



## Acute exacerbations

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## ABC of chronic obstructive pulmonary disease

### Acute exacerbations

This is the ninth in a series of 12 articles

Graeme P Currie, Jadwiga A Wedzicha

An exacerbation of chronic obstructive pulmonary disease (COPD) is a sustained worsening of respiratory symptoms that is acute in onset and usually requires a patient to seek medical help or alter treatment. The deterioration must be more severe than the usual daily variation experienced. Exacerbations are characterised by increased breathlessness, cough, sputum volume or purulence, wheeze, and chest tightness. Other common features are malaise, reduced exercise tolerance, peripheral oedema, accessory muscle use, confusion, and cyanosis. Other (often coexisting) cardiorespiratory disorders can also cause these symptoms, which may lead to diagnostic uncertainty.

Exacerbations of COPD account for up to 10% of all medical admissions to UK hospitals, equating to more than 100 000 admissions a year, with a mean length of stay of over a week. Exacerbations therefore have considerable costs for secondary care and are partly responsible for high occupancy rates of hospital beds. Patients with frequent exacerbations have an accelerated decline in lung function, impaired quality of life, and restricted daily living activities, and, as a consequence, are likely to become housebound. As the disease becomes more severe, the frequency of exacerbations also increases.

### Causes

Exacerbations of COPD are mainly caused by viruses, bacteria, or environmental pollutants, though the precise cause remains unknown in many cases. Viruses play a important aetiological role, with rhinoviruses being implicated most often. How many exacerbations are caused by bacteria is uncertain, as pathogenic bacteria can often be grown from the sputum of clinically stable patients. However, one suggestion is that the isolation of a new strain may be associated with development of an exacerbation.

### Management

#### Oxygen therapy

Patients admitted to hospital with an exacerbation should be given oxygen to maintain the saturation of arterial blood at >90%. For patients with type 2 respiratory failure, give controlled oxygen (24% or 28%) through a Venturi facemask. For patients with type 1 respiratory failure, titrate the oxygen concentration upwards to maintain a saturation of >90%. After giving oxygen for 30-60 minutes, recheck arterial blood gases, especially in those with type 2 respiratory failure. This allows detection of rising carbon dioxide concentration or falling pH due to loss of hypoxic drive.

#### Bronchodilators

Bronchodilators are a fundamental component in managing exacerbations, and all patients should be given inhaled salbutamol. Salbutamol stimulates  $\beta_2$  adrenoceptors to cause smooth muscle relaxation and bronchodilation. Although there are few data to support any additional benefit in acute exacerbations, the short acting anticholinergic ipratropium may be given concomitantly. Both bronchodilators have a duration of action of between four and six hours and are generally well tolerated.

#### Differential diagnosis of an exacerbation of COPD

- Exacerbation of asthma
- Bronchiectasis
- Bronchopneumonia
- Pneumothorax
- Pulmonary embolism
- Upper airway obstruction
- Pleural effusion
- Pulmonary oedema
- Bronchial carcinoma
- Cardiac arrhythmia, such as atrial fibrillation

#### Investigations for patients admitted to hospital with exacerbation of COPD

- Full blood count
- Blood biochemistry and glucose concentration
- Theophylline plasma concentration (in patients using a theophylline preparation)
- Arterial blood gas (documenting the fraction of inspired oxygen)
- Electrocardiography
- Chest radiography
- Blood cultures in febrile patients
- Microscopy, culture and sensitivity of purulent sputum

#### Possible causes of an exacerbation of COPD

- | Bacteria                            | Viruses                       | Pollutants         |
|-------------------------------------|-------------------------------|--------------------|
| ● <i>Haemophilus influenzae</i>     | ● Rhinovirus                  | ● Ozone            |
| ● <i>Streptococcus pneumoniae</i>   | ● Influenza                   | ● Sulphur dioxide  |
| ● <i>Haemophilus parainfluenzae</i> | ● Parainfluenza               | ● Nitrogen dioxide |
| ● <i>Moraxella catarrhalis</i>      | ● Respiratory syncytial virus |                    |
| ● <i>Pseudomonas aeruginosa</i>     | ● Coronavirus                 |                    |

#### Arterial blood gas features of types 1 and 2 respiratory failure

	Respiratory failure	
	Type 1	Type 2
O <sub>2</sub>	Lowered	Lowered
CO <sub>2</sub>	Normal or lowered	Raised
HCO <sub>3</sub>	Normal	Raised or normal
pH	Normal or raised	Normal or lowered



Nebulised bronchodilators are often given during an exacerbation of COPD

## Practice

Bronchodilators can be administered successfully via a metered dose inhaler plus spacer or a nebuliser. Although a nebuliser does not confer any advantage in drug delivery over hand held devices with a spacer, it is independent of patient effort and often more convenient in a busy ward. In patients with hypercapnia or respiratory acidosis, nebulisers should usually be driven by compressed air and supplemental oxygen given via a nasal cannula.

