Gases

This chapter includes monographs on gases with medical or pharmaceutical uses and applications (such as oxygen, carbon dioxide, helium, and nitrogen) as well as those where the medical interest lies primarily in management of their toxicity or adverse effects (such as carbon monoxide or hydrogen sulfide). Also included are some compressed and liquefied gases used as refrigerants and aerosol propellants. Nitric oxide gas is used in bronchopulmonary disorders and is discussed in Cardiovascular Drugs (p.1358). Other gases with medical uses can be found in Disinfectants and Preservatives (p.1622) and General Anaesthetics (p.1779).

Refrigerants and Aerosol Propellants

A number of compressed and liquefied gases are used as refrigerants and as aerosol propellants; these include nitrogen, nitrous oxide, carbon dioxide, propane, and the butanes. Chlorofluorocarbons (CFCs) were widely used but because of environmental hazards their general use has been severely restricted and they are being phased out in medicine and pharmacy. Hydrogenated chlorofluorocarbons (hydrochlorofluorocarbons) and nonchlorinated fluorocarbons (hydrofluorocarbons) are being developed as alternatives, although neither are devoid of environmental effects.

The evaporation of halogenated hydrocarbon propellants produces an intense cold that numbs the tissues, and they have been used as topical analgesics (see Rubefacients and Topical Analgesia, p.5).

Refrigerants and aerosol propellants have been subject to deliberate abuse. Inhalation of high concentrations of halogenated hydrocarbons for their euphoriant effect may result in CNS depression, cardiac arrhythmias, respiratory depression, and death. Propane and butane can act as simple asphyxiants. Heat can cause the decomposition of halogenated hydrocarbons into irritant and toxic gases such as hydrogen chloride and phosgene.

Toxicity. Reviews have covered the toxicity and adverse effects that may occur as a consequence of the deliberate abuse of aerosol propellants[1-4] as well as the hazards associated with occupational exposure.[5] Further references relevant to the toxicity of individual agents are given in the monographs.

1. Volatile substance abuse—an overview. *Hum Toxicol* 1989; **8:** 255–344.
2. Ashton CH. Solvent abuse. *BMJ* 1990; **300:** 1356–6.
3. Anderson HR. Increase in deaths from deliberate inhalation of fuel gases and pressurised aerosols. *BMJ* 1990; **301:** 41.
4. Kurtzman TL, *et al.* Inhalant abuse by adolescents. *J Adolesc Health* 2001; **28:** 170–80.
5. Matthews G. Toxic gases. *Postgrad Med J* 1989; **65:** 224–32.

Bromochlorodifluoromethane

Bromoclorodifluorometano.

$CBrClF_2$ = 165.4.

Profile

Bromochlorodifluoromethane has been used as a fire-extinguishing agent.

◊ Reports of toxicity after the misuse or abuse of fire extinguishers containing bromochlorodifluoromethane,[1-3] and in persons exposed in other ways.[4,5]

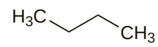
1. Steadman C, *et al.* Abuse of fire-extinguishing agent and sudden death in adolescents. *Med J Aust* 1984; **141:** 115–17.
2. Lerman Y, *et al.* Fatal accidental inhalation of bromochlorodifluoromethane (Halon 1211). *Hum Exp Toxicol* 1991; **10:** 125–8.
3. Gerhardt RT. Acute Halon (bromochlorodifluoromethane) toxicity by accidental and recreational inhalation. *Am J Emerg Med* 1996; **14:** 675–7.
4. Matrat M, *et al.* Reactive airways dysfunction syndrome caused by bromochlorodifluoromethane from fire extinguishers. *Occup Environ Med* 2004; **61:** 712–14.
5. Lo SH, *et al.* Grand rounds: outbreak of hematologic abnormalities in a community of people exposed to leakage of fire extinguisher gas. *Environ Health Perspect* 2006; **114:** 1713–17.

Butane

n-Butane; Butano; E943a.

C_4H_{10} = 58.12.

CAS — 106-97-8.



Pharmacopoeias. In *USNF.*

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

Profile

Butane is used as an aerosol propellant (above). It is widely used as a fuel.

