Adverse Effects

Hydrogen sulfide is a common industrial hazard and is encountered in such places as chemical works, mines, sewage works, and stores of decomposing protein. Concentrations of 0.1 to 0.2% in the atmosphere may be fatal in a few minutes. At concentrations of about 0.005% and above hydrogen sulfide causes anosmia and its unpleasant odour is no longer detectable. Pulmonary irritation, oedema, and respiratory failure usually occur after acute poisoning; prolonged exposure to low concentrations may cause severe conjunctivitis with photophobia and corneal opacity, irritation of the respiratory tract, cough, nausea, vomiting and diarrhoea, pharyngitis, headache, dizziness, and lassitude. There are some similarities to poisoning with cyanides.

◊ General references.

1. WHO. Hydrogen Sulfide. *Environmental Health Criteria 19*. Geneva: WHO, 1981. Available at: http://www.inchem.org/documents/ehc/ehc/ehc019.htm (accessed 05/07/04)

Treatment of Adverse Effects

In poisoning with hydrogen sulfide the patient should be removed from the contaminated atmosphere and an effective airway established. Inhalation of amyl nitrite or parenteral therapy with sodium nitrite have been suggested; this produces methaemoglobin, which may bind sulfide. Oxygen should be given; hyperbaric oxygen therapy has also been suggested. The conjunctival sacs should be carefully washed out if eye irritation is severe. Management is then usually symptomatic and supportive.

◊ References.

1. Gorman DF. Problems and pitfalls in the use of hyperbaric oxygen for the treatment of poisoned patients. *Med Toxicol Adverse Drug Exp* 1989; **4:** 393–9.

Uses

Hydrogen sulfide is widely used in many industrial processes.

Isobutane

E943b; Isobutano; 2-Methylpropane.

C_4H_{10} = 58.12.

Pharmacopoeias. In *USNF*.

USNF 26 (Isobutane). A colourless gas. It is highly flammable and explosive. Store in airtight cylinders at a temperature not exceeding 40°.

Profile

Isobutane is used as an aerosol propellant (p.1688).

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austral.:*** Histofreezer†; ***Fr.:*** Cliptol Sport†; Freeze; ***UK:*** Histofreezer; ***USA:*** Compound W Freeze Off.

Nitrogen

Azot; Azotas; Azote; Dusík; E941; Kvävgas; Nitrogén; Nitrogenium; Nitrógeno; Nitrogenum; Stickstoff; Typpi.

N_2 = 28.0134.

CAS — 7727-37-9.

ATC — V03AN04.

ATC Vet — QV03AN04.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn*. Also in *USNF*.

Ph. Eur. 6.2 (Nitrogen). The monograph applies to nitrogen for medicinal use. A colourless, odourless gas. Soluble 1 in about 62 of water and 1 in about 10 of alcohol by volume at 20° and at a pressure of 101 kpA. Store as a compressed gas or a liquid in appropriate containers.

The BP 2008 directs that nitrogen should be kept in approved metal cylinders, the shoulders of which are painted black and the remainder grey. The cylinder should carry a label stating 'Nitrogen'.

Ph. Eur. 6.2 (Nitrogen, Low-oxygen). The monograph applies to nitrogen used in the production of an inert atmosphere for finished medicinal products that are particularly sensitive to degradation by oxygen. A colourless, odourless gas. Soluble 1 in about 62 of water and 1 in about 10 of alcohol by volume at 20° and at a pressure of 101 kpA. Store as a compressed gas or a liquid in appropriate containers.

USNF 26 (Nitrogen). A colourless, odourless, tasteless gas. It is non-flammable and does not support combustion. Soluble 1 in about 65 of water v/v and 1 in about 9 of alcohol v/v at 20° and at a pressure of 760 mmHg. Store in cylinders.

USNF 26 (Nitrogen 97 Percent). It contains not less than 97% v/v of nitrogen. Store in cylinders or in a low-pressure collecting tank.

Adverse Effects

Nitrogen narcosis has been reported after use of nitrogen at high pressure as in deep-water diving. Under high pressure, nitrogen dissolves in blood and lipid. If decompression is too rapid, nitrogen effervesces from body stores producing gas emboli and leads to the syndrome of decompression sickness. Skin contact with liquid nitrogen causes frostbite or burns.

