results have been reported in patients with carbon monoxide poisoning.[2,3] Its use has therefore been widely recommended, particularly in patients with severe poisoning. However, the availability of hyperbaric oxygen is limited, and it remains unclear which patients should receive therapy; a systematic review considered its value unproven.[1] A controlled trial[4] comparing hyperbaric oxygen with normobaric oxygen (at higher levels than commonly used) in patients with severe poisoning found no benefit from hyperbaric oxygen, but a later study[5] using a different regimen did find a reduction in cognitive sequelae. Hyperbaric oxygen has been successfully used in pregnant patients with carbon monoxide poisoning[6] and its use should possibly be considered earlier in pregnant patients due to the risks to the fetus from hypoxia.

1. Juurlink DN, *et al.* Hyperbaric oxygen for carbon monoxide poisoning. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2005 (accessed 20/06/08).
2. 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.
3. Hawkins M, *et al.* Severe carbon monoxide poisoning: outcome after hyperbaric oxygen therapy. *Br J Anaesth* 2000; **84:** 584–6.
4. Scheinkestel CD, *et al.* Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *Med J Aust* 1999; **170:** 203–10.
5. Weaver LK, *et al.* Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med* 2002; **347:** 1057–67.
6. Van Hoesen KB, *et al.* Should hyperbaric oxygen be used to treat the pregnant patient for acute carbon monoxide poisoning: a case report and literature review. *JAMA* 1989; **261:** 1039–43. Correction. *ibid.* 1990; **263:** 2750.

Uses

Carbon monoxide has been used in low concentrations as a tracer gas in measurements of lung function. Carbon monoxide labelled with carbon-11 may also be used to assess the blood volume.

Chlorofluorocarbons

CFCs; Clorofluorocarbonos.

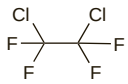
Cryofluorane *(rINN)*

CFC-114; Criofluorano; Cryofluoranum; Dichlorotetrafluoroethane; Propellant 114; Refrigerant 114; Tetrafluorodichloroethane. 1,2-Dichloro-1,1,2,2-tetrafluoroethane.

Криофлуоран

$C_2Cl_2F_4$ = 170.9.

CAS — 76-14-2.



Pharmacopoeias. In *USNF.*

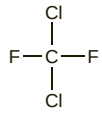
USNF 26 (Dichlorotetrafluoroethane). A clear, colourless gas having a faint ethereal odour. Store in airtight cylinders at a temperature not exceeding 40°.

Dichlorodifluoromethane

CFC-12; Diclorodifluorometano; Difluorodichloromethane; Propellant 12; Refrigerant 12.

CCl_2F_2 = 120.9.

CAS — 75-71-8.



Pharmacopoeias. In *USNF.*

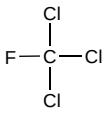
USNF 26 (Dichlorodifluoromethane). A clear, colourless gas having a faint ethereal odour. Store in airtight cylinders at a temperature not exceeding 40°.

Trichlorofluoromethane

CFC-11; Fluorotrichloromethane; Propellant 11; Refrigerant 11; Trichloromonofluoromethane; Triclorofluorometano.

CCl_3F = 137.4.

CAS — 75-69-4.



NOTE. Trichlorofluoromethane is a gas above 24°.

Pharmacopoeias. In *USNF.*

USNF 26 (Trichloromonofluoromethane). A clear, colourless gas having a faint ethereal odour. Store in airtight cylinders at a temperature not exceeding 40°.

Profile

Chlorofluorocarbons are used as refrigerants and as aerosol propellants (p.1688). They may also be used as a spray for topical anaesthesia, the intense cold produced by the rapid evaporation of the spray making the tissues insensitive.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Algispray.

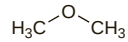
Multi-ingredient: ***Austral.:*** Derm-Freeze; ***USA:*** Aerofreeze; Fluori-Methane†; Fluro-Ethyl.

Dimethyl Ether

Dimethyl Oxide; Éter dimetílico; Methoxymethane; Oxybismethane.

C_2H_6O = 46.07.

CAS — 115-10-6.



Profile

Dimethyl ether is used as a refrigerant, aerosol propellant (p.1688), and topical anaesthetic.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austral.:*** Histofreezer†; ***Fr.:*** Freeze; Histofreezer†; ***Irl.:*** Wartner; ***Israel:*** Wartner; ***NZ:*** Wartner; ***UK:*** Histofreezer; PR Freeze Spray; Ralgex Freeze Spray; Wartner; ***USA:*** Compound W Freeze Off.

