Introduction

Nebulisers are widely used throughout the world in adult and paediatric medical practice, both for emergency and acute treatment, and for domiciliary long term treatment of a variety of respiratory diseases, most commonly airflow obstruction. To date, however, we are aware of no comprehensive review of the laboratory and clinical data which underpin these uses. Likewise, no detailed guidance is available either for clinicians prescribing treatment with nebulisers or planning a nebuliser service, or for nurse practitioners and patients.

In 1994 the Standards of Care Committee of the British Thoracic Society therefore initiated a review of nebuliser treatment in all its aspects. A nebuliser project group was formed. A series of review articles was commissioned and the authors were required to review thoroughly different aspects of nebuliser treatment with reference to the available literature and with the aid of a computer-based reference search. These articles appear on pages S25–106 and include papers on the science of nebulised drug delivery, its use in clinical practice, and practical aspects of the use of nebulisers.

The conclusions from these papers have been condensed into a set of guidelines for nebuliser treatment. Draft guidelines were considered at a plenary symposium at the British Thoracic Society meeting in December 1994 and revised by the project group and a group of specialist advisors at a one day consensus meeting held at the Royal Society of Medicine in May 1995. They have subsequently been modified after wide consultation. As far as possible the individual recommendations have been weighted according to the scale proposed by the Committee of the Scottish Intercollegiate Guidelines Network in their paper on clinical guidelines (see Appendix 4) and the grades are indicated in the text as [A], [B] and [C]. A summary of the guidelines appears on pp S2–3.

There are, in many instances, gaps between usual clinical practice and supporting scientific evidence for that practice. This has been separately recognised by including summaries of the particular areas of uncertainty where further research efforts should be focused (see Appendix 5).

It is intended that these recommendations should form the basis of local guidelines, and thereby improve nebuliser therapy undertaken by respiratory physicians, paediatricians and other hospital specialists, general practitioners, and other staff both in hospital and in primary care.

Many of the recommendations are, of necessity, based on informal consensus, and such recommendations [C] are particularly suitable for further study for audit exercises.

It is intended that this document should be reviewed in 2–3 years time.

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These recommendations have been published with the approval of: The British Thoracic Society, The Respiratory Medicine Committee of the Royal College of Physicians, The Royal College of General Practitioners, The General Practitioners in Asthma Group, The British Paediatric Association (now The Royal College of Paediatrics and Child Health), The British Paediatric Respiratory Group, The National Asthma Campaign (on behalf of asthma patients), The Cystic Fibrosis Trust (on behalf of patients with cystic fibrosis), Breathe Easy (on behalf of patients with COPD), The British Association of Palliative Care Medicine, The British Association of Accident and Emergency Medicine, The British Association of Respiratory Nurse Specialists, The Society of Physiotherapists, The British Association of Respiratory Function Technicians.

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Summary

1 The aim of treatment with nebulisers is to deliver a therapeutic dose of the drug as an aerosol in the form of respirable particles within a fairly short period of time, usually 5–10 minutes.
2 Nebulisers are useful when large doses of inhaled drugs are needed, when patients are too ill or otherwise unable to use hand held inhalers, and when drugs are not available in hand held inhalers.
3 The commonest indication is for the emergency treatment of asthma [A] and exacerbations of chronic obstructive pulmonary disease (COPD) [A]. Other indications include the long term bronchodilator treatment of chronic airflow obstruction [B]; prophylactic drug treatment in asthma [B]; antimicrobial drugs for cystic fibrosis [A], bronchiectasis [C], and HIV/AIDS [A]; and symptomatic relief in palliative care [C].
4 The present British Standard (BS7711) for jet nebulisers indicates that they should provide an aerosol with a respirable fraction of at least 50% at their recommended driving gas flows.
5 Any combination of compressor and nebuliser needs to be assessed for a particular drug solution and drug volume [A]. For the commonly used bronchodilators, output data derived from 0.9% sodium chloride can be used as a general guide [B].
6 For drugs other than bronchodilators there is a particular need only to use equipment known to provide a suitable output [B] and for patients to have specific instructions. Such treatment is best supervised by hospital specialists.
7 Nebulisation time for bronchodilators should be less than 10 minutes [B]. Patients should know how long nebulisation should take when their equipment is working correctly [C]. For bronchodilators the use of a mask or mouthpiece should depend upon convenience and/or patient preference (see paragraph 22).

Asthma

8 In acute severe asthma in children and adults nebulisers should be used as recommended in the British Thoracic Society guidelines on the management of asthma (1993, updated 1997).
9 Nebulised bronchodilators should only be used in chronic severe asthma for the relief of symptoms at step 4 of the asthma guidelines [B]. They should be considered only after a review of the diagnosis, if the air flow obstruction is reversible, and providing the patient is taking regular high dose inhaled prophylactic treatment and complying with the prescribed dose and frequency with a satisfactory technique. Long term regular bronchodilator therapy should not be established without a trial of domiciliary treatment for at least two weeks and incorporating, where possible, peak flow measurements.
10 Patients with brittle asthma may require bronchodilator treatment by nebuliser [C]. They must have clear verbal and written instructions about the indications for treatment, be aware of the need to seek help for acute attacks, and must receive an appropriate educational programme and clinic supervision.
11 Nebulised corticosteroids may be a way in which steroid-dependent asthmatic patients can reduce their maintenance doses of oral corticosteroids. Their superiority for this purpose over large doses of inhaled corticosteroids by hand held inhaler has not yet been demonstrated. It is recommended that, before starting this treatment, patients should be reviewed by a respiratory specialist [C].

COPD

12 The use of nebulised bronchodilators for COPD should be consistent with the British Thoracic Society guidelines for the management of COPD (1997) and similar documents from the European Respiratory Society (1995) and the American Thoracic Society (1995).
13 Nebulised bronchodilators are indicated for acute exacerbations of COPD if treatment with hand held inhalers is insufficient [A]. β agonists or anticholinergics may be used and a combination should be considered in more severe cases, especially if the patient has had a poor response to either type of drug alone [B].
14 Adequate domiciliary bronchodilator treatment for most patients with COPD can be delivered with standard treatment with a hand held inhaler [B].
15 Before long term domiciliary treatment is prescribed, either from hospital or in general practice, every patient should be assessed fully [A].
16 The components of such an assessment should include a review of the diagnosis, peak flow monitoring at home, and sequential testing of different regimens using peak flow and subjective responses [B].
17 After assessment, patients who have a clear subjective and peak flow response to domiciliary nebuliser treatment should be advised to continue it [B]. If there is a subjective response with less than a 15% improvement over baseline peak flow, physicians should use their clinical judgement [C]. Other outcomes should not result in continued domiciliary treatment [C].
18 Short term reversibility studies should not be substituted for longer term assessments [A].
19 Patients having such treatment should usually be advised to use it as required up to four times per day [C] and should have regular reviews at a respiratory clinic.

The elderly

20 Elderly patients with asthma or COPD, who might benefit from treatment with a nebuliser, should be assessed and managed in the same way as younger patients [B].
21 Treatment with high dose β agonists should be used with caution in elderly patients with known ischaemic heart disease [C].
22 Mouthpieces rather than face masks should be considered in elderly patients susceptible to glaucoma and using high doses of anticholinergic drugs [C].

Intensive care unit

23 Aerosol therapy may be less effective in ventilated patients because their lung disease is usually more severe and aerosol deposition from nebulisers (and metered dose inhalers) is reduced during ventilation compared with spontaneous breathing.

# of guidelines

24 Metered dose inhalers, jet nebulisers, and ultrasonic nebulisers can be incorporated into ventilator circuits.
25 Indications for such treatment include bronchodilators for severe acute airflow obstruction [B] and, less certainly, tribavirin (ribavirin) for respiratory syncytial virus infection in infants [C], corticosteroids for bronchopulmonary dysplasia in infants [C], surfactants in infant and adult respiratory distress syndrome [C], and epoprostenol (prostacyclin) for pulmonary hypertension [C].

HIV/AIDS

26 Nebulised pentamidine is used for the primary and secondary prophylaxis of *Pneumocystis carinii* pneumonia [A] but is less effective than other drugs given orally.
27 Nebulised pentamidine may be used to treat mild to moderately severe *Pneumocystis carinii* pneumonia [A] but is ineffective for severe pneumonia [A]. Treatment with other drugs is generally more effective and nebulised pentamidine needs to be combined with intravenous treatment for the first 3–5 days.
28 Nebulised hypertonic 2.7% sodium chloride is used for sputum induction, usually from an ultrasonic nebuliser.

Palliative care

29 The principal indications for treatment with a nebuliser are the palliation of breathlessness and cough. Prescriptions for both should be reviewed within three days to check efficacy [C].
30 Nebulised bronchodilators may relieve breathlessness due to concomitant reversible airflow obstruction but hand held inhalers should be assessed first [B].
31 Lignocaine or bupivacaine may relieve dry persistent unproductive cough [B] but not dyspnoea [A]. Pretreatment with bronchodilators is advisable [C].
32 Nebulised 0.9% sodium chloride as an expectorant, opioids for the relief of terminal dyspnoea, and corticosteroids for dyspnoea, in the presence of lung disease, have been used for palliation, but as yet there is little scientific evidence of their efficacy. It is recommended that their prescription be discussed with palliative care or respiratory physicians.

Cystic fibrosis

33 Nebulised bronchodilators should be considered for the treatment of respiratory exacerbations in cystic fibrosis [B].
34 The response to regular domiciliary bronchodilator treatment is variable. Trials of treatment should be undertaken beforehand [B] at a time when lung function is stable, monitoring by repeat measurements [A] and incorporating treatment with hand held inhalers [B]. Drug doses and combinations should be similar to those recommended for childhood asthma, adult asthma, and COPD.
35 Although there is evidence that bronchodilator drugs increase mucociliary clearance in cystic fibrosis, there is as yet no clinical evidence that this adds to the benefit of physiotherapy.
36 Treatment with nebulised rhDNase should be consistent with recommendations made in published guidelines. Patients should commence treatment under the guidance of a cystic fibrosis centre [C].
37 The indications for prescribing nebulised antibiotics are to delay or prevent early colonisation with *Pseudomonas aeruginosa* progressing to chronic colonisation [B] and to prevent clinical deterioration in patients chronically colonised [A]. Benefits should be assessed by a combination of spirometric tests and clinical observations [A].
38 Nebulised antibiotics should be given by combinations of compressors and nebulisers known to produce appropriately sized aerosols [B]. Mouthpieces rather than face masks should be used, except in infants or younger children [C].

