Today's Treatment

Diseases of the respiratory system

Chronic bronchitis and emphysema

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Any disease that affects one million people in the United Kingdom and causes 30 000 deaths a year must be so familiar to all practising doctors that articles on treatment and management might be considered superfluous, particularly when the effects of treatment are unlikely to be dramatic. No intervention short of a lung transplant is going to affect the irreversible changes of chronic bronchitis and emphysema, but appropriate treatment can help the patient considerably and should reduce the number of hospital admissions. Unfortunately most patients present at a late stage of the disease when symptoms are becoming a problem and considerable airways obstruction is present.¹ I propose therefore to discuss treatment for these symptoms and the two main complications of arterial hypoxaemia-polycythaemia and pulmonary hypertension.

Clinical features

Although chronic bronchitis and emphysema are two pathologically distinct entities resulting from common causes, they often occur together. The definition of neither condition is entirely satisfactory. Emphysema is defined as "an increase in the size of air spaces distal to the terminal bronchiole with destructive changes in the walls" and so can only be accurately assessed at necropsy. Patients with predominant emphysema have a well-preserved respiratory drive and tend to hyperventilate to maintain a reasonable arterial oxygen tension. Their main symptom is breathlessness, so they have received the nickname "pink puffer."

Chronic bronchitis is arbitrarily defined on the basis of chronic sputum production for which no other cause such as bronchiectasis is evident, and in practice it covers patients with a wide range of symptoms with or without airways obstruction. Recent epidemiological work² suggests that the disease should be considered in terms of two separate processes—hypersecretion of mucus, which predisposes to recurrent chest infections, and airways obstruction. The two may coexist, but it is the progressive airways obstruction that leads to severe respiratory disability and accounts for most deaths from bronchitis. These patients suffer from cough and phlegm, ankle swelling, and acute episodes of bronchitis eventually associated with ventilatory failure. They tend to underventilate and so become cyanosed

and polycythaemic and have thus been labelled "blue bloaters." Most patients have both chronic bronchitis and emphysema and fall between the two extreme ends of the clinical spectrum described by the pink puffer and the blue bloater.

Which patients develop bronchitis and emphysema?

The reason for the particularly high prevalence of chronic bronchitis and emphysema in Britain is not entirely clear.¹ It is strongly related to social class, with a seven-fold greater prevalence in social class V than social class I. Cigarette smoking appears to be the single most important factor in causing both diseases but air pollution, occupation, and living conditions are also important. The various factors probably interact in a synergistic manner, so the smoker in a dusty occupation is much more likely to run into trouble than the smoker sitting in an office. It is far from clear, however, why one cigarette smoker develops emphysema, a second chronic bronchitis, and a third no lung trouble at all. Studies of migrants suggest that constitutional factors are much less important than environmental factors. One well-recognised exception, however, is α_1 -antitrypsin deficiency, which is inherited as an autosomal recessive and occurs in 0.02% of the general population and in about 5% of patients with emphysema. In cigarette smokers this causes a predominantly basal form of emphysema, which develops quite early in life, often in the third and fourth decade.

Diagnosis

Usually the diagnosis of chronic bronchitis and emphysema is not difficult, though occasional patients with late-onset asthma can cause confusion. If any doubt exists a trial of steroid treatment should be carried out with pulmonary function monitoring (see below). Upper airways obstruction is usually clearly recognised from the history and inspiratory stridor but is occasionally missed in patients with co-existing lower airways obstruction. More detailed lung function tests or bronchoscopy should settle any uncertainty.

General management

Atmospheric pollution should be minimised and smoking discontinued. Only these measures will influence the rate at which alveoli and airways are destroyed. Patients with mild or moderate airways obstruction who discontinue smoking show a reduction in the rate at which lung function declines and a lower death rate. Patients with severe disability show less benefit when they stop smoking, though it sometimes helps their cough and breathlessness. The diagnosis must therefore

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be made as early as possible so that patients can be strongly discouraged from smoking. Simple measurements of peak expiratory flow rate (PEF) or the forced expiratory volume in one second (FEV₁) made in the surgery will help to identify the patients with airways obstruction who are most at risk. Repeated measurements will chart the rate of deterioration, and will help to assess the benefit of treatment. Patients may need help and advice about work and should aim for a non-dusty environment both at work and at home.

