMO) when compared to those receiving conventional ventilation. ECMO remains a salvage therapy and tends to be used when conventional management has failed[1]. It is invasive and its use remains controversial.

THE ACUTE RESPIRATORY DISTRESS SYNDROME IN AN ADULT PATIENT PRESENTING WITH SEPSIS

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Other adjuncts to the management of patients with severe ARDS have been explored. They include:

• **Prone positioning:** This has been shown to improve oxygenation in up to 70% of cases[3]; this is thought to be secondary to alveolar recruitment and better ventilation-perfusion matching[3]. However, prone positioning does not improve survival rates[4].

• **Exogenous surfactant:** Several large RCTs have since shown no change in mortality following the use of surfactant in adults[3].

• **Inhaled Nitrous Oxide:** Nitrous oxide has vasodilating properties which were thought to improve gas exchange at the alveolar capillary membrane of ventilated alveoli. Research has shown this only manifests as a transient improvement in oxygenation and that its use produces no benefit to survival rates[11], in fact its use has been associated with an increase in mortality in some studies.

• **Corticosteroids:** The use of corticosteroids is not advocated in the management of ARDS. Whilst some promising trends were demonstrated, increased mortality rates were found when patients were started on steroids after 13 days of disease onset[3].

Mr R's subsequent course in Critical Care:
Mr R was successfully converted to high frequency oscillatory ventilation. He made good progress from both a respiratory and cardiovascular perspective and within 72 hours had improved sufficiently to undergo a thoracotomy to achieve complete source control of his sepsis.

His recovery continued and on day 12 he was successfully extubated and a chest x-ray was repeated (Figure 4). It is anticipated that he will go one to make a full recovery. At one year around 50% of ARDS survivors have abnormal lung function, but few of them have functional respiratory disability.

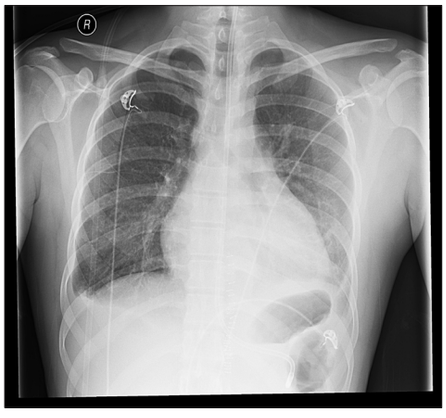
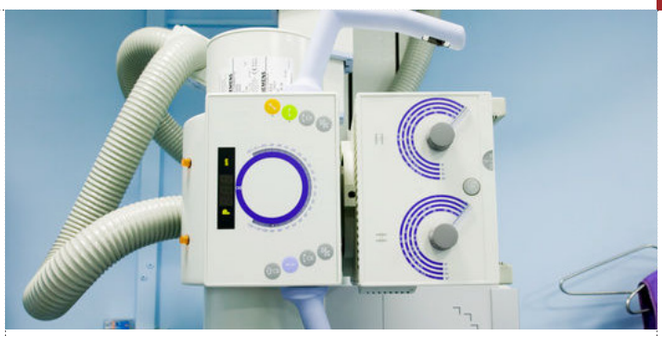


Figure 4



Questions

1. Which of the following does NOT contribute towards a diagnosis of ARDS?

a. Bilateral infiltrates on chest radiograph
b. Arterial oxygen tension (PaCO2) to inspiratory oxygen fraction (FiO2) ratio <200mmHg
c. Homogenous alveolar involvement on CT thorax
d. An acute onset
e. The absence of clinical evidence of atrial hypertension

2. In the management of ARDS, which of these ventilation strategies has been shown to improve oxygenation and survival?

a. Low tidal volume ventilation
b. High PEEP ventilation
c. Airway Pressure Release Ventilation
d. High Flow Oscillatory Ventilation
e. None of the above