Bronchiectasis

39 There are no controlled trial data in adult patients with bronchiectasis to prove the benefit of long term nebulised antibiotics.
40 It is recommended that, if nebulised antibiotics are used because of severe symptoms for frequent exacerbations, patients' responses should be carefully evaluated as for cystic fibrosis [C]. The use of oral antibiotics combined with adequate postural drainage should have previously been shown to be unsuccessful [C].
41 Nebulised bronchodilators may be used for patients with bronchiectasis and severe airflow obstruction [C]. The need for them should be assessed as for patients with COPD.

Domiciliary nebuliser services

42 All patients needing long term domiciliary nebuliser treatment should have access to a local, centrally organised nebuliser service administered by a designated specialist or group of specialists, and under the day to day management of a named and appropriately trained individual or individuals [C].
43 Such a service should include equipment provision, emergency replacements, servicing arrangements, patient and staff education, detailed regimens for assessing patient suitability for long term treatment, and standard written patient instructions [C].
44 It is recommended that patients should be referred by primary care physicians to this centralised service for assessment before they are established on long term treatment.

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Guidelines

Selecting and using nebuliser equipment

AIM OF NEBULISER THERAPY

The aim of nebuliser therapy is to deliver a therapeutic dose of the desired drug as an aerosol in the form of respirable particles within a fairly short period of time, usually 5–10 minutes.

DEFINITIONS

- *Aerosol output*: the mass per minute of particles in aerosol form produced by the nebuliser.
- *Respirable particles*: particles <5 μm diameter.
- *Respirable fraction*: the mass of respirable particles expressed as a percentage of the aerosol output.
- *Respirable output*: the mass of respirable particles produced per minute (aerosol output × respirable fraction).
- *Drug output*: the mass of drug produced per minute as an aerosol.
- *Mass median diameter*: the diameter of the particle such that half the mass of the aerosol is contained in smaller diameter particles and half in larger.
- *Mass median aerodynamic diameter (MMAD)*: the diameter of a sphere of unit density that has the same aerodynamic properties as a particle of median mass from the aerosol.

NEBULISERS

- Jet nebulisers consist of a nebulising chamber in which an aerosol is generated with a flow of gas provided either by an electrical compressor or compressed gas (air or oxygen).
- Ultrasonic nebulisers are self-contained electrical devices in which an aerosol is generated by vibrating fluid placed within them. They can nebulise larger volumes of fluid and are quiet.
- In the sections which follow "nebuliser" means jet nebuliser unless otherwise specified.

DRUG OUTPUT

Unlike the output of most ultrasonic nebulisers, the aerosol output of jet nebulisers is not the same as drug output. Measurement of aerosol output for a particular drug solution therefore gives only a general guide to nebuliser performance. The drug output from different systems needs to be known, particularly since many drug solutions and suspensions such as antibiotics and corticosteroids have physicochemical properties which are quite different from 0.9% sodium chloride (which is often used to measure aerosol output) and the commonly used bronchodilators.

Respirable fraction

The present British Standard (BS7711 Part 3) for jet nebulisers indicates that they should provide a respirable fraction of at least 50% at their recommended driving gas flows.

FACTORS AFFECTING DRUG OUTPUT

Driving gas flow rate

Most jet nebulisers are now designed to work at a flow rate of 6–10 l/min. Flow rates generated by electrical compressors should be measured at the outlet of an attached nebuliser (dynamic flow). The flow required will depend upon the nebuliser design, the dimensions of the connecting tubing and, to a lesser extent, the drug used.

Nebuliser chamber design

Increasing the fraction of droplets intercepted by the internal baffles in a standard jet nebuliser will decrease particle size but increase nebulisation time. Incorporating an open vent into the nebuliser may allow entrainment of air and a faster nebulisation rate. Breath enhanced open vent nebulisers incorporate valve systems and utilise a patient's inspiratory flow to increase the nebulisation rate. However, they may not provide benefit to patients such as infants whose inspiratory flow rates do not exceed the output flow rate from the compressor.

Residual volume

This is the volume of liquid remaining in the nebuliser reservoir when nebulisation has ceased. It will affect the drug output from a given fill volume. If the residual volume is less than 1.0 ml, a fill volume of 2.0–2.5 ml may be adequate; nebulisers with residual volumes of more than 1.0 ml generally require fill volumes of about 4 ml [B].

Fill volumes

Nebuliser chambers have different maximum fill volumes; the volume of drug solution must be known not to exceed the maximum fill volume.

Physical properties of drug solution or suspension

Simple drug solutions, such as commonly used bronchodilators, have a similar nebuliser volume output and particle size distribution to that of 0.9% sodium chloride; the volume output of drug preparations with a higher viscosity or a different surface tension will differ – for example, some antibiotic solutions with a high surface tension (such as amoxycillin) are slow to nebulise whereas others (such as colistin) with a low surface tension are readily nebulised.

Breathing pattern of the patient
This may have a profound effect on the mass of drug delivered to the lungs. It is a particularly important consideration in infants or young children [B]. Steady normal breathing interspersed with occasional deep breaths is likely to be optimal [B].

Summary
Any combination of compressor and nebuliser needs to be assessed for a particular drug solution and drug volume [B]. For the commonly used bronchodilators, output data derived from 0.9% sodium chloride can be used as a general guide [B]. For other drugs there is a particular need to use a nebuliser known to produce suitable output or to obtain such data for any proposed combination [B].

COMPRESSORS AND NEBULISERS PRESENTLY AVAILABLE

Examples of compressors and nebulisers presently available in the UK are given in the paper entitled "Selecting and using nebuliser equipment" on pages S92–101.

SUBSIDIARY FACTORS AFFECTING CHOICE OF EQUIPMENT

- Compressors vary in size, shape, weight, cost, running cost and noise level.
- Nebuliser chambers preferably should not contain components that can be easily swallowed.
- Simple jet nebulisers should consist of a removable top and a single component chamber.
- Nebulisers should be able to be easily assembled and disassembled by patients.

USING NEBULISERS

Nebulisation time
The nebulisation time is the time from starting nebulisation until continuous nebulisation has ceased. The time taken to deliver a drug is important for patient compliance. Nebulisation time for bronchodilators should be less than 10 minutes [B].

Nebulisation end point
"Dryness" is a difficult end point for patients to recognise [B]. It may be better for patients to be advised to nebulise for about a minute after "spluttering" occurs. Patients need to know how long this should take when their equipment is working correctly [C].

Tapping
Tapping the nebuliser chamber when the solution begins to "splutter" increases the volume output [B].

Face masks and mouthpieces
Bronchodilator responses are the same whether masks or mouthpieces are used. The choice should therefore depend upon convenience – for example, masks are better for emergencies – and patient preference. Face masks should be tight-fitting. Patients should breathe with an open mouth [A]. For ipratropium bromide, mouthpieces should be preferred to masks if there is a possibility of glaucoma. For antibiotics, rhDNase and corticosteroids, mouthpieces should be used.

Cleaning
Nebulisers used for bronchodilator therapy should be disassembled, washed in warm water with a little detergent at least once a day, and carefully dried. The nebuliser should be run empty for a moment or two before the next use.

Multiple uses
In the UK, where nebuliser chambers packs are marked by the manufacturer as "single use" they may only be used once and should then be discarded; where they are marked "single patient use" they are reusable items that are capable of being reused, with or without reprocessing, by an individual patient.

NEBULISERS FOR ANTIBIOTICS (as for adult and paediatric cystic fibrosis and bronchiectasis)

- These should be prescribed twice a day for domiciliary use [C].
- Antibiotics should preferably be nebulised using a compressor with a flow rate of 6 l/min and a breath-enhanced open vent nebuliser (table 1) [C]. Solutions should not be hypertonic [A] and should be reconstituted immediately before use. Needles and syringes should be changed according to the manufacturers' recommendations.
- Bacteria may grow in damp equipment. It is recommended that nebulisers used for antibiotics should be cleaned after each use [C]. The nebuliser should be disconnected from the tubing and the compressor turned on for a short period to clear moisture from the tube. All parts of the nebuliser should be disassembled and, together with the mouthpiece, washed in warm water with a little detergent, rinsed, and dried thoroughly [C].

Table 1 Order of preference for compressor/nebuliser systems for nebulised antibiotics

1	Standard flow rate compressor (6 l/min) with a breath-enhanced open vent nebuliser. This is suitable for adults and children over two years.
2	High flow rate compressor (8 l/min) with a breath-enhanced open vent nebuliser.
3	High flow rate compressor (8 l/min) with a Venturi nebuliser. This is recommended if compliance is a problem as nebulisation time is reduced. [C]
4	Standard flow rate compressor (6 l/min) with a Venturi nebuliser.

Mouthpieces rather than face masks should be used except for infants or younger children who will not tolerate one.

- Standard jet nebulisers, tubing, and mouthpieces used for antibiotics should be changed every three months [C]. Durable nebulisers (which last 12 months) should be boiled for 5–10 minutes in water with a little detergent after every 30 uses [C].
- All nebuliser equipment should be single patient use [C]. Separate compressors should be used for patients colonised with *Pseudomonas aeruginosa* and *Burkholderia cepacia* [C].
- In hospital respect should be given to local infection control policies. Patients should nebulise antibiotics in a separate area. The nebuliser should be fitted with a venting system – for example, a high efficiency expiratory filter or tubing out of the window [C]. Two filters should be used – one in the morning and one in the evening – to allow them to dry thoroughly between uses.
- At home (unless there is an affected sibling with cystic fibrosis when hospital recommendations should apply), patients may nebulise antibiotics in a separate room with a closed door and open window without a venting system or filter [C]. However, the use of a venting system or filter is preferable with some antibiotics because there is a risk that droplets may make furniture sticky and degrade soft furnishings.

EDUCATION OF STAFF AND PATIENTS ABOUT NEBULISER TREATMENT

- A nebuliser service should provide information for ward staff, general practitioners, community nurses, community pharmacists, practice nurses, and patients (and their carers).
- Topics to be covered should include:
  (a) descriptions of equipment and its use;
  (b) drugs: their use, doses and frequencies;
  (c) equipment maintenance;
  (d) action to take if treatment becomes less effective;
  (e) action to take and emergency telephone number to use in case of equipment breakdown.
- Before domiciliary use all patients should have a first treatment under supervision.
- As a guide, examples of such information are given in Appendices 1 and 2. A detailed booklet is available from the nebuliser service, Department of Respiratory Medicine, City Hospital, Nottingham NG5 1PB, UK.