◊ References.

1. Roblin P, *et al.* Liquid nitrogen injury: a case report. *Burns* 1997; **23:** 638–40.
2. Kernbach-Wighton G, *et al.* Clinical and morphological aspects of death due to liquid nitrogen. *Int J Legal Med* 1998; **111:** 191–5.
3. Koplewitz BZ, *et al.* Gastric perforation attributable to liquid nitrogen ingestion. *Pediatrics* 2000; **105:** 121–3.
4. Kim DH, Lee HJ. Evaporated liquid nitrogen-induced asphyxia: a case report. *J Korean Med Sci* 2008; **23:** 163–5.

Uses and Administration

Nitrogen is used as a diluent for pure oxygen or other active gases and as an inert gas to replace air in containers holding oxidisable substances. Liquid nitrogen is used as a cryotherapeutic agent for the removal of warts (p.1584) and for preservation of tissues and organisms.

Oxygen

Deguonis; E948; Happi; Kyslík; Ossigeno; Oxigén; Oxígeno; Oxygène; Oxygenium; Oxygenum; Sauerstoff; Tlen.

O_2 = 31.9988.

CAS — 7782-44-7.

ATC — V03AN01.

ATC Vet — QV03AN01.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet*.

Ph. Eur. 6.2 (Oxygen). A colourless, odourless gas. Soluble 1 in about 32 of water by volume at 20° and at a pressure of 101 kPa. Store as a compressed gas or liquid in appropriate containers.

The BP 2008 directs that oxygen should be kept in approved metal cylinders, the shoulders of which are painted white and the remainder black. The cylinder should carry a label stating 'Oxygen'. In addition, 'Oxygen' or the symbol 'O_2' should be stencilled in paint on the shoulder of the cylinder.

Ph. Eur. 6.2 (Air, Medicinal; Aer Medicinalis; Medical Air BP 2008). It is compressed ambient air containing not less than 20.4% and not more than 21.4% of oxygen. A colourless, odourless gas. Soluble 1 in about 50 of water by volume at 20° and at a pressure of 101 kPa. Store as a gas in suitable containers.

Ph. Eur. 6.2 (Air, Synthetic Medicinal; Aer Medicinalis Artificiosus; Synthetic Air BP 2008). It is a mixture of nitrogen and oxygen containing between 21.0% and 22.5% of oxygen. A colourless, odourless gas. Soluble 1 in about 50 of water by volume at 20° and at a pressure of 101 kPa. Store as a compressed gas in suitable containers.

USP 31 (Oxygen). A colourless, odourless, tasteless gas that supports combustion more energetically than does air. Soluble 1 in about 32 of water v/v and 1 in about 7 of alcohol v/v at 20° and at a pressure of 760 mmHg. Store in cylinders or in a pressurised storage tank.

USP 31 (Medical Air). A natural or synthetic mixture of gases consisting largely of nitrogen and oxygen. It contains not less than 19.5% and not more than 23.5% of oxygen. Store in cylinders or in a low pressure collecting tank.

USP 31 (Oxygen 93 Percent). It contains not less than 90% v/v and not more than 96% v/v of oxygen, the remainder consisting mostly of argon and nitrogen. Store in cylinders or in a low-pressure collecting tank.

Adverse Effects

Oxygen toxicity depends upon both the inspired pressure (a function of concentration and barometric pressure) and the duration of exposure, the safe duration decreasing as the pressure increases. At lower pressures of up to 2 atmospheres absolute, pulmonary toxicity occurs before CNS toxicity; at higher pressures, the reverse applies. Symptoms of pulmonary toxicity include a decrease in vital capacity, cough, and substernal distress. Symptoms of CNS toxicity include nausea, mood changes, vertigo, twitching, convulsions, and loss of consciousness.

Hyperbaric oxygen therapy. In a review of hyperbaric oxygen therapy[1] the following were mentioned as potential complications: barotrauma (ear or sinus trauma, tympanic membrane rupture, or rarely pneumothorax or air embolism); oxygen toxicity (CNS toxicity or pulmonary toxicity); and reversible visual changes.