### Corticosteroids

Unless they are contraindicated, oral corticosteroids should be given to all patients with an exacerbation of COPD. Several studies have shown that they improve lung function and shorten the length of hospital stay. Severely ill patients or those who are unable to swallow can initially be given 100-200 mg of intravenous hydrocortisone. For straightforward exacerbations, current guidelines recommend that 30-40 mg of prednisolone is given for 7-14 days, with no additional benefit being gained with longer courses of treatment. Instruct patients on when and how to discontinue oral corticosteroids and be aware of potential adverse effects (discussed in article 7 of this series). Patients taking oral corticosteroids for less than three weeks do not usually need to taper off the dose.

### Antibiotics

Despite viruses and pollutants being implicated in many exacerbations of COPD, antibiotics are still widely used. Antibiotics are most effective in severe exacerbations with increased sputum volume and purulence. It is important to tailor the choice of antibiotic to local patterns of sensitivity and resistance, although amoxicillin is a suitable first choice. Patients who are allergic to penicillin should be given a macrolide (such as erythromycin or clarithromycin).

### Aminophylline

Aminophylline has only modest benefits at best in treating exacerbations of COPD, and its use is controversial. In a meta-analysis of four trials, aminophylline in conjunction with conventional treatment failed to confer any advantage over placebo in terms of lung function, symptoms, or length of hospital stay. However, its use was associated with a greater incidence of adverse effects such as nausea and vomiting.

Current guidelines suggest adding aminophylline to standard therapy for patients with moderate to severe exacerbations or those not responding to nebulised bronchodilators.

### Respiratory stimulants

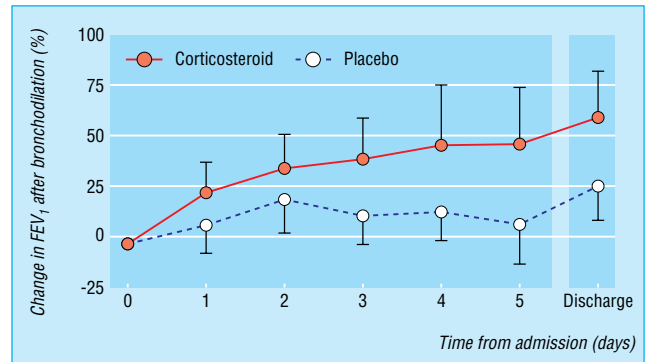
Since the introduction of non-invasive ventilation the use of doxapram has become far less common in hypercapnic respiratory failure. It may have some use if non-invasive ventilation is contraindicated or not immediately available, but whether it confers benefit when used alongside non-invasive ventilation is uncertain. Doxapram is given by continuous intravenous infusion and stimulates both respiratory and non-respiratory muscles. Its use is often limited by adverse effects such as agitation, tachycardia, confusion, and hallucinations.

### Non-invasive ventilation

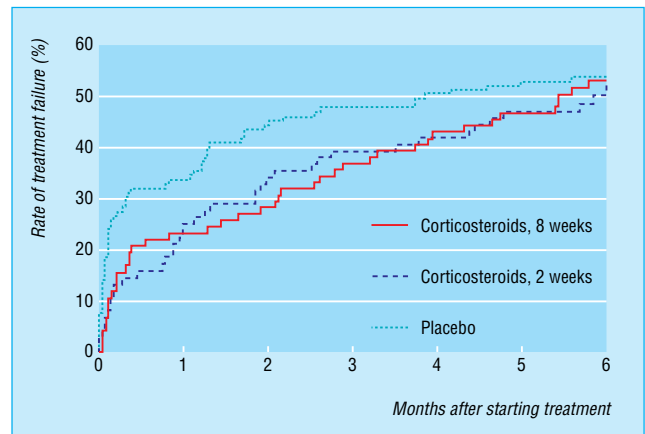
Non-invasive ventilation has revolutionised the management of hypercapnic respiratory failure due to COPD and will be discussed in the next article in this series.