Nebulisers in children

GENERAL

- A metered dose inhaler and spacer (if necessary, with a face mask) is a cheaper and more convenient delivery system than a nebuliser [B]. However, some infants and children cannot tolerate face masks and spacers, in which case nebulisers are needed.
- Where possible, children should be encouraged to breathe through the mouth. If old enough, they should use a mouthpiece rather than a mask [C].
- A maximum time for treatment should be given to parents of children using particular drug/nebuliser/compressor combinations. Shorter nebulisation times may improve compliance [B].

ASTHMA

- Nebulisers should be used as recommended in the British Thoracic Society guidelines on the management of asthma (1993, updated 1997).[1 2]
- For regular treatment at home alternative delivery methods such as a metered dose inhaler and spacer, or a dry powder inhaler should first be assessed [B].
- For treatment of acute exacerbations recognition of the severity of the illness and prompt treatment are of paramount importance (Chart 1). Treatment with a metered dose inhaler and spacer may be as effective and cheaper than nebulisation [A] but is not yet widely undertaken.
- In severe acute asthma frequent bronchodilator therapy may be helpful [B]. Doses of 1–3 mg/hour terbutaline or 0.3 mg/kg salbutamol hourly (to a maximum 10 mg/hour) have been used in trials so far. More randomised controlled trials are now needed to determine the optimum dose and duration of treatment.
- Continuous nebulisation is still being evaluated for very severe attacks with patients being monitored in intensive care. Early experience with this method is encouraging.

NEBULISERS FOR DISEASES IN CHILDREN OTHER THAN ASTHMA

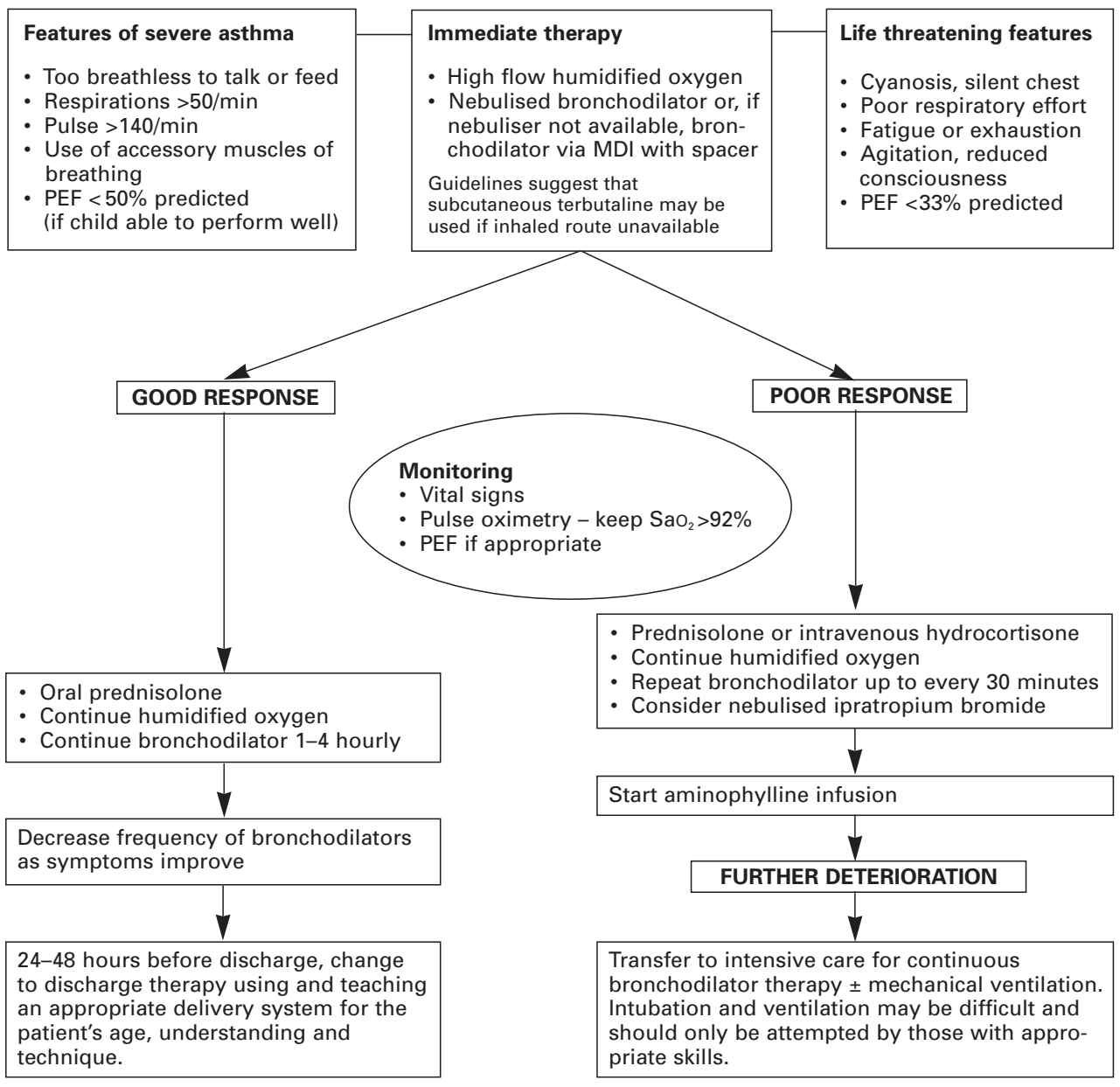
Croup

- Nebulised adrenaline (0.5 ml/kg of a 1:1000 solution) is used to avoid intubation, to stabilise children prior to transfer to intensive care [B], and in stridor following intubation [C]. The effect is short lived (1–2 hours). It should not be used in children who are shortly to be discharged or on an outpatient basis [C].
- Nebulised steroids (for example, 500 μg budesonide) may also reduce symptoms in croup in the first two hours [B]. No data are available on longer term use or on the effect of this treatment on the eventual outcome.

Bronchiolitis

- Nebulised ribavirin may be considered in infants at high risk or those with severe disease [B].
- Administration is by a small particle aerosol generator containing a solution of 20 mg/ml, operated for 12–18 hours per day for 3–7

Chart 1
Nebulisers in acute severe childhood asthma



Drug dosages:
The following dosages have been suggested in published guidelines:

Salbutamol – *Nebulised*, 5 mg or 0.15 mg/kg.
MDI + Spacer, 100 μg, one actuation then inhale, repeat up to 20 times.

Terbutaline – *Nebulised*, 10 mg or 0.3 mg/kg.
MDI + Spacer, 250 μg, one actuation then inhale, repeat up to 20 times.
Subcutaneous, 2.5 mg.

Steroids – Prednisolone 2 mg/kg/day for three days, max 40 mg/day, or hydrocortisone 100 mg six hourly IV.

Aminophylline – *Intravenous infusion*, Loading dose, omit if already on theophylline, 5 mg/kg over 20 minutes, then 1 mg/kg/hour.

Ipratropium – *Nebulised*, 250 μg six hourly.

days. Ribavirin has not been shown to reduce the length of hospital stay, or the need for oxygen or assisted ventilation. It is not used for the majority of infants with respiratory syncytial virus positive bronchiolitis in the UK.

Bronchopulmonary dysplasia (BPD)

- Uncontrolled data suggest that inhaled steroids may improve lung mechanics and short term measures of outcome in neonates [B].
- The best dose, drug delivery device, and the optimum timing of administration are not known.
- The side effect profile and the long term effects of inhaled steroids in these children have not been determined.

Nebulisers in adult asthma

- There are indications for the use of nebulised drugs in both acute [A] and chronic severe asthma [A].
- Nebulisers should be used in asthma as recommended in the British Thoracic Society guidelines on the management of asthma (1993, updated 1997).[1 2]

NEBULISERS IN ACUTE SEVERE ASTHMA

- The use of nebulisers in acute severe adult asthma is shown in Chart 2.
- Oxygen should be used as the driving gas whenever possible [A]. Treatment should otherwise be given using either an electrical compressor or compressed air.

NEBULISERS IN CHRONIC ASTHMA

- Nebulised bronchodilators may be given either to patients with chronic persistent asthma or those with sudden catastrophic severe asthma (brittle asthma).
- If nebulised treatment is prescribed patients must:
  (a) have clear instructions from a doctor, specialist nurse, or pharmacist;
  (b) be instructed not to treat acute attacks at home without also seeking help;
  (c) receive an education programme;
  (d) have regular subsequent follow up, including peak flow monitoring, at an asthma clinic and be seen by a doctor, specialist nurse, or physiotherapist.

Chronic persistent asthma

- Nebulised bronchodilators should only be used to relieve persistent daily wheeze at Step 4 or above of the BTS guidelines on the management of asthma.[1]
- The use of nebulisers should only be considered:
  (a) after a review of the diagnosis;
  (b) if the airflow obstruction is significantly reversible by bronchodilators (minimum increase in forced expiratory volume in one second (FEV_1) 0.21 or peak expiratory flow rate (PEFR) 60 l/min) [B];
  (c) after the patient has demonstrated correct use of his or her usual hand held inhaler;
  (d) after a larger dose of bronchodilator – for example, 4–6 actuations of a hand held inhaler six hourly, with a spacer if necessary – has been tried for at least two weeks [C];
  (e) if the patient is taking regular high dose inhaled corticosteroid anti-inflammatory treatment and is complying with the prescribed dose and frequency [A].

Assessment of nebuliser treatment for chronic persistent asthma

- Before long term nebulised bronchodilator therapy is prescribed, clinically useful bronchodilatation without unacceptable side effects should be demonstrated, preferably with a home trial monitoring peak flow for up to two weeks on standard treatment and then for up to two weeks on nebulised treatment.
- Peak flows should be measured twice daily before nebulisation, on rising and before going to bed. In addition, a peak flow measurement should be taken 30 minutes after treatment in the morning.
- Not every patient will benefit from high dose nebulised therapy and an increase from mean baseline peak flow (measured over at least five days) of 15% or more should be demonstrated before recommending treatment [B].
- The dose of β agonist for chronic asthma is usually 2.5 mg salbutamol or 5 mg terbutaline. The dose of ipratropium bromide is usually 250 μg or 500 μg.