1. Grim PS, *et al.* Hyperbaric oxygen therapy. *JAMA* 1990; **263:** 2216–20.

Retinopathy of prematurity. In the 1940s and 1950s an epidemic of retinopathy of prematurity, affecting perhaps 10 000 babies, was attributed to excessive use of oxygen in neonates. This resulted in the use of oxygen being reduced or curtailed and the incidence of the condition fell dramatically. However, in the 1970s and later an unexpected resurgence of retinopathy of prematurity occurred (probably *not* due to excessive oxygen use). It was suggested[1,2] that oxygen plays only a minor part and that retinopathy of prematurity is a multifactorial condition that affects the most immature and sick children; the increased incidence may reflect the improved survival of these very premature neonates. A study[3] of supplemental oxygen in infants with prethreshold retinopathy of prematurity suggested that therapy was safe, but a beneficial effect could not be confirmed. However, a retrospective study[4] in premature neonates given supplemental oxygen found that retinopathy of prematurity was more common in those maintained at higher oxygen saturations.

1. Anonymous. Retinopathy of prematurity. *Lancet* 1991; **337:** 83–4.
2. Holmström G. Retinopathy of prematurity. *BMJ* 1993; **307:** 694–5.
3. The STOP-ROP Multicenter Study Group. Supplemental therapeutic oxygen for prethreshold retinopathy of prematurity (STOP-ROP), a randomized, controlled trial. I: Primary outcomes. *Pediatrics* 2000; **105:** 295–310.
4. Tin W, *et al.* Pulse oximetry, severe retinopathy, and outcome at one year in babies of less than 28 weeks gestation. *Arch Dis Child Fetal Neonatal Ed* 2001; **84:** F106–F110.

Precautions

Any fire or spark is highly dangerous in the presence of increased oxygen concentrations especially when oxygen is used under pressure.

Metal cylinders containing oxygen should be fitted with a reducing valve by which the rate of flow can be controlled. It is important that the reducing valve should be free from all traces of oil or grease, as otherwise a violent explosion may occur. Combustible material soaked in liquid oxygen is potentially explosive and the low temperature of liquid oxygen may cause unsuitable equipment to become brittle and crack. Liquid oxygen should not be allowed to come into contact with the skin as it produces severe 'cold burns'.

Oxygen intended for aviation or mountain rescue must have a sufficiently low moisture content to avoid blocking of valves by ice on freezing.

High concentrations of oxygen should be avoided in patients whose respiration is dependent upon hypoxic drive, otherwise carbon dioxide retention and respiratory depression may ensue.

Neonates. The use of supplemental oxygen in neonates is controversial.[1] Although the use of 100% oxygen for the resuscitation of asphyxiated term neonates has been standard, there is some evidence that the use of room air (21% oxygen) is equally effective and possibly safer than 100% oxygen although a systematic review[2] concluded that there was insufficient evidence for recommendations to be made. Guidelines[3,4] for neonatal resuscitation state that the use of less concentrated oxygen or room air in preference to 100% oxygen is reasonable, but that supplemental oxygen should be available if room air is used initially. Use of supplemental oxygen in preterm neonates has been associated with an increased risk of retinopathy of prematurity, although other factors are probably also involved (see under Adverse Effects, above). However, another study[5] has reported that supplemental oxygen has beneficial effects on sleep patterns in premature neonates. Although there is some evidence for a link between neonatal oxygen therapy and childhood cancer, this remains to be confirmed.[6]

1. Higgins RD, *et al.* Executive summary of the workshop on oxygen in neonatal therapies: controversies and opportunities for research. *Pediatrics* 2007; **119:** 790–6.
2. Tan A, *et al.* Air versus oxygen for resuscitation of infants at birth. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2005 (accessed 07/06/06).
3. Resuscitation Council (UK). Resuscitation Guidelines 2005: newborn life support. Available at: http://www.resus.org.uk/pages/nls.pdf (accessed 07/06/06)
4. The American Heart Association. 2005 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Part 13: neonatal resuscitation guidelines. *Circulation* 2005; **112:** (suppl 1): IV188–IV195. Also available at: http://circ.ahajournals.org/cgi/reprint/112/24_suppl/IV-188 (accessed 07/06/06)
5. Simakajornboon N, *et al.* Effect of supplemental oxygen on sleep architecture and cardiorespiratory events in preterm infants. *Pediatrics* 2002; **110:** 884–8.
6. Spector LG, *et al.* Childhood cancer following neonatal oxygen supplementation. *J Pediatr* 2005; **147:** 27–31.