General measures include weight reduction for obese patients and small and frequent meals for very breathless patients. Exercise should be encouraged within comfortable limits to maintain general fitness and morale. Because these patients have a high death rate during influenza epidemics vaccination is recommended for those at risk. Otherwise treatment is largely aimed at alleviating symptoms or controlling secondary complications such as polycythaemia.

Treatment of symptoms

ACUTE EXACERBATION OF BRONCHITIS

Although exacerbation of bronchitis often follows upper respiratory viral infections green sputum usually denotes a bacterial infection, most commonly with *Haemophilus influenza*. In these patients episodes of infection should be treated promptly, and the symptoms will normally respond to a seven-day course of a suitable antibiotic. In an uncomplicated episode sputum culture is unnecessary, being often unhelpful and sometimes misleading. The antibiotics of choice are tetracycline, 250 mg four times a day; co-trimoxazole, two tablets twice daily (trimethoprim, 160 mg twice daily, and sulphamethoxazole, 800 mg twice daily); ampicillin, 250 mg four times a day; and amoxicillin 250 mg four times a day. Patients known to have chronic bronchitis should be told either to contact their doctor at the first sign of a chest infection or to keep a spare supply of antibiotics at home. Treating exacerbations promptly is for most patients a better approach than long-term chemoprophylaxis, which would help some patients marginally in the short term but cause large problems with resistant organisms in the future. Some patients who deteriorate, with increased dyspnoea and "congestion" in the chest, have no overt signs of infection but they usually respond to a short course of antibiotics. Physiotherapy helps when the sputum is tenacious and is essential when the patient is drowsy. Any suggestion of drowsiness or confusion is an indication for admission to hospital.

COUGH AND PHLEGM

Cough and phlegm may improve when the patient stops smoking. The recent development of cough may indicate an infection and will respond to the antibiotics listed above. Otherwise it may settle with either linctus simplex or a linctus containing antihistamines such as diphenhydramine (Benylin) linctus or pseudoephedrine and triprolidine (Actifed) compound linctus. Stronger cough suppressants such as linctus codeine may also depress ventilation. Intractable cough is fortunately rare in these patients but if it does occur inhaled lignocaine might be considered though it carries the risk of increasing airways obstruction.³ Mucolytic agents have been strongly advocated for patients with tenacious sputum but generally have been rather disappointing. Steam inhalations or a hot drink are probably as effective and considerably cheaper.

ANKLE SWELLING

Ankle swelling will usually respond to a thiazide diuretic such as bendrofluazide, 5 mg daily, with a potassium supplement, though stronger diuretics such as frusemide or bumetanide may

be needed. Digoxin is not indicated since the oedema is due more to fluid retention than to heart failure. These patients appear to be more prone to arrhythmias after digoxin, particularly atrial tachycardias, which can be difficult to treat.

BREATHLESSNESS

The objective improvement in pulmonary function tests after bronchodilators is usually small but is often considered well worth while by the patient. Most widely used are the β_2 -selective, β -adrenergic agonists in metered aerosol form. Salbutamol (100 μ g per puff) or terbutaline (250 μ g per puff) are usually effective for 3-4 hours and can be given either as required or on a regular basis of 1 or 2 puffs four times a day. On the whole these drugs are better given by inhalation than as oral tablets since they then achieve more bronchodilatation and fewer side effects such as tremor, but the patient must inhale correctly. Although some patients are helped by theophylline drugs such as choline theophyllinate, 200 mg thrice daily, their value is limited by the variable absorption and the frequency of gastrointestinal symptoms. The newer theophylline preparations such as Phyllocontin and Nuelin give more predictable absorption and are said to have fewer side effects.