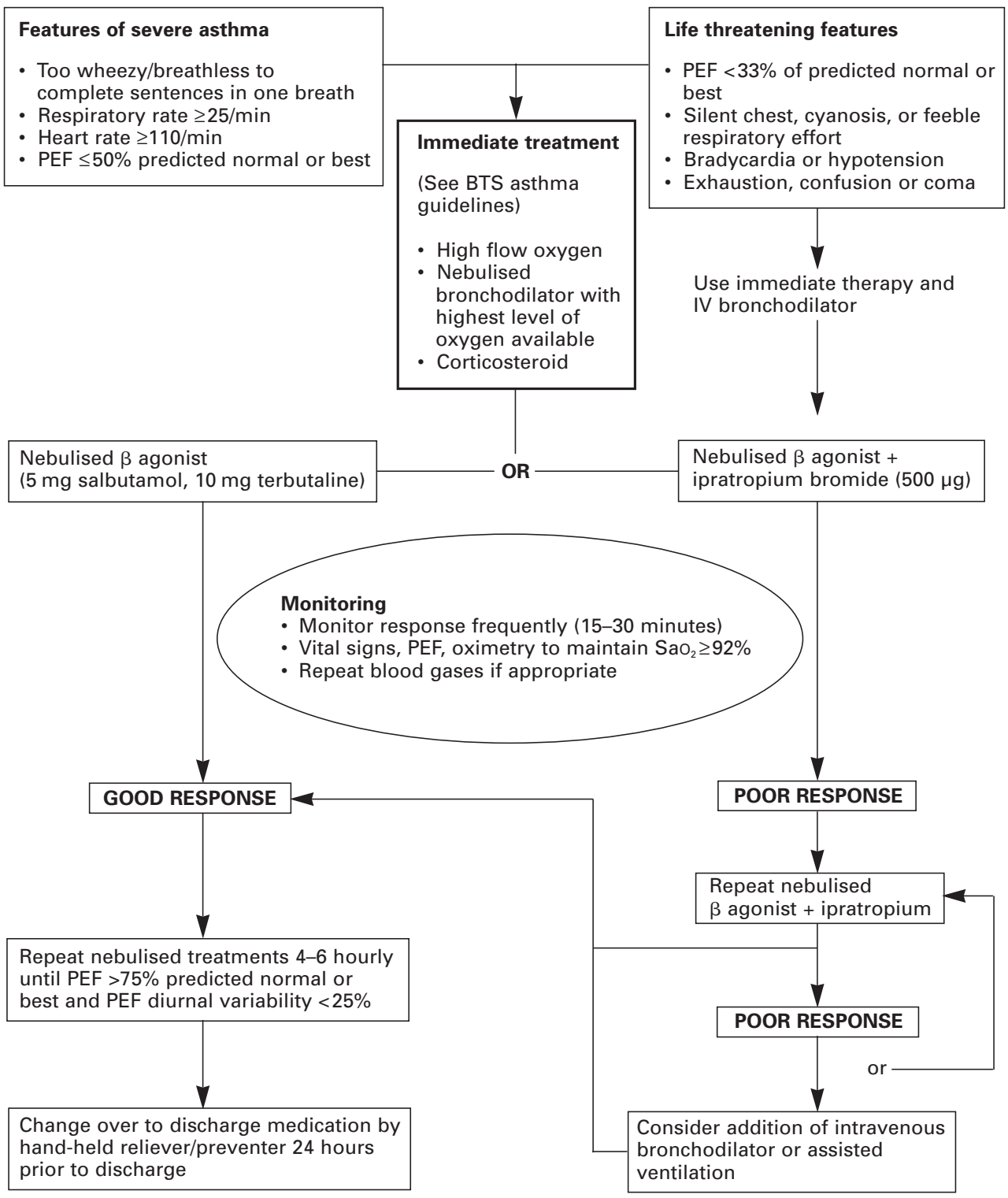
Brittle asthma

- A few asthmatic subjects develop sudden severe attacks despite little preceding instability. They require treatment with a β agonist in a high dose, often by nebuliser (for example, salbutamol 5 mg or terbutaline 10 mg).

Nebulised corticosteroids

- There are at present no published randomised controlled trials of the effectiveness of nebulised corticosteroids in adults with asthma. Their use may allow steroid dependent asthmatic patients to reduce their maintenance doses of oral corticosteroids. It is recommended that patients should be reviewed by a respiratory specialist before they are prescribed.

Chart 2
Nebulisers in acute severe adult asthma



This flow chart should be used in conjunction with published asthma guidelines.

Nebulisers in chronic obstructive pulmonary disease (COPD)

These recommendations refer to nebuliser treatment for chronic obstructive pulmonary disease (COPD). The definition of the disease and degrees of severity, together with recommendations for overall treatment strategies, will be available in the forthcoming British Thoracic Society guidelines for the management of COPD (1997) and are available in a similar document from the European Respiratory Society[3] and the American Thoracic Society.[4]

ACUTE EXACERBATIONS OF COPD

- If the exacerbation is relatively mild, bronchodilators should be given by a hand held inhaler using 200–400 μg salbutamol or 500–1000 μg terbutaline [B].
- In more severe cases nebulised salbutamol (2.5–5 mg) or terbutaline (5–10 mg) or ipratropium bromide (500 μg) should be given 4–6 hourly for 24–48 hours or until the patient is improving clinically [B].
- Combined nebulised treatment (2.5–10 mg of a β agonist with 250–500 μg ipratropium bromide) should be considered in more severe cases, especially if the patient has had a poor response to either treatment given alone [C].
- If the patient is sufficiently ill to require hospital admission, arterial blood gas tensions should always be measured. If these show that the patient has carbon dioxide retention and acidosis, or if gas tensions cannot be measured (for example, in general practice), the nebuliser should then be driven by air (not high flow oxygen) [C].
- Nebulised bronchodilator treatment should be changed to treatment with a hand held inhaler and patients should be observed for 24–48 hours before discharge from hospital [C].

DOMICILIARY NEBULISER TREATMENT FOR SEVERE COPD

- Adequate bronchodilator medication for most patients with COPD can be delivered with standard doses given by hand held inhalers – for example, salbutamol 200 μg or terbutaline 500 μg, or ipratropium bromide 40–80 μg given up to four times daily [A].
- A few patients may benefit from high dose bronchodilator treatment delivered by a nebuliser.
- It is recommended that, before such treatment is prescribed either from hospital or in general practice, every patient should be assessed fully by a respiratory physician or by another appropriate hospital specialist or general practitioner who has had training in the supervision of nebuliser treatment [C].

ASSESSMENT OF PATIENTS

The components of such an assessment should include:

(a) a review of the diagnosis;
(b) peak flow monitoring at home;
(c) sequential testing of different regimens using peak expiratory flow (PEF) and subjective responses.

Peak flow monitoring

- Patients should record their best of three PEF readings twice daily (morning and evening, before treatment) for a minimum of one week on each treatment [B].
- The average peak flow should be calculated from at least five days recordings.
- A patient's ability to record peak flow reliably should be checked.

Response definition

Pending new evidence, a response to treatment may be defined as an increase of more than 15% over the baseline PEF. Baseline PEF is defined as the average of two weeks PEF recording on standard inhaler therapy as above. For all increases in dose, both subjective responses – for example, breathing better/same/worse – and PEF response should be compared with standard inhaler treatment [C].

Assessment regimen

- A hand held inhaler which the patient can use efficiently should be selected. The subjective and peak flow response to standard doses of bronchodilators given with this device should be formally assessed [B].
- An assessment of the patient's peak flow response to oral steroids or high dose inhaled steroids given for at least two weeks should be carried out if this has not been done previously [C].
- For patients who are still symptomatic on standard bronchodilators, the response to higher doses of bronchodilator treatment using the same device should be assessed – for example, 1 mg terbutaline or 400 μg salbutamol with 160 μg ipratropium bromide four times daily (unlicensed recommendation). Many patients will respond well to such treatment and will not need a subsequent nebuliser trial [B].
- If patients have a poor response or no response to an increase in dose of their bronchodilator they should have a formal assessment of home nebuliser treatment while continuing to record twice daily peak flows and symptom scores for one or two weeks for each drug or drug combination.
- Formal instruction should be given in the use of the nebuliser equipment and the first dose should be given under supervision. Nebuliser drug regimens to consider include:
  (a) a β agonist such as salbutamol 2.5–5 mg or terbutaline 5–10 mg four times daily;

(b) ipratropium bromide 250 or 500 μg four times daily;
(c) a nebulised β agonist combined with ipratropium bromide (doses as above) [B].

- Patients who have a clear subjective and peak flow response to domiciliary nebulised treatment should be advised to continue it. If there is a subjective response with less than a 15% improvement in peak flow, the physician must use clinical judgement to make a recommendation [C]. Other outcomes should not result in continued domiciliary treatment [C].
- There is evidence that hospital "reversibility" tests cannot usefully predict which patients should or should not receive long term nebulised bronchodilator therapy [A].
- Patients should be advised to use nebulised bronchodilator treatment as needed, up to four times per day. (In practice, most patients choose four times daily treatment) [C].
- Follow up of such patients should include regular review at a respiratory clinic.

Nebulisers in the elderly

- In patients aged over 65 years nebulisers are mostly used to deliver high dose bronchodilator medication to those with severe COPD or asthma, but they will also occasionally be needed for patients with milder disease who are unable to use hand held inhalers.
- Elderly patients who might benefit from treatment with nebulisers should be assessed and managed as indicated in the accompanying sections on nebuliser services, asthma, and COPD.
- Elderly patients who do not have cognitive impairment can keep peak flow records just as well as younger patients and these should be used in a similar manner [B].
- A relatively high proportion of elderly patients may not be able to use metered dose inhalers satisfactorily due to impaired cognitive function or memory loss, weak fingers, or poor coordination.
- It is recommended that the use of alternative devices to a metered dose inhaler by the patient or his or her carer should then be assessed – for example, a metered dose inhaler with spacer and tight fitting face mask [C]; a Haleraid or breath activated inhaler [B]; a dry powder inhaler [B]; or a nebuliser [B].
- With advancing age, the response to β agonists declines more rapidly than the response to anticholinergics. For this reason, anticholinergic treatment by hand held inhaler or nebuliser should also be considered [B].
- Ischaemic heart disease is increasingly prevalent with advancing age. High dose β agonist treatment with nebulisers or other devices should be used with caution in elderly patients with known ischaemic heart disease in whom the first dose may require ECG monitoring at a hospital [C].
- Beta agonists are especially likely to cause tremor in the elderly. High doses should be avoided unless necessary [C].
- Prostatism and glaucoma are more common in the elderly. Treatment by mouthpiece rather than face mask should be considered when high doses of anticholinergics are used to avoid the risk of acute glaucoma or blurred vision [C].