3. Which of the following statements is FALSE regarding APRV and HFOV?

a. HFOV can be delivered via a standard ventilator
b. APRV can be delivered via a standard ventilator
c. Lead to hypercapnia
d. The OSCAR trial has demonstrated improvements in oxygenation with HPOV.
e. HPOV is a commonly used technique if conventional ventilation fails

4. In a patient with a confirmed diagnosis of ARDS who has failed to maintain adequate oxygenation on both conventional ventilation and high frequency oscillatory ventilation, which of the following options would be the next step in the patient's management?

a. Intravenous salbutamol
b. Inhaled nitrous oxide
c. Extracorporeal Membrane Oxygenation
d. Intravenous Corticosteroids
e. Exogenous surfactant

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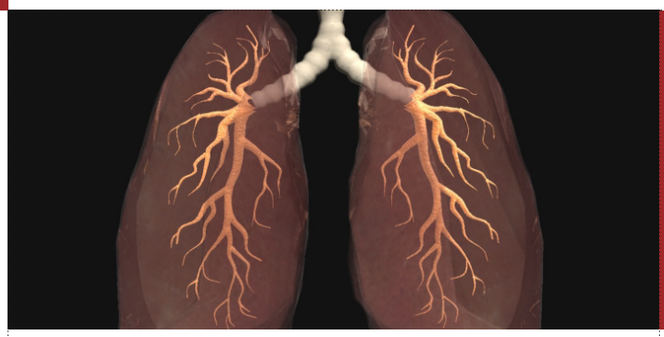

The Acute Respiratory Distress Syndrome in an adult patient presenting with Sepsis. Patient Management.

5. Which of the following is NOT a lung protective strategy?

a. The use of high PEEP in conventional ventilation
b. Low tidal volume ventilation
c. Using low concentrations of inspired oxygen
d. Maintaining mean airway pressures < 30cmH2O
e. Permissive hypercarbia

Answers

1. c)
Homogenous alveolar involvement on CT thorax. CT thorax actually demonstrates that ARDS affects the lungs in a heterogeneous manner. As a result there are varying degrees of alveolar compliance within the lungs, which will react variably to different ventilator settings, (i.e. the use of high tidal volumes to recruit affected sections of the lung and may cause barotrauma in healthy areas of the lung. This forms the basis for low tidal volume ventilation in ARDS.

2. (e)
None of the above. The only strategy that improves survival is the use of low tidal volumes. High PEEP has been shown to improve oxygenation, but confers no survival benefit. There have also been some studies that show improvements in oxygenation with APRV and HPOV, but as yet there is no definitive evidence as to the survival outcome.

3. (a)
HPOV can be delivered via a standard ventilator. HPOV cannot be delivered by a standard ventilator, but requires a specialised delivery system. Both methods of ventilation will lead to an inevitable rise in arterial carbon-dioxide concentration. This is accepted- "permissive hypercapnia" and ventilatory parameters are adjusted only if the pH reaches an unacceptable acidic state- usually <7.25. The OSCAR trial is still underway and although early results have shown some improvements in oxygenation, that is still under investigation.

4. (c)
Extracorporeal membrane oxygenation. Extracorporeal membrane oxygenation has been shown to improve survival rates when compared to normal ventilatory methods. Despite this it remains a salvage therapy in the treatment of ARDS. None of the other management options have been shown to produce any benefit to survival rates.

5. (e)
Permissive hypercarbia. Low tidal volumes have been widely documented as a lung protective strategy, notably by the ARDS network trial (2000). High PEEP is thought to be protective as it prevents the repeated opening and closing of alveoli (atelectotrauma). High FiO_2 causes lung damage by free radical formation and so FiO_2 should be titrated to the lowest possible level. Limiting airway pressures reduces barotraumas by preventing sustained over distension of lung tissue. Hypercarbia is not in itself a lung protective strategy, more a consequence of lung protective strategies.

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THE OBESITY HYPOVENTILATION SYNDROME

IS Stone and DE Simcock

The obesity hypoventilation syndrome.
Patient Management.