Uses and Administration

Oxygen is given by inhalation to correct hypoxaemia in conditions causing respiratory failure (below) and in conditions where the oxygen content of the air breathed is inadequate such as high-altitude disorders (p.1168). Oxygen is of value in the treatment of poisoning with a number of substances, including carbon monoxide (p.1688), cyanides (p.2045), and dichloromethane (p.2021). It provides enhanced oxygenation in inhalation injury. Oxygen is also given by inhalation to subjects working in pressurised spaces and to divers to reduce the concentration of nitrogen inhaled. It is used as a diluent of volatile and gaseous anaesthetics.

Oxygen is usually given by means of nasal prongs or via a face mask; these can usually deliver concentrations of up to 60%. Tight-fitting anaesthetic-type masks, or delivery via an endotracheal tube or oxygen tent, can provide higher concentrations of up to 100%. Face masks are often used for domiciliary oxygen therapy when flow rates are 2 or 4 litres/minute. Oxygen is usually supplied compressed in metal cylinders although oxygen concentrators, which produce oxygen-enriched air, are useful for domiciliary therapy, especially in patients using large quantities of oxygen. Oxygen may also be supplied at low temperature in insulated containers as liquid oxygen.

In respiratory failure in conditions not usually associated with retention of carbon dioxide, such as pneumonia, pulmonary oedema, or fibrosing alveolitis, oxygen should be given in high concentrations (usually 40 to 100%). Concentrations of 40 to 60% should be used in acute severe asthma even though carbon dioxide retention may have increased as the patient's condition deteriorated. High concentrations of oxygen should always be reduced as soon as possible to the lowest concentration needed to

correct hypoxaemia in order to prevent development of any associated oxygen toxicity, including increased carbon dioxide retention. High concentrations of oxygen should be used in carbon monoxide poisoning and, in selected patients, treatment with hyperbaric oxygen considered.

In respiratory failure associated with chronic obstructive pulmonary disease (conditions such as chronic bronchitis and emphysema) oxygen is usually given initially at an inspired concentration of up to 28%. High concentrations are to be avoided as they may enhance carbon dioxide retention and narcosis.

Oxygen at a pressure greater than 1 atmosphere absolute, i.e. hyperbaric oxygen therapy (below), is given by enclosing the patient in a special high-pressure chamber. It may be used in carbon monoxide poisoning, as an adjunct in the treatment of severe anaerobic infections, especially gas gangrene, and for the treatment of decompression sickness and gas emboli.

◊ General references.

1. Naylor-Shepherd MF, *et al.* Oxygen homeostasis: theory, measurement, and therapeutic implications. *DICP Ann Pharmacother* 1990; **24:** 1195–1203.
2. Gribbin HR. Management of respiratory failure. *Br J Hosp Med* 1993; **49:** 461–77.
3. Tarpy SP, Celli BR. Long-term oxygen therapy. *N Engl J Med* 1995; **333:** 710–14.
4. Bateman NT, Leach RM. ABC of oxygen: acute oxygen therapy. *BMJ* 1998; **317:** 798–801.
5. Rees PJ, Dudley F. ABC of oxygen: oxygen therapy in chronic lung disease. *BMJ* 1998; **317:** 871–4.
6. Rees PJ, Dudley F. ABC of oxygen: provision of oxygen at home. *BMJ* 1998; **317:** 935–8.
7. Treacher DF, Leach RM. ABC of oxygen: oxygen transport: basic principles. *BMJ* 1998; **317:** 1302–6.
8. Leach RM, Treacher DF. ABC of oxygen: oxygen transport: tissue hypoxia. *BMJ* 1998; **317:** 1370–3.
9. Balfour-Lynn IM, *et al.* Home oxygen for children: who, how and when? *Thorax* 2005; **60:** 76–81.