Nebulisers in the intensive care unit

GENERAL

Nebulised drug therapy may be less effective in patients undergoing mechanical ventilation because ventilated patients will have more severe lung disease and aerosol deposition from nebulisers and metered dose inhalers is reduced during mechanical ventilation compared with spontaneous breathing. There are few published studies proving the efficacy of aerosol drug treatments in ventilated patients, and it is often necessary to make clinical judgements on the need for it using clinical data from spontaneously breathing subjects.

INDICATIONS

- *Severe acute airflow obstruction*: β agonists, anticholinergic drugs [B].

Of possible value:

- *Respiratory syncytial virus infection in infants*: tribavirin (ribavirin) [C].
- *Bronchopulmonary dysplasia in infants*: corticosteroids [C].
- *Adult and infant respiratory distress syndrome*: surfactants (beractant, colfosceril palmitate, poractant alpha, pumactant) [C].
- *Pulmonary infection*: antibiotics [C].
- *Pulmonary hypertension*: epoprostenol (prostacyclin) [C].

METHODS OF AEROSOL ADMINISTRATION

Until further evidence becomes available, any of the following three methods of aerosol administration appears to be appropriate for mechanically ventilated patients.

Metered dose inhaler

The medication can be administered by metered dose inhaler into a spacer connected to the inspiratory limb of the ventilator circuit with actuation at the onset of lung inflation. Humidification should be interrupted for a few minutes before administration. The amount of drug reaching the lungs has been estimated as 1.5–2% in infants and 4–6% in adults.

Jet nebuliser

An inspiratory phase activated jet nebuliser connected to an aerosol holding chamber

placed in the inspiratory limb of the circuit, or at least connected to the T piece in the inspiratory tubing no greater than 30 cm from the Y piece, can be used. A high nebuliser gas flow is required and the drug solution should be diluted to fill the nebuliser to capacity. Humidification should be discontinued for a few minutes before and throughout nebulisation. Aerosol deposition from jet nebulisers has been measured in vivo as 1.2–3.0% in adults.

Ultrasonic nebuliser

An ultrasonic nebuliser connected to the inspiratory limb of the circuit may also be used. The drug solution should be diluted to fill the nebuliser to capacity and humidification should be discontinued for a few minutes before and throughout nebulisation. Aerosol deposition in vivo has been estimated as 1.3% in infants using the Pentasonic. In vivo data are lacking in adults.

CLEANING OF NEBULISERS

Nebulisers used in ventilator circuits should not be left permanently in line and should be cleaned and changed between nebulisations. There is a risk of small particle bacterial aerosols which can be avoided by this simple measure.

DRUG TREATMENT

- Nebulised β agonists and ipratropium bromide improve lung function in ventilated patients with acute airflow obstruction and should be used in combination with systemic steroids, antibiotics, and intravenous bronchodilators.
- In the management of respiratory syncytial virus (RSV) infection in mechanically ventilated infants, the small particle aerosol generator (SPAG) should be used for ribavirin until other equipment has been shown to be as effective or more so [B].
- Nebulised corticosteroids may improve lung function in ventilated infants with bronchopulmonary dysplasia, although further studies are needed to confirm this [B]. Administration by metered dose inhaler should be equally or more effective than the use of the Whisper jet nebuliser, but this remains to be proven.

Nebulisers in HIV infection and AIDS

NEBULISED PENTAMIDINE FOR PNEUMOCYSTIS CARINII INFECTION

Prophylaxis

- When used for primary and secondary prophylaxis of *P carinii* pneumonia, nebulised pentamidine is less effective than oral co-trimoxazole or dapsone/pyrimethamine which should be used before nebulised pentamidine is tried [A].
- Primary prophylaxis against *P carinii* pneumonia is required if an HIV positive patient has (a) a CD4 (T helper) lymphocyte count of $<200/mm^3$ or a CD4:total lymphocyte count of 1:5 [A], (b) oral thrush or unexplained fever, regardless of CD4 count [A], or (c) an alternative AIDS defining diagnosis such as Kaposi's sarcoma [A].
- Secondary prophylaxis is required after an episode of *P carinii* pneumonia [A].

P carinii pneumonia

- First line treatment for *P carinii* pneumonia of mild to moderate severity is intravenous high dose co-trimoxazole or pentamidine; second line treatment is clindamycin with primaquine or dapsone with trimethoprim or atovaquone. All these regimens are more effective than nebulised pentamidine and a more rapid response to treatment is obtained [A].
- Nebulised pentamidine is ineffective for treatment of severe *P carinii* pneumonia [A].

Method

- Patients should not smoke cigarettes for two hours before treatment [A]. All patients should be pretreated with a β agonist bronchodilator [A]. Further doses of β agonist should be given if bronchoconstriction occurs during treatment.
- Data sheet precautions concerning the handling of pentamidine by health care workers should be observed.
- Ready made pentamidine solution (300 mg in 5 ml) or dry powder vials (300 mg) with 3–5 ml water for injection may be nebulised.
- For prophylaxis 150 mg pentamidine should be given once a month via a System 22 Mizer or 300 mg pentamidine via a Respirgard II nebuliser [A].
- If nebulised pentamidine is used for treatment a dose of 600 mg per day is recommended, given by a Respirgard II nebuliser for 21 days [A], with intravenous pentamidine 4 mg/kg once daily for the first 3–5 days to reduce the risk of extrapulmonary pneumocystis [B].

SPUTUM INDUCTION FOR THE DIAGNOSIS OF LUNG INFECTION

Patients inhale 20–30 ml of hypertonic saline for 10–15 minutes, usually from an ultrasonic nebuliser [A].

Method

- Patients should starve for at least two hours before the procedure to reduce the risk of nausea and retching and should remove any dentures [A]. Rigorous cleaning of the mouth, teeth, gums, and cheeks is needed to remove oral debris which would otherwise

take up stain and obscure cysts of *P carinii* [A].

- A high output ultrasonic nebuliser – for example, the UltraNeb 99m (DeVilbiss) or DP100 (DP Medical) – is recommended. The reservoir is loaded with 20–30 ml of 2.7% sodium chloride, 1 mmol/ml [A].
- The first sputum sample is frequently unrepresentative of the lower respiratory tract and is discarded. Subsequent material is sent for microbiological and cytological analysis [A]. The yield for *P carinii* and other organisms is less than from bronchoalveolar lavage [A].
- Unpredictable arterial oxygen desaturation may occur during sputum induction and persist afterwards so monitoring of oxygen saturation with a transcutaneous oximeter is recommended and exercise testing should not be performed immediately after this procedure [A].

Nebulisers in palliative care

- Nebulisers may be used for the palliation of patients with cough or breathlessness related to advanced disease. Any prescription should be reviewed within three days to check efficacy.
- Bronchodilators may be indicated for the palliation of breathlessness due to concurrent reversible airflow obstruction [B].
- Local anaesthetics such as 2% lignocaine (2–5 ml) or 0.25% bupivacaine (2–5 ml) are indicated for the palliation of non-productive cough, particularly if due to large airway tumour, bronchial stent, or diffuse lung disease [B]. They should not be used for the palliation of breathlessness [B].
- Pretreatment with a β agonist by hand held inhaler or nebuliser is recommended because there is a risk of bronchospasm. Patients should be advised not to eat or drink for about an hour after treatment because of the ensuing reduced sensitivity of the cough reflex [C].
- Normal saline (0.9% sodium chloride in a dose of, for example, 5 ml six hourly) may be tried to loosen tenacious secretions, but as yet there is no supporting scientific evidence [C].
- Nebulised opioids are used for the palliation of breathlessness. However, there is conflicting evidence of benefit in patients with breathlessness due to COPD [B]. A recent randomised trial in patients with cancer showed no benefit over placebo. Only solutions suitable for systemic use should be nebulised – for example, morphine 5–20 mg; diamorphine 5 mg; fentanyl 50–100 μg. The optimal dose, scheduling, and relative efficacy of opioid drugs are unknown. The dose needed will depend upon whether the patient is currently on an opioid or is opioid naive. Because there is a risk of bronchospasm, patients should be given β agonists by hand held inhaler or nebuliser beforehand.
- The possible indications for nebulised corticosteroids, such as budesonide 500 μg 12 hourly, include stridor, lymphangitis carcinomatosa, radiation pneumonitis, or cough after insertion of an endobronchial stent. However, there is no scientific evidence to support this practice [C].
- Likewise, there is as yet no evidence that nebulised corticosteroids are superior to hand held inhalers or oral steroids in these settings.

Nebulisers in cystic fibrosis

DOMICILIARY BRONCHODILATOR TREATMENT

- Bronchospasm responsive to bronchodilators makes a variable contribution to the overall airways obstruction in cystic fibrosis. Neither bronchial provocation tests, reversibility tests, nor clinical characteristics can reliably predict those patients who will benefit from longer term treatment with bronchodilators [B].
- A therapeutic trial of regular treatment is particularly appropriate in patients who wheeze or if there is a marked improvement in symptoms or pulmonary function following a test dose [A]. There is no patient group in whom bronchodilators are always contraindicated.
- There have been no comparative studies of nebulisers and hand held inhalers to determine which should be tried first [B].
- Trials of regular bronchodilator therapy should be performed at a time of stable lung function [B] and monitored by repeat measurements [A]. β agonists and anticholinergic drugs should be assessed separately and in combination doses similar to those recommended for childhood and adult asthma and COPD [A].
- Patients with negative results should be reassessed annually [C].

EXACERBATIONS

- Bronchodilators should be considered for routine prescription during treatment of respiratory exacerbations [B]. Drug doses should be similar to those recommended for adult asthma and COPD.

PHYSIOTHERAPY

- Bronchodilators increase mucociliary clearance in cystic fibrosis and may be useful before physiotherapy to mobilise secretions [C]. However, there is as yet no objective evidence that this adds to the benefit of physiotherapy.