Abstract

Obesity is a rapidly increasing health problem. Obesity hypoventilation syndrome (OHS) is defined as the combination of obesity (BMI>30), awake hypercapnia ($PaCO_2$ >6 KPa) accompanied by sleep disordered breathing. The condition is under diagnosed and under appreciated, and puts a significant burden on health care, prolonging length of hospital stay and an increased need for intensive care and mechanical ventilation. Interrelating mechanisms thought to cause OHS include respiratory load and mechanics, central respiratory drive, sleep disordered breathing and leptin resistance.

In this review, we will discuss the definition, clinical presentation and diagnosis as well as differential diagnosis of OHS. We will summarise the epidemiology, review the current understanding of the pathophysiology and discuss the recent advances in treatment.

Clinical history

A 45 year old, non-smoking lorry driver is referred with a 5-year history of reduced exercise tolerance, 25kg weight gain and headaches, which are worse on waking and settle during the course of the morning. He also reports bothersome ankle swelling.

He complains of fragmented sleep with episodes of choking and gasping for breath. He describes nocturia on at least five occasions each night. His wife reports loud snoring and has witnessed episodes where his breathing actually stops, frightening her to the extent that she wakes him up to "remind him to breathe". She also reports that his mood has become erratic and that he seems unable to concentrate on even the most basic of tasks.

He awakes unrefreshed from sleep and is finding driving more difficult. His symptoms do not progress during the day and there is no history of limb weakness, swallowing difficulties, diplopia or sensory abnormalities to suggest a neurological cause for his problems.

His past medical history includes hypertension, dyslipidaemia and impaired glucose tolerance. He does not use sedatives and drinks alcohol occasionally.

Clinical examination

He appears well, but morbidly obese with a BMI of 50. There is no tongue enlargement, tonsillar hypertrophy, nasal obstruction or retrognathia. The jugular venous pressure is not elevated and his pulse and heart sounds were normal. There is globally reduced expansion of the thoracic cage with no evidence of scoliosis and an otherwise normal respiratory examination with oxygen saturations of 94% breathing room air. There were no paradoxical movements of the abdomen suggestive of diaphragmatic paralysis. There was no evidence of muscle wasting, weakness, ptosis nor glossopharyngeal dysfunction.

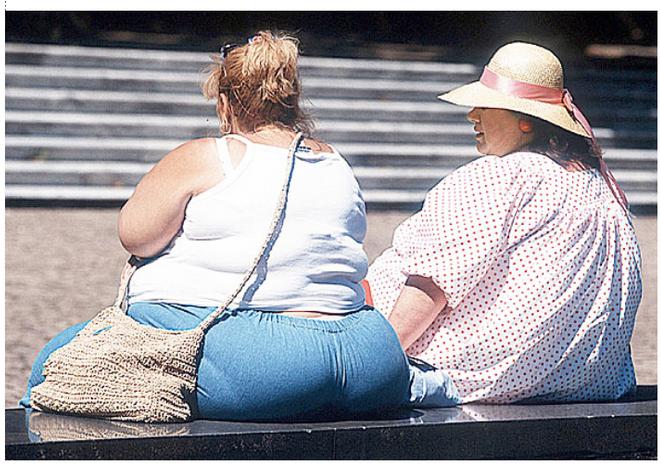
Baseline investigations

Arterial blood gas revealed compensated type 2 respiratory failure: pH 7.36, PO2 10.0KPa, PCO2 8.2Kpa, HC03 35mmol.

Bloods including full blood count, urea and electrolytes, thyroid function tests, magnesium and phosphate were all normal.

Epworth sleepiness score was 16/24 (24 point validated score of somnolence, >10 is excessive daytime sleepiness).

Simple spirometry revealed a restrictive ventilatory defect with FEV1 3.3l, FVC 4.5l, FEV/FVC 82% and was referred for full pulmonary function testing with postural measurements (looking for diaphragmatic weakness), lung volumes, reversibility testing and gas transfer factor.