### General hospital care

Measures to prevent venous thromboembolism with low molecular weight heparin should be considered in all patients



Effect of oral corticosteroids compared with placebo on forced expiratory volume in one second (FEV<sub>1</sub>) of patients with an exacerbation of COPD



Effects of oral corticosteroids for an exacerbation of COPD, showing no difference between short and long courses (2 and 8 weeks) on rates of treatment failure



Consider giving antibiotics when sputum is purulent and of greater volume than usual

### Guidance for adding aminophylline to standard therapy for COPD exacerbations

#### Patients not taking oral theophylline

- Give loading dose of 5 mg/kg over  $\geq 20$  minutes with cardiac monitoring
- Subsequent maintenance infusion of 0.5 mg/kg/hour

#### Patients already taking theophylline

- Omit loading dose of aminophylline
- Before starting maintenance infusion of 0.5 mg/kg/hour, plasma concentration of theophylline should ideally be obtained
- Measure daily plasma theophylline concentration and alter infusion rate to maintain a concentration of 10-20 mg/l (55-110  $\mu\text{mol/l}$ ).

admitted with an exacerbation of COPD. Attention should also be given to adequate hydration and nutritional input. Many patients with COPD have important comorbidities—such as ischaemic heart disease, left ventricular dysfunction, and diabetes—which must not be overlooked.

## Recovery

### Assisted hospital discharge

Any intervention that hastens a patient's recovery and discharge from hospital may be useful in the overall management of an exacerbation. In recent years, "assisted hospital discharge" schemes have been developed whereby patients with non-severe exacerbations of COPD can be discharged almost immediately with appropriate nursing and medical back up. As well as providing patients with a package of care, this practice also facilitates the identification of a deterioration in clinical condition and readmission to hospital if necessary.

Studies have shown that rates of hospital readmission and mortality among patients on assisted discharge schemes are not significantly different from those among individuals receiving standard inpatient care. Moreover, such schemes have produced substantial cost savings and increased the availability of inpatient beds. However, not all patients admitted with an exacerbation of COPD are suitable for assisted discharge.

### Monitoring while in hospital

Clinical assessment and routine observations are useful in assessing the rate of recovery from an exacerbation. Frequent measuring of arterial blood gases is required to monitor patients with decompensated respiratory acidosis. Daily recordings of peak expiratory flow rates are less useful unless the patient has reversible obstructive lung disease. It is useful to record spirometry before discharge as this helps to confirm the diagnosis (in patients who have not previously had it performed), provides information on the severity of airflow obstruction, and allows progress to be assessed at subsequent outpatient follow-up.

### Outpatient follow-up

Arrange hospital outpatient clinic follow up for four to six weeks after discharge in most patients. As well as allowing monitoring of changes in lung function, this is an opportunity to provide education, check inhaler technique, consider augmentation of pharmacotherapy, check oxygen saturation and arterial blood gases if required, and reassess smoking status.

Explain to patients that they should report symptoms suggestive of an exacerbation of COPD to their general practitioner at an early stage. This is important since early and prompt treatment results in a quicker recovery than if treatment is delayed. Moreover, patients who fail to recognise or promptly report worsening symptoms have a greater risk of being admitted to hospital and generally have a poorer quality of life.

## Recurrent exacerbations

Many patients with COPD have frequent exacerbations, necessitating repeated hospital admissions. This is especially so for individuals with hypercapnic respiratory failure who have had treatment with non-invasive ventilation. Indeed, within a year after hospital discharge, most of these patients will be readmitted and require further non-invasive ventilation, with as many as half dying. Further studies are required to identify factors associated with readmission and to devise strategies to address this common problem.

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After discharge from hospital with an exacerbation of COPD, most patients should be reviewed at the hospital outpatient clinic

### Relative contraindications to assisted hospital discharge in patients with an exacerbation of COPD

- Acute onset
- Confusion
- Worsening peripheral oedema
- Uncertain diagnosis
- Poor performance status
- Concomitant unstable medical disorders
- New chest radiograph abnormalities
- Acidosis or marked hypoxia or hypercapnia
- Adverse social conditions

### Further reading

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The figure of effects of oral corticosteroids on FEV<sub>1</sub> was adapted from Davies et al. *Lancet* 1999;354:456-60. The figure comparing short and long courses of oral corticosteroids was adapted from Niewoehner et al. *N Engl J Med* 1999;340:1941-7.