Abuse. Reports of toxicity associated with the abuse of butane.[1-9]

1. Gunn J, *et al.* Butane sniffing causing ventricular fibrillation. *Lancet* 1989; **i:** 617.
2. Siegel E, Wason S. Sudden death caused by inhalation of butane and propane. *N Engl J Med* 1990; **323:** 1638.
3. Roberts MJD, *et al.* Asystole following butane gas inhalation. *Br J Hosp Med* 1990; **44:** 294.
4. Williams DR, Cole SJ. Ventricular fibrillation following butane gas inhalation. *Resuscitation* 1998; **37:** 43–5.
5. Rieder-Scharinger J, *et al.* Multiorganversagen nach Butangasinhalation: ein Fallbericht. *Wien Klin Wochenschr* 2000; **112:** 1049–52.
6. Wehner F, *et al.* Tödliche Inhalation von Butan-Propan-Gas. *Arch Kriminol* 2002; **209:** 164–8.
7. El-Menyar AA, *et al.* A teenager with angiographically normal epicardial coronary arteries and acute myocardial infarction after butane inhalation. *Eur J Emerg Med* 2005; **12:** 137–41.
8. Harris D, Mirza Z. Butane encephalopathy. *Emerg Med J* 2005; **22:** 676–7.
9. Doogue M, Barclay M. Death due to butane abuse—the clinical pharmacology of inhalants. *N Z Med J* 2005; **118:** U1732.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Arg.:*** Batistol†; Frionex; ***Fr.:*** Cliptol Sport†.

Carbon Dioxide

Anglies dioksidas; Carbone, dioxyde de; Carbonei dioxidum; Carbonei Dioxydum; Carbonic Acid Gas; Carbonic Anhydride; Dióxido de carbono; E290; Hiilidioksidi; Koldioxid; Oxid uhličitý; Szén-dioxid; Węgla dwutlenek.

CO_2 = 44.01.

CAS — 124-38-9.

ATC — V03AN02.

ATC Vet — QV03AN02.

NOTE. Carbon dioxide is about 1⁄ times as heavy as air.

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

Ph. Eur. 6.2 (Carbon Dioxide). A colourless gas. Soluble 1 in about 1 of water by volume at 20° and at a pressure of 101 kpA. Store liquefied under pressure in suitable containers.

The BP 2008 directs that carbon dioxide should be kept in approved metal cylinders which are painted grey and carry a label stating 'Carbon Dioxide'. In addition, 'Carbon Dioxide' or the symbol 'CO_2' should be stencilled in paint on the shoulder of the cylinder.

USP 31 (Carbon Dioxide). A colourless, odourless gas. Its solutions are acid to litmus. One volume dissolves in about 1 volume of water. Store in cylinders.

Adverse Effects

Above a concentration of 6%, carbon dioxide causes headache, dizziness, confusion, palpitations, hypertension, dyspnoea, increased depth and rate of respiration, and CNS depression. Concentrations of about 20% and higher produce convulsions and loss of consciousness; inhalation of 50% carbon dioxide is reported to produce central effects similar to anaesthetics. The inhalation of high concentrations may produce respiratory acidosis.

Abrupt withdrawal of carbon dioxide after prolonged inhalation commonly produces pallor, hypotension, dizziness, severe headache, and nausea or vomiting.

Skin contact with solid carbon dioxide may cause frostbite.

Uses and Administration

Carbon dioxide has been added to the oxygen in certain types of pump oxygenators to maintain the carbon dioxide content of the blood.

Although carbon dioxide stimulates respiration, it is seldom used for this purpose. Treatment of carbon monoxide poisoning with carbon dioxide/oxygen mixtures is discouraged due to the risk of respiratory acidosis.

Inhalation of carbon dioxide has been tried for relief of intractable hiccup (p.976). Carbonated vehicles are useful for masking the unpleasant taste of some medicinal preparations.

Solid carbon dioxide, or 'dry ice' has a temperature of –80° and has been used to treat warts (p.1584) and naevi by cryotherapy.

Carbon dioxide may be used as the insufflating gas for laparoscopy and as a contrast agent in radiography (p.1474).

Carbon Monoxide *(USAN)*

Anglies monoksidas; Carbone, monoxyde de; Carbonei monoxidum; Hiilimonoksidi; Karbon Monoksit; Kolmonoxid; Monóxido de carbono; Węgla tlenek.

CO = 28.01.

CAS — 630-08-0.

Description. Carbon monoxide is a colourless, odourless, tasteless, highly flammable gas.

Adverse Effects

Carbon monoxide is produced by incomplete combustion of organic materials and is highly toxic when inhaled; infants, small children, and elderly people are particularly susceptible. Although the number of cases of poisoning in countries such as the UK has fallen as the availability of coal gas has declined and as changes have been made to motor vehicles to improve their exhaust fumes, carbon monoxide is still a major cause of poisoning. Common sources of carbon monoxide include poorly maintained and ventilated heating systems and improperly burnt fuel in domestic fires.

When inhaled, carbon monoxide combines with haemoglobin in the blood to form carboxyhaemoglobin, which is unable to transport oxygen; the symptoms of carbon monoxide poisoning are largely due to anoxia. The skin and tissues may turn a classic cherry red in patients poisoned with carbon monoxide although this is seen most often after death.