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Further investigations

He went on to have a multichannel limited sleep study, with measurements of nasal airflow, chest wall movements, oximetry, heart rate, body position and snoring recordings, after initial assessment ruling out other causes of hypercapnia and hypoventilation. The sleep study confirmed sleep disordered breathing in the form of obesity hypoventilation syndrome (Figure 1).

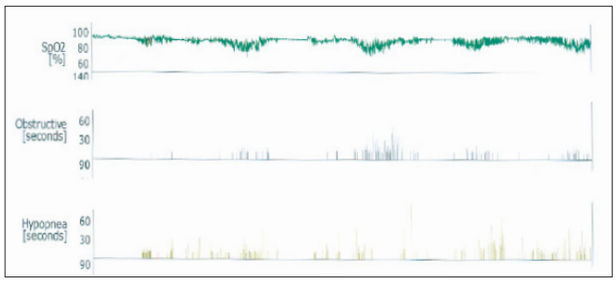


Figure 1: Eight-hour sleep study summary (time x-axis), showing oxygen saturation and nasal airflow data with episodes of prolonged desaturation down to SPO_2 75%. The desaturation episodes are not always associated with obstructive events, indicating hypoventilation.

Introduction

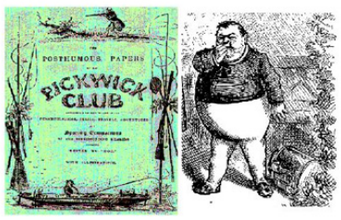
Obesity is a rapidly increasing health problem[1]. In England the proportion of men classed as obese increased from 13.2% in 1993 to 23.1% in 2005 and from 16.4% to 24.8% for women during the same period[2].

Obesity hypoventilation (OHS), defined as the combination of obesity, awake hypercapnia and sleep disordered breathing, is under diagnosed and under appreciated. It is a condition that often complicates the admission of the severely obese inpatient resulting in excess morbidity and mortality, and an increased need for intensive care and mechanical ventilation[3]. The clinical case presented above highlights a number of the key clinical features of OHS (Table 1).

Snoring
Nocturnal awakening
Waking up startled
Sensation of choking
Nocturia
Witness reports of apnoeas
Unrefreshed sleep
Daytime Hypersomnolence
Low mood/irritable
Poor concentration
Ankle swelling
Morning headaches

Table 1: The clinical features of the obesity hypoventilation syndrome.

Origins and definitions



When first discovered, obstructive sleep apnoea (OSA) and OHS were grouped together and labelled (in reference to the hypersomnolent Charles Dickens character "Fat Joe" of the Pickwick Papers), as "Pickwickian Syndrome". The case report described hypoventilation while awake with secondary polycythaemia and cor pulmonale[4]. Further investigation of these patients established the presence of pauses in respiration during sleep (apnoeas) – caused by partial or complete collapse of the airway, which could lead to sleep disturbance (arousals) and hypersomnolence[5]. This was termed obstructive sleep apnea (OSA), 15% of whom had awake hypercapnia; the obesity hypoventilation syndrome[6]. The terminology was then further classified by the observation that a proportion of these patients had hypercapnia without any apnoeas or hypopnoeas; the sleep hypoventilation syndrome (SHS) (summarised in Table 2).

Obesity hypoventilation is defined as the combination of obesity (BMI >30), awake hypercapnia (PaCO2 >6), accompanied by sleep disordered breathing (7.)

	BMI	Awake PCO_2	Sleep study findings
Simple obesity	>30	Normal	<5 apnoeas*,hypopnoeas** or respiratory related arousals per hour (i.e. ∫AHI <5)
Obstructive Sleep Apnoea (OSA)	Variable	Normal	>5 apnoeas*,hypopnoeas** or respiratory related arousals per hour (i.e. ∫AHI>5)
Obesity Hypoventilation Syndrome (OHS)	≥ 30	6KPa***	i) as in OSA (90% of patient) ii) sleep hypoventilation where one or both of the following occur (10% of patients) • increase in PCO2 >1.5 compared to daytime • desaturation not explained by apnoea/hypopnoea iii) i) and ii) combined

Table 2: The differences between obesity, OSA and OHS[7].