CORTICOSTEROIDS

- Although it is theoretically possible that routine, regular use of inhaled corticosteroids may benefit patients with cystic fibrosis in a number of ways, clinical data are lacking. The routine use of nebulised corticosteroids cannot be recommended on the basis of present knowledge.

rhDNase

- Treatment with rhDNase should be consistent with recommendations made in published guidelines – for example, the 1994 Cystic Fibrosis Trust guidelines for the treatment of cystic fibrosis with dornase alpha (Pulmozyme).[5]
- Patients should commence rhDNase therapy under the guidance of a cystic fibrosis centre [C]. Most patients with moderate disease can be managed as outpatients; those with severe unstable disease should start treatment as inpatients [C].
- Because of the cost of rhDNase and the importance of continued evaluation of this new therapy, the response of patients needs to be assessed repeatedly by monitoring spirometric values, the frequency of respiratory exacerbations, and the patient's report of any improvement in symptoms [C]. Patients with mild to moderate disease can be assessed after one to two weeks of treatment [A]. More severely affected patients may need 12 weeks of treatment to record a positive response [B].
- rhDNase should be given using the equipment supplied with the drug or that used in published trials – for example, the CR50 compressor with Sidestream nebuliser, the Pulmo-Aide compressor with Hudson Updraft II or Acorn nebuliser, or the Proneb compressor with Pari LC nebuliser.
- Improvements in pulmonary function and a reduction in the frequency of respiratory exacerbations should be demonstrated.
- Any adult patient who has inflammation of the lower airways should be considered for a trial of rhDNase [A]. It is potentially beneficial in mild [A], moderate [A], and severe [B] lung disease.
- Children likely to benefit are:
  (a) those over five years of age;
  (b) those with purulent sputum (or, in young children, a productive cough);
  (c) those who have had more than one exacerbation of respiratory infection requiring intravenous antibiotics in the last 12 months;
  (d) those with a forced vital capacity (FVC) less than 80% predicted for height when in a stable stage; and
  (e) those who have been compliant with previous treatments [A].
- Selection and assessment of all patients should be performed in a regional cystic fibrosis centre [C]. Treatment should be initiated under the direct supervision of a cystic fibrosis specialist [C].

Table 2 Commonly used nebulised antibiotics in cystic fibrosis

Antibiotics	*Daily dose*
Colistin*	2 mega units 12 hourly
Gentamicin	80–160 mg 12 hourly
Tobramycin	80–160 mg 12 hourly

* Colistin (Colomycin) is the only antibiotic licensed in the UK for inhalation.

Table 3 Solutions of colistin

Dose (mega units)	*Volume fill (ml)*	*Solvent*
2	4	2 ml water + 2 ml 0.9% sodium chloride
2	2.5	1.5 ml water + 1 ml 0.9% sodium chloride
2	3	2 ml water + 1 ml 0.9% sodium chloride

ANTIBIOTICS

- Nebulised antibiotics (table 2) are indicated to delay or prevent early colonisation with *P aeruginosa* progressing to chronic colonisation [A] and for the prevention of clinical deterioration in patients chronically colonised with *P aeruginosa* [A].
- The benefit of nebulised antibiotics may be assessed by maintenance of spirometric values, reduced sputum production, reduced requirement for intravenous antibiotics, and patient reported benefit [A].
- Nebulised antibiotics should be withdrawn if there is failure to demonstrate benefit as judged by the patient or clinician, poor patient compliance, side effects, or persistent isolation of *B cepacia* with failure to culture other sensitive bacteria [C].
- Nebulised antibiotics may cause bronchoconstriction in adults. At the time of initial prescription each patient should be assessed in hospital with a test dose of an isotonic solution of colistin (table 3). Before the test is performed, and in routine domiciliary use, patients should be pretreated with a nebulised bronchodilator [A].
- Spirometric tests should be performed before and after administration of the test dose. Maximum bronchoconstriction occurs in over 85% of patients within 15 minutes. Patients should be asked about the development of chest tightness [B].
- In children it is not yet known whether long term treatment with nebulised antipseudomonal antibiotics from the time of diagnosis prevents the onset of colonisation with *P aeruginosa*.
- When *P aeruginosa* is first isolated it is reasonable to give a two week course of parenteral or oral antipseudomonal antibiotics together with nebulised colistin [C].

Nebulisers in bronchiectasis

ANTIBIOTICS

- A therapeutic trial of long term nebulised antibiotics with careful evaluation is justified in individual patients when background symptoms, severity of acute exacerbations, or risk of progression warrant antibiotic therapy, provided that oral antibiotics combined with regular postural drainage have been unsuccessful [C].
- Any changes in the volume of purulent sputum and patient well being between acute exacerbations and the severity and frequency of exacerbations should be carefully assessed to evaluate the efficacy of the treatment [C].
- Nebulised antibiotics should usually only be used as an adjunct to regular postural drainage and, for acute exacerbations, oral or intravenous antibiotics [C].
- The doses and frequency of treatment with nebulised antibiotics are similar to those for adults with cystic fibrosis.

BRONCHODILATORS

- Nebulised bronchodilator therapy is indicated in a small number of patients with bronchiectasis and the need should be evaluated as for patients with asthma and COPD [B].

Recommendations for running a domiciliary nebuliser service

ORGANISATION

- All patients needing nebuliser treatment should have access to a nebuliser service [C].
- The service should be provided locally on behalf of a department, trust, or district according to local needs [B].
- It should be organised and administered centrally by a designated consultant or a group of consultants with a consensus view [C].
- Day to day management should be by a named and appropriately trained individual, such as a respiratory nurse specialist, physiotherapist, physiological measurement technician, or medical scientist, with technical and clerical support [C]. Contracts should recognise the expertise and time needed to run a nebuliser service [C].
- The service should include:
  (a) provision of compressors, nebulisers and disposables;
  (b) provision of equipment for emergency replacement in case of breakdown [C];
  (c) a system for repair, servicing and maintenance [B];
  (d) patient and staff education [C];
  (e) detailed schemes for assessing the suitability of patients for long term treatment [A];
  (f) standard written instructions for patients about the use and cleaning of equipment and the local arrangements for servicing and replacement including telephone numbers for emergency replacements [C].

It is recommended that patients of primary care physicians should be referred to a centralised service for assessment before they are established on long term treatment [B].

A mechanism for training staff in running a nebuliser service should be in place [C].

EQUIPMENT

- Compressors should conform to BS5724 or IEL 601-1. By June 1998 all compressors and nebulisers in Europe will have to comply with the European Medical Devices Directive [A].
- A compressor should be matched with a nebuliser to give an adequate rate of output with a high proportion of particles of appropriate size for a therapeutic effect. The performance of any chosen combination of compressor and nebuliser should be verified for each class of drug used (bronchodilators, steroids, antibiotics) from published data or new laboratory measurements [A].
- A service should provide foot pump, battery, or 12 volt adapted compressors for occasional emergency use and for patients on holiday [C].
- Nebulisers should be easy for patients to use and clean [C].
- Supplies of mouthpieces or face masks should be available for patients on different drug treatments [B].

SERVICING AND MAINTENANCE

- All equipment should be checked for electrical safety and performance before issue [B].
- Compressors should be serviced regularly, at least annually [C], although further studies are needed to examine a policy of filter replacement and full servicing "on demand" which is much cheaper.
- Patients should be aware that, if a nebuliser is not working, the compressor should be checked.
- Compressors should be available for loan or replacement while servicing or repairs are being carried out [B].
- Two sets of nebulisers and disposables such as tubing should be provided initially. Standard equipment needs replacing every 3–6 months, although some more durable units may need to be replaced less frequently [B].

SERVICE RECORDS

- It is recommended that the records of a nebuliser service are kept on a computerised data base [C].

RESOURCES

- In the UK, if the prescribing physician decides that nebulising equipment is essential

for a patient's treatment then it is the responsibility of the NHS to provide it and to provide a repairs, maintenance, and electrical safety check service (NHS Management Executive EL (92) 20) [C].

- In the UK, NHS patients should not usually be advised to buy their equipment themselves. If they do, the prescribing physician or general practitioner must ensure that patients are assessed in the same way before long term treatment is begun, that they have oral and written instructions, and that replacement and servicing arrangements are in place. After equipment is issued for long term treatment patients should be reviewed in a clinic or in the surgery within three months and thereafter at least annually [C].

1 British Thoracic Society. Guidelines on the management of asthma. *Thorax* 1993;**48**:S1–24.
2 British Thoracic Society. The British guidelines on asthma management: 1995 review and position statement. *Thorax* 1997;**52**(Suppl 1):S1–21.
3 European Respiratory Society. Optimal assessment and management of chronic obstructive pulmonary disease (COPD). Consensus statement of the European Respiratory Society (ERS). *Eur Respir J* 1995;**8**:1398–420.
4 American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. Official statement of the American Thoracic Society. *Am J Respir Crit Care Med* 1995;**152**:S77–120.
5 Cystic Fibrosis Trust. *Guidelines for the treatment of cystic fibrosis (CF) with dornase alpha (Pulmozyme)*. London: Cystic Fibrosis Trust, 1994.

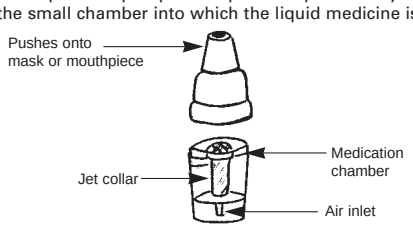
Appendix 1: Instructions for patients using home nebulisers

Instructions for patients using home nebulisers

Your nebuliser system consists of the following parts

Compressor Tubing Nebuliser Mouthpiece/mask

The **compressor** is the portable pump which provides power for your nebuliser.
The **nebuliser** is the small chamber into which the liquid medicine is put and through which the air is blown to make a mist.



The nebuliser

The medicine that is required will be explained to you and your GP will provide it on a long term basis.

Your treatment: Drug Dose When to take

....

....

For each treatment, use your nebuliser for up to ..... minutes.
Do not fill the nebuliser chamber with the drug until you are ready to use it.

Most people use their nebuliser on a fairly regular basis. If you are an asthmatic and use it only for acute episodes of asthma, then you will be provided with a peak flow meter and instructions on what to do and who to contact, should the need arise.

IF YOUR NEBULISER FAILS TO GIVE THE USUAL RELIEF OR THE EFFECT IS SHORTER THAN NORMAL, THIS IS A WARNING SIGN. YOU SHOULD SEEK URGENT MEDICAL ADVICE.

CLEANING
Wash the mouthpiece/mask and nebuliser (drug chamber) in warm water with a little detergent, rinse thoroughly and dry well ideally after every use, and once a day as a minimum. Attach the tube and run the nebuliser empty for a few moments after cleaning it. **If your equipment is dirty or moist, you can pick up a chest infection from it.**
Once a week, disconnect the electricity and wipe the compressor and tubing with a damp cloth.

SUPPLIES
Disposables (masks, mouthpieces, nebulisers, filters, tubing) can be obtained from

.....

NEBULISER PROBLEMS
If your nebuliser takes much longer than normal to run, or it bubbles with no mist, repeat the cleaning process. If this still does not work, replace it.

COMPRESSOR BREAKDOWN
If your compressor breaks down, you should use your hand-held inhaler until you are able to get help. In case of breakdown:

CONTACT NAME .....