Cluster headache. Inhalation of 100% oxygen can provide rapid and effective treatment of cluster headache attacks (p.616) but practical difficulties associated with its use result in other drugs being preferred. It has been noted that the evidence of value is limited.

References.

1. Fogan L. Treatment of cluster headache: a double-blind comparison of oxygen v air inhalation. *Arch Neurol* 1985; **42:** 362–3.
2. Rozen TD. High oxygen flow rates for cluster headache. *Neurology* 2004; **63:** 593.
3. Bennett MH, *et al.* Normobaric and hyperbaric oxygen therapy for migraine and cluster headache. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2008 (accessed 21/08/08).

Hyperbaric oxygen therapy. The use of hyperbaric oxygen therapy, which involves the intermittent inhalation of 100% oxygen under a pressure of greater than 1 atmosphere in a specialised chamber, has been reviewed.[1-3] In the 1960s hyperbaric therapy was used for disorders such as *myocardial infarction*, *stroke*, *senility*, and *cancer* but clinical studies and experience have shown little benefit and enthusiasm has since waned. Hyperbaric oxygen therapy has also been tried in *multiple sclerosis* but there is little evidence of benefit. There are, however, other disorders for which the evidence supporting the efficacy of hyperbaric oxygen is much stronger.

Hyperbaric oxygen is a safe and effective primary therapy for *decompression sickness* and *air or gas embolism*. The effect is achieved through the mechanical reduction in bubble size in the blood brought about by an increase in ambient pressure; the increased oxygenation of blood due to the additional pressure used for these conditions (often 6 rather than 2 or 3 atmospheres) is also beneficial.

The role of hyperbaric oxygen therapy in *carbon monoxide poisoning* is unclear but it should be considered in selected patients (see p.1688). Its mechanism of action is not fully understood; it increases the rate at which carboxyhaemoglobin concentrations decline, increases intracellular delivery of oxygen, and may also reduce lipid peroxidation and thus spare neuronal cell membranes.

Hyperbaric oxygen is used as adjunctive therapy in *clostridial infections (gas gangrene)* (p.171). Early treatment appears to reduce systemic toxic reactions (probably by inhibiting the production of alpha toxin by the anaerobic bacteria, *Clostridium*) thus enabling patients to tolerate surgery more readily; additionally there is a clearer demarcation of viable and nonviable tissue. *Necrotising fasciitis* (p.180) is another infection in which hyperbaric oxygen therapy may be useful.

There is some evidence that hyperbaric oxygen may be useful in other types of *wounds*. In an *acute crush injury* therapy may reduce oedema via vasoconstriction and reverse ischaemia by increased oxygen delivery. In *problem wounds*, including venous ulcers, therapy may increase the tissue oxygen tension and stimulate angioneogenesis but it is emphasised that it is adjunctive therapy and not a replacement for meticulous local care. Hyperbaric oxygen therapy might also reduce the risk of major amputation in patients with chronic *diabetic foot ulcer*.[4,5] Improved healing of leg ulcers has been reported[6] with use of hyperbaric oxygen therapy in patients with livedoid vasculopathy. Other wounds in which therapy may be beneficial include thermal burns and compromised skin grafts and flaps. The management of burns and wounds is described on p.1578 and p.1585, respectively.

Radiation therapy can damage normal adjacent tissue resulting in tissue hypoxia and eventual cell death. Hyperbaric oxygen therapy appears to aid in salvaging such tissue by stimulating angioneogenesis in marginally viable tissue and has been demonstrated to be beneficial in osteoradionecrosis, radiation-induced haemorrhagic cystitis (p.2178), and other radiation-damaged soft tissue.[7]

There has been interest in the use of hyperbaric oxygen in children with *cerebral palsy*, although a randomised study[8] found that it was no better than pressurised air. However, improved neurological outcomes have been reported with hyperbaric oxygen therapy in neonates with hypoxic-ischaemic encephalopathy.[9]