**Aponeas: the cessation of airflow at the nostrils and mouth for at least 10 seconds.*
***Hypoponea: 50% reduction in airflow at the nostrils for more than 10 seconds.*
****Important to exclude other causes of hypercapnia – see Table 3.*
∫ AHI: Apnoea-Hypopnoea Index.

Epidemiology

The true prevalence of obesity hypoventilation is not known. The prevalence of OHS is higher in men, although the difference is not as marked as found in OSA. Among obese patients admitted to hospital one study found 31% had daytime hypercapnia unexplained by other causes[3]. There is no clear racial or ethnic predominance, however, due to cephalometric differences, Asian patients with OSA associated OHS develop it at a relatively lower BMI compared to Caucasians.

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Pathophysiology of OHS

A number of interrelating mechanisms are proposed, leading to the obesity hypoventilation syndrome (Figure 2):

1. Respiratory load and mechanics: "can't breathe"

There is reduction in total lung capacity, vital capacity, functional residual capacity as well as increases in residual volume compared to similarly obese patients without hypercapnia. There is a 50% reduction in chest wall compliance and a threefold increase in lung resistance. These individuals tend to develop positive airway pressures (PEEP) at the end of exhalation, known as intrinsic PEEP (PEEPi). Altered mechanics, compliance and need to overcome PEEPi lead to an increase in the work of breathing possibly and muscle fatigue[8]. Patients with OHS are able to voluntarily hyperventilate and clear CO_2, therefore respiratory mechanics alone do not explain the development of awake hypercapnia[9].

2. Central respiratory drive: "won't breathe"

Recent studies have demonstrated increase load on the respiratory system. Eucapnic individuals have an increased ventilatory drive to breathe[1]. Those with OHS have a blunted neural drive leading to a failure to reduce CO_2. Obese patients also have reduced diaphragmatic efficacy, up to 50% compared to the non-obese, leading to a reduction in physiological reserve in the setting of increased demand.

3. Role of sleep disordered breathing

Repetitive oxygen desaturation occurring due to associated OSA leads to attenuation of central neural drive to breathe akin to the situation observed at altitude and in congestive cardiac failure. Additionally, in those with OHS there may be a failure to clear CO_2, by brief hyperventilation, in the post-apnoeic/hypopnoeic period leading to a rise in CO_2 and bicarbonate levels, further obtunding the drive to breathe[11].

In the patients who do not have a raised AHI, periods of hypoxia and hypercapnia can develop as a result of abnormal breathing patterns during specific stages of sleep. A clear reduction in minute ventilation has been shown between wakefulness and sleep in this group of patients with no change in respiratory rate implying that this reduction is due to decreased tidal volumes. Although hypoventilation is noted in non-rapid eye movement sleep, it is most striking during rapid eye movement sleep with a 39% reduction compared to ventilation during wakefulness[12].

Leptin resistance

Leptin, the product of the Ob gene, is secreted by adipocytes and acts on the hypothalamus to suppress appetite and increase ventilatory drive. Leptin deficient mice develop morbid obesity, hyperphagia, insulin resistance and hypoventilation. Serum leptin levels correlate with body fat percentage. OHS patients have been found to have higher serum leptin levels, suggesting the development of leptin resistance that may lead to hypoventilation and hypercapnia[13].

Impaired ventilatory control
- Functional
  - OHS
  - Hypothyroidism
  - Drugs (opiates/sedatives)
  - Metabolic derangement (low k+, po4-, Mg2+)
- Structural
  - Brainstem infarction/neoplasm
- Idiopathic
  - Primary alveolar hypoventilation

Neuromuscular disorders
- Myopathies
  - Muscular dystrophy
- Neuropathies
  - Diaphragmatic paralysis
    Amyotrophic lateral sclerosis
  - Guillain-Barre syndrome
- Neuromuscular junction problems
  - Myasthenia gravis

Chest wall abnormalities
- Kyphoscoliosis
- Thoracoplasty

Airway obstruction
- Upper
  - Tracheal stenosis
  - OSA
  - Polyps
  - Tonsillar hypertrophy
- Lower
  - COPD

Parenchymal lung disease
- ILD

Table 3: The causes of chronic hypoventilation[10].