Helium

E939; Helio; Hélium.

He = 4.002602.

CAS — 7440-59-7.

ATC — V03AN03.

ATC Vet — QV03AN03.

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Helium). A colourless, inert gas. Store as a compressed gas or liquid at cryogenic temperatures, in appropriate containers.

USP 31 (Helium). A colourless, odourless, tasteless gas which is not combustible and does not support combustion. Very slightly soluble in water. Store in cylinders.

Profile

As helium is less dense than nitrogen, breathing a mixture of 80% helium and 20% oxygen requires less effort than breathing air. Thus mixtures containing various concentrations of oxygen ('Heliox') have been used in patients with respiratory disorders. Due to the low solubility of helium, mixtures of helium and oxygen are used by divers or others working under high pressure to prevent the development of decompression sickness (caisson disease); they are preferred to compressed air as they do not cause nitrogen narcosis. Helium has been used in pulmonary function testing.

Breathing helium increases vocal pitch and causes voice distortion. Cerebral artery gas embolism has been reported after inhalation of helium from a pressurised container.

◊ Reviews.

1. Rodrigo GJ, *et al.* Use of helium-oxygen mixtures in the treatment of acute asthma: a systematic review. *Chest* 2003; **123:** 891–6.
2. Colebourn CL, *et al.* Use of helium-oxygen mixture in adult patients presenting with exacerbations of asthma and chronic obstructive pulmonary disease: a systematic review. *Anaesthesia* 2007; **62:** 34–42.
3. Harris PD, Barnes R. The uses of helium and xenon in current clinical practice. *Anaesthesia* 2008; **63:** 284–93.

Hydrochlorofluorocarbons

HCFCs; Hidroclorofluorocarbonos.

Chlorodifluoroethane

Clorodifluoroetano; Propellant 142b; Refrigerant 142b. 1-Chloro-1,1-difluoroethane.

$C_2H_3ClF_2$ = 100.5.

CAS — 75-68-3.

Chlorodifluoromethane

Clorodifluorometano; Propellant 22; Refrigerant 22.

$CHClF_2$ = 86.47.

CAS — 75-45-6.

Profile

Hydrochlorofluorocarbons are used as refrigerants and as aerosol propellants (p.1688).

Hydrofluorocarbons

HFAs; HFCs; Hidrofluorocarbonos; Hydrofluroalkanes.

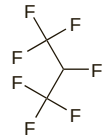
Apaflurane *(BAN, rINN)*

Apaflurano; Apafluranum; Heptafluoropropane; HFA-227; HFC-227. 1,1,1,2,3,3,3-Heptafluoropropane.

Апафлуран

C_3HF_7 = 170.0.

CAS — 431-89-0.

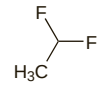


Difluoroethane

Difluoroetano; Ethylene Fluoride; HFC-152a; Propellant 152a; Refrigerant 152a. 1,1-Difluoroethane.

$C_2H_4F_2$ = 66.05.

CAS — 75-37-6.



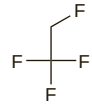
Norflurane *(BAN, USAN, rINN)*

Fluorocarbon 134a; GR-106642X; HFA-134a; HFC-134a; Norflurano; Norfluranum; Propellant 134a; Refrigerant 134a. 1,1,1,2-Tetrafluoroethane.

Норфлуран

$C_2H_2F_4$ = 102.0.

CAS — 811-97-2.



Profile

Hydrofluorocarbons are used as refrigerants and as aerosol propellants (p.1688). They are nonchlorinated and cause less ozone depletion than chlorinated fluorocarbons, which may lead to less detrimental effects on the environment. They are being used to replace chlorinated fluorocarbons as propellants in medicinal inhalers.

◊ References.

1. Denyer LH, *et al.* GR106642X, a non-chlorinated propellant for use in metered-dose inhalers: safety, tolerability and pharmacokinetics in healthy volunteers. *Br J Clin Pharmacol* 1994; **38:** 509P.
2. Taggart SCO, *et al.* GR106642X: a new, non-ozone depleting propellant for inhalers. *BMJ* 1995; **310:** 1639–40.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***USA:*** Gebauers Spray & Stretch.

Hydrogen Sulfide

Hydrogen Sulphide; Siarkowodór; Sulfuro de hidrógeno; Sulphuretted Hydrogen.

H_2S = 34.08.

CAS — 7783-06-4.

Description. Hydrogen sulfide is a colourless flammable gas with a characteristic odour.

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