1. Grim PS, *et al.* Hyperbaric oxygen therapy. *JAMA* 1990; **263:** 2216–20.
2. Tibbles PM, Edelsberg JS. Hyperbaric-oxygen therapy. *N Engl J Med* 1996; **334:** 1642–8.
3. Leach RM, *et al.* ABC of oxygen: hyperbaric oxygen therapy. *BMJ* 1998; **317:** 1140–3.
4. Wang C, *et al.* Hyperbaric oxygen for treating wounds: a systematic review of the literature. *Arch Surg* 2003; **138:** 272–9.
5. Roeckl-Wiedmann I, *et al.* Systematic review of hyperbaric oxygen in the management of chronic wounds. *Br J Surg* 2005; **92:** 24–32.
6. Juan W-H, *et al.* Livedoid vasculopathy: long-term follow-up results following hyperbaric oxygen therapy. *Br J Dermatol* 2006; **154:** 251–5.
7. Pasquier D, *et al.* Hyperbaric oxygen therapy in the treatment of radio-induced lesions in normal tissues: a literature review. *Radiother Oncol* 2004; **72:** 1–13.
8. Collet J-P, *et al.* Hyperbaric oxygen for children with cerebral palsy: a randomised multicentre trial. *Lancet* 2001; **357:** 582–6.
9. Liu Z, *et al.* Clinical effectiveness of treatment with hyperbaric oxygen for neonatal hypoxic-ischaemic encephalopathy: systematic review of Chinese literature. *BMJ* 2006; **333:** 374–6.

Respiratory failure. Respiratory failure occurs when the arterial plasma partial pressure of oxygen (P_aO_2) and of carbon dioxide (P_aCO_2) cannot be maintained within normal physiological limits.[1] Respiratory failure can be classified into 2 types, both of which are characterised by a low P_aO_2 (hypoxaemia). However, in type I the P_aCO_2 is normal or low whereas in type II, referred to as ventilatory failure, P_aCO_2 is raised (hypercapnia). Some conditions, for example asthma, can produce either type of respiratory failure.

Management of respiratory failure mainly involves giving oxygen to reverse hypoxaemia, and specific therapy for any underlying condition. Respiratory stimulants may be considered in some situations.

In type I respiratory failure oxygen is used in high concentrations. Nasal prongs and certain face masks can provide concentrations of up to 60% but if concentrations higher than this are needed then tight-fitting anaesthetic-type masks or methods of delivery such as endotracheal intubation have to be used.

In type II respiratory failure both high and low concentrations are used according to need.

Patients with *acute severe asthma* (p.1108) should usually be given oxygen at high concentrations of 40 to 60%. In patients with exacerbations of chronic respiratory disorders such as *chronic obstructive pulmonary disease* (COPD, p.1112) the aim is to improve hypoxaemia without increasing hypercapnia and respiratory acidosis.[2] The initial concentration of oxygen to give in COPD exacerbations is controversial. During the transfer to hospital, UK guidelines[3] recommend starting at 40% and titrating upwards if the oxygen saturation falls below 90% and downwards if the patient becomes drowsy or if the saturation exceeds 93 to 94%. Special care is needed for patients with known type II respiratory failure, especially if they require a long ambulance journey or receive oxygen at home for a prolonged period before an ambulance arrives, as uncontrolled oxygen therapy can result in suppression of respiratory drive, carbon dioxide narcosis, and respiratory arrest. In hospital, arterial blood gases should be used to guide treatment. Other guidelines[4] consider that lower initial oxygen concentrations of 24 to 28% are usually sufficient. Patients with exacerbations of chronic ventilatory failure already have an increased central drive to the respiratory muscles and therefore respiratory stimulants such as doxapram have a limited role but may be indicated for short-term use if hypercapnia worsens as a result of oxygen. For most patients with chronic obstructive pulmonary disease, non-invasive ventilation is the initial treatment of choice for hypercapnic ventilatory failure during exacerbations.[3] Respiratory stimulants may be considered in the management of *postanaesthetic hypoventilation*. Although naloxone can reverse respiratory depression caused by opioid analgesics careful dosage adjustment is required as it can also abolish analgesia. Specific antagonists such as naloxone and flumazenil are also used to treat hypoventilation associated with opioid and benzodiazepine overdosage, respectively. If oxygen therapy fails to raise P_aO_2 in respiratory failure and there is worsening hypercapnia and respiratory acidosis the use of artificial ventilation should be considered.