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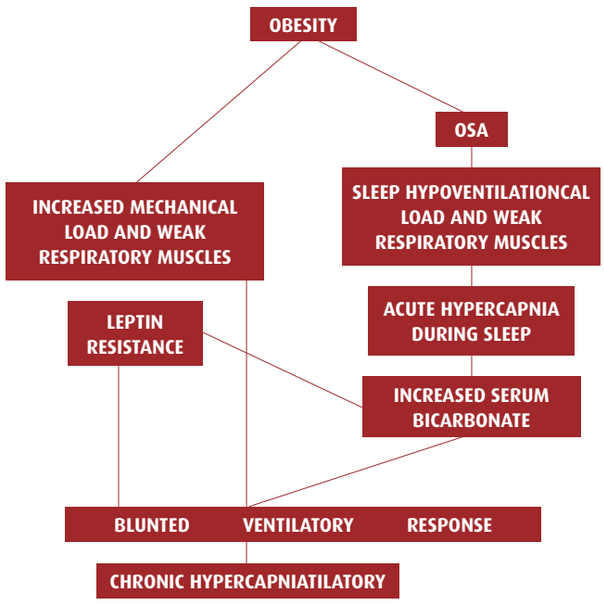

Figure 2: Complex potential interaction of obesity, sleep disordered breathing and leptin resistance leading to OHS (adapted from Reference 8).

Diagnosis

The diagnosis is made if four conditions are met:

1. BMI>30.
2. Daytime hypercapnia ($PaCO_2$>6kPa) on ABG.
3. Evidence of OSA/OHS on sleep study (Figure 1 and Table 2).
4. Other causes of hypoventilation and hypercapnia have been excluded (Table 3).

Treatment

The optimal management of patients with OHS requires a truly multidisciplinary approach involving endocrinologists, respiratory physicians, dieticians, psychologists and bariatric surgeons.

Weight loss

Weight loss leads to reversal of the physiological abnormalities that result in the development of OHS. Losing 10kg improves vital capacity and causes a significant reduction in daytime $PaCO_2$. It has been shown to reduce the AHI and the extent of desaturation during apnoeic episodes[13].

There have been recent studies demonstrating successful weight loss using a very low energy liquid diet in the context of sleep disordered breathing[14], although long-term adherence to such a regimen is questionable. Over recent years there has been a substantial increase in the number of centres offering bariatric surgery in the form of gastric bypass or banding, which results in durable weight loss, reversal of type 2 diabetes in 80% of patients and significant reductions in all-cause mortality through improvements in OSA, OHS, lung volumes, arterial blood gases and pulmonary hypertension[7, 15].

Weight loss is frequently slow to be realised with the optimal weight loss target and long-term outcomes yet to be determined.

Continuous positive airway pressure (CPAP) and non- invasive ventilation (NIV).

The improvement seen following long-term use of CPAP is thought to occur as a result of a direct effect on a number of the different pathophysiological mechanisms involved in the development of OHS. CPAP overcomes upper airway obstruction by mechanically splinting the airway open throughout the respiratory cycle. It also reduces upper airway oedema, increases functional residual capacity and lung mechanics in severely obese patients and overcomes PEEPi to reduce the work of breathing. Positive pressure ventilation, used long term, is usually delivered via a nasal mask, although a number of different interfaces are available.