Interest in atropine-like compounds, particularly ipratropium bromide, has recently revived. In clinical trials this drug (2 puffs or 360 μ g four times a day) appears to cause more bronchodilatation than the more widely used β -adrenergic agonists but more studies are needed to assess its value in clinical practice. It may be helpful to patients with pronounced airway irritability and cough.

Steroids usually give no benefit in chronic bronchitis and emphysema, but they are worth a trial in patients with a large response to β -adrenergic agonists, great variability in their airways obstruction, or sputum eosinophilia. A fairly large dose of prednisone—for example, 40 mg daily—should be started when the patient's condition is stable and continued for 3-4 weeks, with monitoring of pulmonary function tests before, during, and at the end of the trial. If patients show a good response (at least 20% improvement in FEV₁ or PEF) an inhaled steroid (beclo-methasone dipropionate 100 μ g or betamethasone 17-valerate 200 μ g, both four times a day) should be added and the prednisone reduced to the minimum dose needed to maintain improvement. They should not continue to take prednisone unless they have a definite and worth while response.

Surgery may help a few patients with a large emphysematous bulla, particularly when there is little generalised emphysema and the breathlessness is due to compression of relatively normal lung by the bulla.⁴ Unfortunately bullae usually present in patients with severe generalised emphysema when the results of surgery will be disappointing. Detailed investigations are needed to assess the patient's suitability for surgery.

SEVERE BREATHLESSNESS

Patients with emphysema may develop such severe breathlessness that they have difficulty even with simple activities such as eating. Domiciliary oxygen treatment is often prescribed, though the symptomatic benefit to most patients is small—partly because of the inconvenience of being attached by tubing to the cylinder. Portable oxygen circumvents this problem but the extra effort needed to carry the apparatus often outweighs any advantage from the oxygen. All patients with domiciliary oxygen in Southampton were recently asked whether, given the choice, they would prefer to keep their salbutamol inhaler or their oxygen cylinder and most chose the salbutamol inhaler.

In patients with distressing breathlessness oral diazepam should be considered. The benefit of relieving the breathlessness must be weighed against the risk of precipitating or increasing respiratory failure. Diazepam should not be used during exacerbations of bronchitis but it may help patients with terminal

emphysema when other measures have failed. Ideally the patient should start on a small dose such as 2 mg thrice daily, with occasional monitoring of carbon dioxide pressure (PCO_2) so that the dose can be increased to achieve the maximum benefit without a large increase in PCO_2 .

Recently attempts have been made to relieve severe breathlessness by vagotomy or by radiotherapy to the most severely emphysematous part of the lung.⁵ Both approaches are experimental and need further evaluation.

Treatment of complications

POLYCYTHAEMIA

Secondary polycythaemia is seen most commonly in the blue bloater, though they do not often have haemoglobin values above 18 g/dl and the risk attached to untreated polycythaemia is not clearly established. Vascular thromboses do not appear to be particularly common, and there is still controversy about how much polycythaemia contributes to the pulmonary hypertension.⁶ There are therefore no generally agreed criteria for treating secondary polycythaemia; many doctors start treatment when the haemoglobin reaches 19 or 20 g/dl, or less in younger patients.

The best form of treatment is not generally agreed either; venesection, long-term oxygen, and drugs have all been tried. Venesection is probably the most widely used and the procedure itself does not usually present problems. Since it causes a temporary increase in some clotting factors and over-rapid fluid depletion may create problems an exchange transfusion to replace blood with dextran 40 has been advocated.⁷ The haemoglobin will usually return to its previous value over 3-6 months, after which venesection will need to be repeated. These patients should not be allowed to become iron deficient and may require iron treatment.

Prolonged oxygen treatment can be given at home and will reduce the polycythaemia in most patients. This method, though more inconvenient, produces a more gradual fall in haemoglobin with less fluctuation than repeated venesection. Radioactive phosphorus and drugs such as dapsone and pyrimethamine⁸ have also been used but their potential side effects, particularly overcorrection anaemia and folate deficiency, have limited their use.