Severe respiratory failure in *neonates* may result from various disorders. Use of surfactant or inhaled nitric oxide may be of benefit in some cases but extracorporeal membrane oxygenation (ECMO), where blood is removed from the neonate, oxygenated, and re-injected in a continuous circuit that also removes carbon dioxide, may be required.[5] ECMO has also been used in older children and in adults,[6] but is less well established.

1. Gribbin HR. Management of respiratory failure. *Br J Hosp Med* 1993; **49:** 461–77.
2. Plant PK, Elliott MW. Chronic obstructive pulmonary disease 9: management of ventilatory failure in COPD. *Thorax* 2003; **58:** 537–42.
3. National Collaborating Centre for Chronic Conditions. Chronic obstructive pulmonary disease: national clinical guideline on management of chronic obstructive pulmonary disease in adults in primary and secondary care. *Thorax* 2004; **59** (suppl 1): 1–232. Also available at: http://thorax.bmj.com/content/vol59/suppl_1/ (accessed 18/12/07)
4. McKenzie DK, *et al.* The COPDX plan: Australian and New Zealand guidelines for the management of chronic obstructive pulmonary disease 2007. Available at: http://www.copdx.org.au/guidelines/documents/COPDX_Sep28_2007.pdf (accessed 18/12/07)
5. Barrington KJ, Finer NN. Care of near term infants with respiratory failure. *BMJ* 1997; **315:** 1215–18.
6. Peek GJ, *et al.* Extracorporeal membrane oxygenation: potential for adults and children? *Hosp Med* 1998; **59:** 304–8.

Wounds. Hyperbaric oxygen therapy may have a role in the management of infected and problem wounds (see above). Supplemental normobaric oxygen has been tried in the prevention of postoperative wound infections, but results of controlled studies[1-3] have been contradictory and its role is not established.

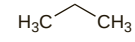
1. Greif R, *et al.* Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med* 2000; **342:** 161–7.
2. Pryor KO, *et al.* Surgical site infection and the routine use of perioperative hyperoxia in a general surgical population: a randomized controlled trial. *JAMA* 2004; **291:** 79–87.
3. Belda FJ, *et al.* Supplemental perioperative oxygen and the risk of surgical wound infection: a randomized controlled trial. *JAMA* 2005; **294:** 2035–42.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Fr.:*** Kalinox; Medimix; ***S.Afr.:*** Entonox; ***UK:*** Entonox; Equanox.

Propane

Dimethylmethane; E944; Propano; Propyl Hydride.
C_3H_8 = 44.10.
CAS — 74-98-6.



Pharmacopoeias. In *USNF*.
USNF 26 (Propane). A colourless gas. It is highly flammable and explosive. Store in airtight cylinders at a temperature not exceeding 40°.

Profile

Propane is used as a refrigerant and as an aerosol propellant (p.1688). It is also widely used as a fuel.

◊ Reports of toxicity associated with the abuse or misuse of propane.[1-6]

1. James NK, Moss ALH. Cold injury from liquid propane. *BMJ* 1989; **299:** 950–1.
2. Siegel E, Wason S. Sudden death caused by inhalation of butane and propane. *N Engl J Med* 1990; **323:** 1638.
3. Tsoukali H, *et al.* Death during deliberate propane inhalation. *Forensic Sci Int* 1998; **93:** 1–4.
4. McLennan JJ, *et al.* Propane-associated autoerotic fatalities. *Am J Forensic Med Pathol* 1998; **19:** 381–6.
5. Grosse K, Grosse J. Propanmissbrauch: extreme Dosissteigerung durch Toleranzentwicklung. *Nervenarzt* 2000; **71:** 50–3.
6. Jackowski C, *et al.* Autoerotic accident by inhalation of propane-butane gas mixture. *Am J Forensic Med Pathol* 2005; **26:** 355–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Austral.:*** Histofreezer†; ***Fr.:*** Cliptol Sport†; Freeze; Histofreezer†; ***Ger.:*** Olbas; ***Irl.:*** Wartner; ***Israel:*** Wartner; ***NZ:*** Wartner; ***UK:*** Histofreezer; Wartner; ***USA:*** Compound W Freeze Off.