The best ventilatory mode is yet to be determined in the setting of OHS and both continuous and bi-level modes of ventilation are effective[16]. Although there is no universally agreed protocol the algorithm shown (Figure 3) is a good example of the general strategy employed[13]. Following evaluation by sleep study, CPAP is used initially if there is evidence of co-existing OSA (90% of cases). SHS is suggested by the absence of obstructive events (AHI <5) and is an indication for bi-level positive airway pressure ventilation (BiPAP). BiPAP is also employed if there is sustained hypercapnoea and/or hypoxia. Newer BiPAP machines are capable of delivering high inspiratory pressures negating the need for volume controlled non-invasive modes of ventilation in morbidly obese individuals.

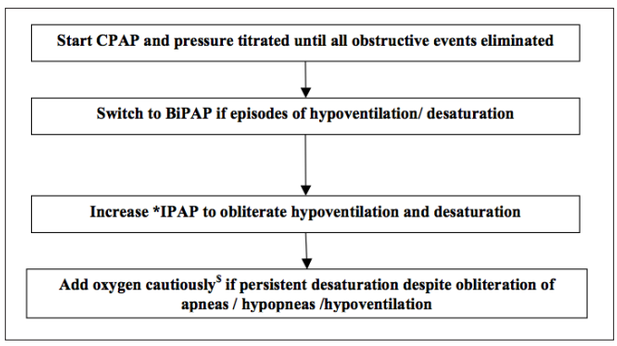

Figure 3. An example of an algorithm for the management of OHS.

* IPAP: Inspiratory Positive Airway Pressure. $ Assessment with overnight CO_2 monitoring or early morning Arterial blood gases required when prescribing oxygen in OHS.

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Pharmacotherapy

Progesterone

Medroxyprogesterone increases hypercapnic chemosensitivity and thus improves ventilation in OHS. It has no effect on apnoeas or somnolence and there is very little evidence regarding its long-term use and so it is not currently recommended.

Other drugs (such as acetazolamide), in principle, reduce CO_2 levels but are not used in routine practice due to no efficacy or safety data in the population[13].

Conclusion

OHS is an increasingly common problem, under appreciated and under diagnosed. Successful treatment strategies exist, and in the case of non-invasive respiratory support, are immediately apparent to the individual and help prevent adverse sequelae and mortality. Prevalence data and long-term outcomes of treatment are not yet know, prompting the need for further evaluation and clinical studies. A coordinated approach to the obese individual, involving different medical specialities and health care professionals will ultimately improve quality and effectiveness of care given to this unique group of individuals.