The symptoms of carbon monoxide poisoning are varied and depend on the degree and duration of exposure. Unconsciousness may occur suddenly but is commonly preceded by headache, dizziness, weakness, nausea, and vomiting, which may be misdiagnosed as a viral illness or food poisoning. Other symptoms may include skin lesions, excessive sweating, pyrexia, increased respiration, mental dullness and confusion, visual disturbances, convulsions, hypotension, tachycardia or other cardiac arrhythmias, myocardial ischaemia, and possibly myocardial infarction. Death may result from respiratory failure, pulmonary oedema, cardiovascular failure, or cerebral damage. The lethal concentration of carboxyhaemoglobin in the blood is about 50% or more. Concentrations over 1000 ppm of carbon monoxide in inspired air may be fatal in 1 hour. Neurological and psychiatric sequelae may develop some weeks later in the survivors of severe poisoning and therefore a prolonged follow-up of such patients is advised; symptoms include memory impairment, apathy, mutism, irritability, personality change, gait disturbance, and urinary and faecal incontinence. Chronic carbon monoxide exposure may present as a non-specific illness with headache, nausea, and flu-like symptoms.

◊ General references.

1. Meredith T, Vale A. Carbon monoxide poisoning. *BMJ* 1988; **296:** 77–9.
2. Crawford R, *et al.* Carbon monoxide poisoning in the home: recognition and treatment. *BMJ* 1990; **301:** 977–9.
3. Ernst A, Zibrak JD. Carbon monoxide poisoning. *N Engl J Med* 1998; **339:** 1603–8.
4. WHO. Carbon Monoxide. *Environmental Health Criteria 213.* Geneva: WHO, 1999. Available at: http://www.inchem.org/documents/ehc/ehc/ehc213.htm (accessed 05/07/04)
5. Satran D, *et al.* Cardiovascular manifestations of moderate to severe carbon monoxide poisoning. *J Am Coll Cardiol* 2005; **45:** 1513–16.
6. Prockop LD, Chichkova RI. Carbon monoxide intoxication: an updated review. *J Neurol Sci* 2007; **262:** 122–30.

Treatment of Adverse Effects

The patient should be removed from the contaminated atmosphere and an effective airway established. Oxygen (100%) should be given until the blood carboxyhaemoglobin concentration has fallen below dangerous levels (usually 5%). Management is then usually symptomatic and supportive with attention being given to the possible need to treat or correct any cardiovascular disorders, metabolic acidosis, or cerebral oedema. Hyperbaric oxygen therapy may be considered in pregnant patients or in severe poisoning (if the patient is, or has been, unconscious; if the carboxyhaemoglobin concentration exceeds 20%; or if there are neurological symptoms or cardiac complications) but is of unproven benefit (see below) and its use is controversial.

◊ References.

1. Anonymous. Treatment of carbon monoxide poisoning. *Drug Ther Bull* 1988; **26:** 77–9.
2. Ely EW, *et al.* Warehouse workers' headache: emergency evaluation and management of 30 patients with carbon monoxide poisoning. *Am J Med* 1995; **98:** 145–55.

Hyperbaric oxygen therapy. The use of hyperbaric oxygen therapy in the management of carbon monoxide poisoning is controversial.[1] It is of theoretical benefit since it increases the rate at which carboxyhaemoglobin dissociates, and beneficial 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.

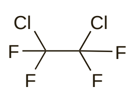
Cryofluorane *(rINN)*

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.*

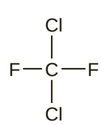
USNF 26 (Dichlorotetrafluoroethane). A clear, colourless gas having a faint ethereal odour. Store in airtight cylinders at a temperature not exceeding 40°.

Dichlorodifluoromethane

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

CCl_2F_2 = 120.9.

CAS — 75-71-8.



Pharmacopoeias. In *USNF.*

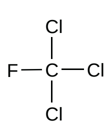
USNF 26 (Dichlorodifluoromethane). A clear, colourless gas having a faint ethereal odour. Store in airtight cylinders at a temperature not exceeding 40°.

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.

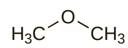
Multi-ingredient: *Austral.:* Derm-Freeze; ***USA:*** Aerofreeze; Fluori-Methane†; Fluro-Ethyl.

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

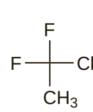
HCFCs; Hidroclorofluorocarbonos.

Chlorodifluoroethane

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

$C_2H_3ClF_2$ = 100.5.

CAS — 75-68-3.

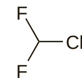


Chlorodifluoromethane

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.

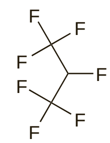
Apaflurane *(BAN, rINN)*

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.

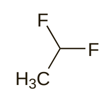


Difluoroethane

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

$C_2H_4F_2$ = 66.05.

CAS — 75-37-6.



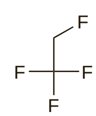
Norflurane *(BAN, USAN, rINN)*

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.