TEL NO (working hours) .....

Emergency number for breakdown .....

Important points:
- **Nebulisers should only be used on a doctor's recommendation.**
- **If you have been prescribed regular preventative treatment, this is still needed even if you have a nebuliser.**
- **Your compressor should be serviced once a year. Filters on the compressor should be changed when discoloured.**
- **Disposable parts should be changed every three months, or annually if the long-lasting type.**
- **Side effects – ask the clinic what to expect.**
- **Holidays – ask the clinic about portable compressors.**

MORE DETAILED ADVICE IS AVAILABLE IF YOU WISH – PLEASE ASK WHOEVER GAVE YOU YOUR NEBULISER.

EXTRA INSTRUCTIONS:

Thorax 1997;**52**(Suppl 2)

Appendix 2: Summary of nebuliser guidelines for ward and community staff

Wherever possible, this protocol should be used in conjunction with the BTS nebuliser guidelines.

Principal aim of nebulisation

Nebulisers change a liquid drug into a mist or suspension of very small droplets in air or oxygen. They are used to deliver drugs into the lungs in a mist of particles small enough to reach the bronchioles and, in some cases, the alveoli.[1]

Nebulisers are preferable to hand held inhalers when:

- large drug doses are needed;[2]
- controlled coordinated breathing is difficult, e.g. in sick patients with acute severe asthma or an exacerbation of COPD;
- in chronic lung disease if hand held inhalers have been found ineffective;
- in babies if inhalers, spacer, and mask are not working;
- some drugs such as antibiotics and lignocaine are unavailable in hand held inhalers.

Drugs for nebulisation

Bronchodilators: β agonists such as salbutamol (Ventolin) and terbutaline (Bricanyl) and anticholinergics such as ipratropium bromide (Atrovent).
Steroids: for example, budesonide (Pulmicort) respules.
Antibiotics: for example, colistin and gentamicin for cystic fibrosis.
rhDNase: for cystic fibrosis.[3]
Pentamidine: sometimes for HIV positive patients as treatment or prophylaxis for *Pneumocystis carinii* pneumonia.
Lignocaine: in terminal care to relieve cough.
0.9% sodium chloride: sometimes to assist physiotherapy.

N.B. Water should not be used as it may cause bronchoconstriction when nebulised.[4]

Parts of the nebulising system

SOURCE OF THE DRIVING GAS

(a) Compressor: air pump powered by electricity or by battery for portable use, used at home or in hospital.
(b) Compressed air from cylinder or piped on wall, flow rates 6–8 l/min (hospital).
(c) Compressed oxygen from cylinder or piped on wall (only in acute asthma) (hospital).[5]

MOUTHPIECES AND MASKS

Masks (with straps) are better in:

(a) Acutely ill patients when holding the nebuliser is tiring (although some severely breathless patients may find this claustrophobic).
(b) Babies and young children when co-ordination is difficult.

Mouthpieces should be used:

(a) For nebulised steroids to prevent deposition on the face.
(b) For nebulised antibiotics so a filter can be used to prevent exhalation of antibiotic into air.
(c) Sometimes for anticholinergics as they may exacerbate glaucoma.

Nebulisation

- A gas flow rate of 6–8 l/min is usually used to nebulise 50% of the particles to 2–5 μm diameter to aid deposition into the small airways.[6]
- Flow meters on cylinders may be less accurate than electrical compressors at the high pressure required. Compressors are cheaper to run.
- In patients with acute severe asthma oxygen is used, if possible, to nebulise bronchodilators as patients are hypoxic.[7] In all other lung diseases air should be used unless oxygen is prescribed. In some patients low flow oxygen can be given via nasal cannulae while nebulising drugs with air. Oxygen should not be routinely used for nebulisers in patients with COPD because there is a risk of carbon dioxide retention in some.
- The volume of fluid in the nebuliser chamber is usually 2.0–4.5 ml. Most wards have nebulisers which only leave 0.5 ml of fluid as residual after nebulisation,[6] in which case it is sufficient to start with 2–2.5 ml of drug fluid. Bronchodilators such as β agonists and ipratropium bromide are sometimes mixed together to make up to 4.5 ml.
- For bronchodilators 10 minutes should be sufficient for nebulisation.[6] Antibiotics, steroids, and pentamidine may need to take longer to use as much drug as possible. For these and other solutions which are more viscous, especially chosen equipment is necessary.[7]
- Special filters prevent antibiotic particles that are harmful to staff or family from getting into the atmosphere; these filters need to be dried between use to be effective so two should be supplied.
- Nebulisers (drug chamber) come in disposable versions which last up to three months and durable versions which last up to a year. Any scratches, damage, or discolouration means the nebuliser and tubing should be changed. Durable nebulisers can be boiled, sterilised, or autoclaved according to the manufacturers' instructions.

- The mouth should be rinsed out after nebulising steroids and antibiotics to prevent development of oral thrush.

METHOD OF INHALATION

The patient should be instructed to sit upright or in a chair, to take normal steady breaths (tidal breathing), not to talk during the nebulisation, and to keep the nebuliser upright.

Be aware of the best time for each patient to nebulise. Nebulisers just before meals may spoil an already small appetite, but others who are severely breathless may need the bronchodilatation to give them breath to eat.

CLEANING

Each patient should have their own tubing, nebuliser, and mouthpiece/mask, even if they share a compressor. In order to avoid crystallisation and growth of micro-organisms in the residual fluid the nebuliser should be emptied after each use and washed at least once a day in warm water with a little detergent and dried with a soft tissue.[8] Drugs should be put into the nebuliser immediately before use as they no longer contain preservative.

Outpatient nebuliser service

Nebuliser treatment for patients at home will usually be run by a centralised local nebuliser service where nebulisers are used in accordance with the hospital protocol.[9]

Before they go home with a nebuliser patients should be taught how to use, clean and assemble it, and when to call for help.[10] This should also be written down clearly for them to keep handy. If they are asthmatic it is essential they know when and which treatment to take and when to call their general practitioner, rather than waiting too long to come to hospital.

This Appendix has been prepared by a multidisciplinary team of respiratory physicians, general practitioners, a consultant microbiologist, infection control nurse specialists, physiotherapist, lung function technicians, respiratory nurse specialists, and ward nurses.

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Appendix 3: Summary of nebuliser guidelines for general practitioners

Purpose

Nebulisers provide doses of drugs to the lungs as an aerosol. They are useful:

(a) when large doses of drugs are needed;
(b) when patients are too ill or otherwise unable to use hand held inhalers;
(c) when drugs are not available in hand held inhalers – for example, lignocaine, antibiotics.

Indications

1 Most commonly, for the emergency treatment of asthma and exacerbations of COPD.
2 Less frequently for:
(a) the long term treatment of chronic air flow obstruction with bronchodilators;
(b) prophylactic drug treatment – for example, corticosteroids and disodium cromoglycate in asthma;
(c) antimicrobial treatment in cystic fibrosis, bronchiectasis, and HIV/AIDS;
(d) symptom relief in palliative care.

Long term treatment

The BTS recommends that long term treatment with nebulised drugs should usually be initiated only after assessment by a hospital specialist such as a chest physician or a paediatrician, and by general practitioners only after specific training.

Equipment

Jet nebulisers are generally the most suitable. They consist of an electrical compressor with a standard flow rate of 6–8 l/min or a higher flow rate of >8 l/min, and disposables including connecting tubing, the nebuliser chamber (performance depends on design), mouthpiece or mask (these are interchangeable but masks are better for emergencies and infants).

Nebuliser use

DRUG VOLUME

Most nebulisers work with drug volumes of 2–5 ml. If the system used has a residual volume of more than 1.0 ml (shown on packing) the drug volume should be made up with 0.9% sodium chloride (not water) to a minimum of 4.0 ml.

NEBULISING TIME

"Dryness" should not be used as an end point. Patients should be advised to nebulise until about a minute after "spluttering" occurs. This should take 5–10 minutes. An upper limit for treatment time should be specified. Patients should tap the nebuliser cup towards the end of treatment.

CLEANING

Patients using nebulisers regularly should clean them daily, and patients using them intermittently should clean them after each use. The nebuliser and mouthpiece or mask should be disconnected, disassembled, washed in warm water with a little detergent, and allowed to dry overnight. The nebuliser should be run for a few seconds with no drugs in it before the next treatment.

MAINTENANCE

Disposable components (plastic tubing, the nebuliser cup, mask or mouthpiece) should be changed every three to four months (available from chemists, manufacturers, or local nebuliser service). Compressors need servicing annually by the local nebuliser service or manufacturer.

BREAKDOWN

Patients must know what to do if their equipment breaks down. If nebulisation is slow the nebuliser should be disassembled and washed and treatment tried again. If it is still inefficient a spare one should be used. If nebulisation is still slow or the compressor is faulty the patient should ask for medical help and meanwhile self-treat with multiple doses of hand held inhalers (previously advised).

Patients must know who to contact in the event of an emergency – for example, the local nebuliser service or practice nurse.

OXYGEN

Patients with acute severe attacks of asthma need additional oxygen. Nebulisers will run with a flow rate of 6–8 l/min. If available cylinders do not produce this flow rate, electrical compressors should be used for immediate treatment. Simultaneous use of oxygen by nasal cannulae at 4 l/min is appropriate.

PATIENT INSTRUCTION

Firstly, patients must be shown how to use their nebuliser. The first treatment should always be done under supervision. For longer term use patients should have written instructions provided by their local nebuliser service or derived from the BTS guidelines.

When to use nebuliser treatment

For the treatment of acute severe and chronic persistent asthma and of COPD, nebuliser treatment should be a component of disease management as in the published BTS asthma[1 2] and COPD[3 4] guidelines.

ACUTE SEVERE ASTHMA

Adults

Severity: cannot complete sentences, RR >25/min, HR >110/min, PEF <50% best.

Treatment: oxygen plus oral steroids plus nebulised β agonist, e.g. salbutamol 5 mg or terbutaline 10 mg, repeated 4–6 hourly if better. If not, add ipratropium bromide 500 μg to β agonist and consider admission to hospital.

Children

Severity: cannot talk or feed, RR >50/min, HR >140/min, PEF <50% predicted.

Treatment: oxygen plus nebulised salbutamol 5 mg (or 0.15 mg/kg) or terbutaline 10 mg (or 0.3 mg/kg) repeated 1–4 hourly if better. If not, repeat at 30 minutes after adding ipratropium bromide 250 μg. Continue 1–4 hourly and consider transfer to hospital and oral steroids.