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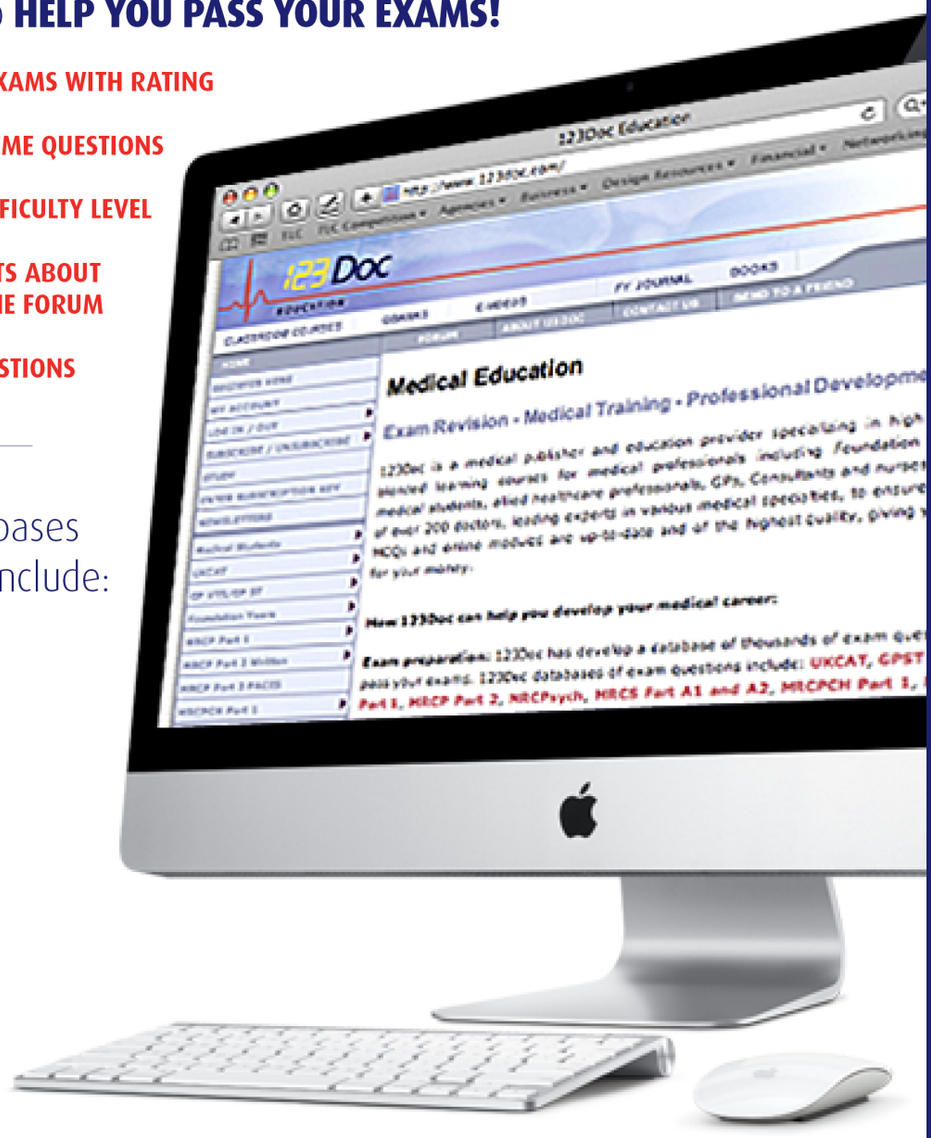

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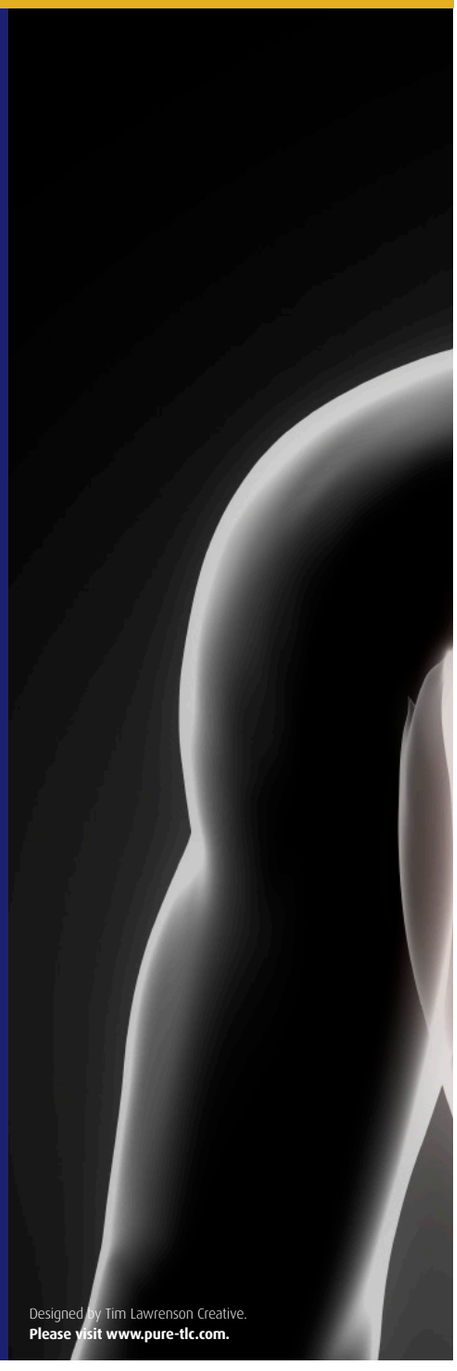

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