PULMONARY HYPERTENSION

Recent studies have shown that long-term domiciliary oxygen when taken for 15 hours a day will reduce pulmonary hypertension. This can be managed by patients who go out to work but obviously a considerable amount of co-operation and adaptation is necessary. A large Medical Research Council study is currently looking at the longer-term effects of this fairly expensive treatment on life expectancy and morbidity, and until these results are available it should not be generally recommended.

Pulmonary embolism and thrombosis, not uncommon findings at necropsy in these patients, will accentuate the pulmonary hypertension. Diagnosis can be difficult since ventilation-perfusion scans will be abnormal anyway, and small additional losses of perfusion may not be detectable. Anticoagulants should be considered when the condition is strongly suspected on clinical grounds.

Prevention

The recent small reduction in the death rate from chronic bronchitis and emphysema, particularly in women, has been attributed largely to implementation of the 1956 and 1968 Clean Air Acts. Improved treatment may have contributed to some extent, but it appears to have little to offer once cor pulmonale supervenes since the prognosis has hardly changed over the

past 20 years. This is not surprising since most treatment is symptomatic and does not affect the underlying disease. How many patients die from the complications of bronchitis, such as pulmonary hypertension, rather than respiratory failure is not known, and treating the complications will be effective only if these are a significant cause of morbidity and mortality.

Since treatment of established bronchitis is disappointing attempts have been made to identify people particularly at risk. Relatives of all patients with α_1 -antitrypsin deficiency should be screened and if homozygous should be told of the severe risk they run if they continue to smoke. The effect of smoking on heterozygotes is still debated but they would be wise not to smoke.

Screening the general population would be much more difficult. Various tests for detecting early airway narrowing have been suggested, such as measurement of the frequency dependence of compliance, maximum expiratory flow-volume curves, and closing volume; but none have shown the sensitivity and reproducibility needed for a useful screening test and they are, moreover, all complicated tests unsuitable for screening large populations. Patients found to have early airway narrowing may in any case be unwilling to stop smoking when asymptomatic. Furthermore, those at risk of other conditions caused by cigarette smoke may be falsely reassured by a satisfactory result from the screening test.

Since the most important cause of chronic bronchitis is cigarette smoking and since smokers find it difficult to stop smoking, the logical attack on this problem is to discourage children from starting to smoke. Money spent on finding out how this can be achieved might result in the greatest gains in the long term. Meanwhile we need to detect signs of chronic bronchitis as early as possible, urge those affected to stop smoking, treat symptoms as they arise, and in a small minority consider treating polycythaemia and pulmonary hypertension.

References

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Is manic-depressive psychosis inherited?

Scientific work on this subject has been admirably reviewed.¹ The risk to children of those suffering from manic-depressive illness is about 12%,² but it is less in cases of late onset. The risk for the grandchildren is probably 2-3%. When advising relatives about genetic risks it must be remembered that most patients with manic-depressive illness can be effectively treated with lithium carbonate.

¹ Price, J, in *Recent Developments in Affective Disorders*, ed A Coppen and A Walk, ch 4. Ashford, Headley Bros, 1968.

² Stenstedt, A, *Acta Psychiatrica et Neurologica Scandinavica*, 1952, suppl 79.

Should diabetic patients avoid cola-type drinks?

Diabetics may drink only unsweetened or calorie-free cola drinks. These will not interfere with diabetic control. The main pharmacologically active principle in such drinks is caffeine. A 12 oz bottle contains 35-55 mg (compared with 100-150 mg in a cup of coffee). The therapeutic dose of caffeine is 150-250 mg. Even at high doses any tendency for the blood sugar concentration to increase as a result of enhanced tissue glycolysis would be offset by concomitant stimulation of motor activity. In short, normal amounts of calorie-free cola-type drinks are not contraindicated in diabetes.