"BRITTLE" ASTHMA (patients needing to self-treat with nebulisers for sudden attacks)

These patients are uncommon but are difficult to treat. It is recommended that a written treatment plan is agreed with a local hospital specialist. Patients should be encouraged to seek medical help early in an attack. Suggested drug regimens are as above plus oral steroids.

CHRONIC PERSISTENT ASTHMA

Regular nebulised bronchodilator treatment should only be undertaken after formal evaluation of its benefit (a service provided by most specialist units) and where treatment with a hand held inhaler at appropriate doses has failed.

ACUTE EXACERBATIONS OF COPD

Mild episodes

Hand held inhaler: salbutamol 200–400 μg or terbutaline 500–1000 μg four hourly.

Moderately severe

Hand held inhaler: salbutamol 400 μg or terbutaline 1000 μg four hourly or nebuliser.

Severe (cyanosed, RR >25/min, cannot make sentences, reduced activity)

Consider admission to hospital, meanwhile nebulise β agonists as for acute asthma or ipratropium bromide 250–500 μg 4–6 hourly. If more severe or not improving, consider combination of a β agonist with ipratropium bromide 500 μg 4–6 hourly. Do not nebulise with oxygen. A 24% Venturi mask is suitable in between treatments.

CHRONIC SEVERE COPD

Most patients are managed well by hand held inhalers. Only a few will benefit from higher dose treatment.

Patients should be referred to a local specialist for assessment. This should include a review of the diagnosis, home peak flow monitoring, and evaluation of different treatment regimens.

If GPs wish to initiate long term treatment, the same standard of assessment is appropriate. Patients wishing to purchase their own compressor should be discouraged from commencing long term treatment without a similar assessment.

THE ELDERLY

(a) Asthma and COPD: treatment as above.
(b) Rarely, β agonists may precipitate angina. A first treatment should be supervised.
(c) Because glaucoma may be worsened by ipratropium, the use of a mouthpiece should be considered.

PALLIATIVE CARE

Advanced neoplastic disease

Nebulisers may be used for symptom relief in patients known to have advanced neoplastic or other disease. Treatment should be reviewed within three days to check efficacy.

Breathlessness with diffuse airflow obstruction (not stridor)

Consider bronchodilators as for COPD.

Severe non-productive cough

Lignocaine 2%, 2–5 ml; bupivacaine 0.25%, 2–5 ml repeated up to four hourly, preceded by a β agonist given by hand held inhaler (2–4 actuations). Nil by mouth for one hour afterwards.

Poor expectoration

Consider 2–5 ml 0.9% sodium chloride repeated up to four hourly.

Other uses of nebulisers

These are uncommon. Nebulisers tend to be needed in patients with complex problems and treatment is best begun and supervised by appropriate hospital or hospice specialists. The other possible uses include antibiotics in patients with cystic fibrosis and severe bronchiectasis, rhDNase in cystic fibrosis, pentamidine in HIV/AIDS, corticosteroids in patients with chronic persistent asthma, and opioids and corticosteroids in the palliation of dyspnoea.

1 British Thoracic Society. Guidelines on the management of asthma. *Thorax* 1993;**48**:S1–24.
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Appendix 4: Grading scheme for recommendations in the guidelines

The criteria for the grading of recommendations in the guidelines are based upon a paper by Petrie *et al* published on behalf of the Scottish Intercollegiate Guidelines Network.[1]

Levels of evidence

Level	*Type of evidence (based on AHCPR 1992)*[2]
Ia	Evidence obtained from meta-analysis of randomised controlled trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well designed controlled study without randomisation
IIb	Evidence obtained from at least one other type of well designed quasi-experimental study
III	Evidence obtained from well designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grading of recommendations

Grade	*Type of recommendations (based on AHCPR 1992)*[2]
A (levels Ia, Ib)	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation
B (levels IIa, IIb, III)	Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation
C (level IV)	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality

1 Petrie, GJ, Barnwell E, Grimshaw J, on behalf of the Scottish Intercollegiate Guidelines Network. *Clinical guidelines: criteria for appraisal for national use.* Edinburgh: Royal College of Physicians, 1995.

2 Agency for Health Care Policy and Research. *Acute pain management, operative or medical procedures and trauma 92-0032. Clinical practice guideline.* Rockville, Maryland, USA: Agency for Healthcare Policy and Research Publications, 1992.

Appendix 5: Suggestions for further research

Basic science

- Adequate information is not available in most cases to inform clinicians or patients of how much of a specific drug a patient might receive from a given nebuliser. At present the Medicines Control Agency and the Medical Devices Agency do not require such data from drug companies or nebuliser manufacturers. Output of a given drug from different nebulisers may vary by 200% or more, and the output of a given nebuliser may vary dramatically depending on the drug nebulised. It is suggested that each compressor-nebuliser and drug combination should be evaluated separately and standards established for publishing this information.
- At present it is not possible to predict accurately drug delivery to the lungs from in vitro studies of nebuliser performance. The relationship between in vitro studies (including the effect of breathing patterns) and pharmokinetic and radioisotope studies of drug delivery to the lungs needs to be more closely examined.

Paediatrics

- More information is needed on the way in which different inhalation modes and breathing patterns affect the deposition of nebulised drugs in young children and infants.
- There is increasing evidence that hand held inhalers with spacers and face masks may be as effective as nebulisers in the treatment of asthma in most situations and comparative studies would allow the role of nebulisers (if any) to be more accurately defined.
- The efficacy and safety of inhaled steroids in children with bronchopulmonary dysplasia needs further evaluation.

Adult asthma

- More information is needed on the possibility of substituting multiple actuations of hand held inhalers for nebulisers.
- We are ignorant of the best treatment for asthmatic subjects who do not respond well to initial treatment with a nebulised β agonist.
- Controlled trials are urgently needed to establish the role of nebulised corticosteroids compared with increased doses given by hand held inhalers.

COPD

- Nebulised bronchodilator treatment is commonly prescribed for patients with COPD but the choice of medication and the dosage and frequency of dosing have not been established by well controlled studies (either for hospital patients with COPD or for home nebuliser users).
- When patients are admitted to hospital with an acute exacerbation of COPD it is customary to administer nebulised bronchodilator treatment for a few days and then change to hand held inhaler treatment prior to discharge. The timing of this change over has not been subjected to scientific scrutiny.
- It is a common problem to decide the most appropriate management for patients who feel considerably better when taking nebulised therapy but in whom little or no physiological improvement is seen. There is uncertainty at present as to whether "clinical judgement" is appropriate under these circumstances. Detailed studies to analyse the apparent improvement and to assess the placebo effect of nebuliser treatment in double blind comparisons are urgently needed.

The elderly

- There is some evidence that the bronchodilator response to inhaled β agonists declines at a faster rate than the bronchodilator response to inhaled anticholinergics. Further information would allow judgement about the earlier use of anticholinergic treatment in the elderly.
- There is a theoretical risk of nebulised β agonists causing serious dysrhythmias in the elderly who have an increased incidence of heart disease. The evidence that this is more than a theoretical risk is limited and further studies are needed.

Intensive care

- More work is needed to establish the optimum methods of aerosol delivery to ventilated patients and could include radionuclide scanning studies.
- We know little about the optimum method for the delivery of drugs with different physicochemical properties, how aerosol delivery is affected by different ventilators and modes of ventilation such as pressure cycled or positive end expiratory pressure (PEEP), and how aerosol delivery is affected by lung disease and abnormal lung function such as reduced compliance. These data are needed to establish the right conditions for clinical trials on ventilated patients, particularly with respect to drugs other than bronchodilators.

Palliative care

- The evidence for clinical benefit in this area depends far too much on anecdotal experience and controlled studies are urgently

needed. The emphasis for outcome measurements should probably be validated quality of life indicators and not simply functional improvements.

- The role of nebulised opioids will need re-examination in the light of the results of double blind studies now in progress. If it is shown that benefit is simply related to the systemically available drug, then the indications for nebulised treatment will need to be radically reassessed. Data are needed on the relative merits of lignocaine and bupivacaine for cough. The optimal concentration of solutions and specific indications for treatment need to be established.
- The extent to which either oral or high dose nebulised steroids are useful in conditions such as stridor and lymphangitis carcinomatosa needs assessment. Comparative studies of nebulised and oral medication are probably needed before detailed examination of dose ranges and schedules for nebuliser treatment.
- It is not known whether nebulised drugs should be given on a regular or "as required" basis.

Cystic fibrosis

- The efficacy of bronchodilator therapy, both in the treatment of acute respiratory exacerbations and in maintaining respiratory function and decreasing morbidity and mortality with long term treatment, is not known. To answer these questions placebo controlled trials are needed, which would probably need to be multicentre. Subsidiary problems are the investigation of the role of single or combination treatment with β agonists and anticholinergic drugs and the way in which these should be scheduled.
- Prospective studies are needed to determine the effect of long term nebulised corticosteroids on respiratory function, frequency of respiratory exacerbations, daily symptoms, and inflammatory markers. It is not known to what extent nebulised corticosteroids are helpful in the treatment of respiratory exacerbations, and whether patients with coexistent asthmatic characteristics benefit more than other patients with cystic fibrosis. As for asthma, it is not known whether inhaled corticosteroids could be given as effectively by hand held inhaler as by nebulisers.
- The role of rhDNase in the management of an acute respiratory exacerbation or in patients with mild disease is uncertain. It is not yet known whether it is effective in longer term treatment. Whether rhDNase can be given as well or better by other delivery system needs investigation.
- Although nebulised β agonists are commonly used as adjuncts to physiotherapy, few data are available to confirm that this is any more useful than saline alone (or no treatment).

Antibiotics in cystic fibrosis and bronchiectasis

- Appropriate nebuliser systems need to be identified for every drug used. Ideally these need to be established with respect to drug deposition in the lungs as well as in vitro measurements of drug output and particle size.
- In bronchiectasis the indications for treatment are uncertain and the clinical role of nebulised antibiotics is unproven. An opportunity exists for a multicentre study in well characterised patients.
- The optimum doses of nebulised antibiotics, the frequency of treatment, and whether treatment should be intermittent or continuous are not known.
- Many other issues have been underresearched. These include antibiotic resistance, long term drug side effects, and the need for vents or filters for domiciliary treatment.

Nebuliser use

- Only unpublished data are available to support the conclusions that patients cannot easily recognise when nebulisers are spluttering or running dry and that 10 minutes is, for most patients, a reasonable maximum time for treatment. These practical issues need confirmation from larger studies.