Haemodialysis may be indicated to increase the removal of methyl alcohol and its toxic metabolites. Peritoneal dialysis has been used but is less efficient. Haemodialysis may be considered if the blood-methyl alcohol concentration is greater than 500 micrograms/mL, if there is severe metabolic acidosis unresponsive to sodium bicarbonate, or there is visual disturbance, CNS toxicity, renal failure, or severe electrolyte disturbance. If haemodialysis is used, a constant blood-ethanol concentration may be ensured either by increasing the ethanol infusion rate or by addition of ethanol to the dialysate fluid.

Treatment should not be stopped prematurely since oxidation and excretion of methyl alcohol may continue for several days; patients should, therefore, be closely observed and monitored. Suitable supportive treatment should be carried out as required.

Folinic acid and folic acid have been given in the treatment of methyl alcohol toxicity because they may enhance the metabolism of formic acid.

◊ References.

1. Barceloux DG, *et al.* American Academy of Clinical Toxicology Ad Hoc Committee on the Treatment Guidelines for Methanol Poisoning. American Academy of Clinical Toxicology practice guidelines on the treatment of methanol poisoning. *J Toxicol Clin Toxicol* 2002; **40:** 415–46.

Pharmacokinetics

Methyl alcohol is readily absorbed from the gastrointestinal tract and distributed throughout the body fluids. It may also be absorbed after inhalation or through large areas of skin. Oxidation by alcohol dehydrogenase with formation of formaldehyde and formic acid takes place mainly in the liver and also in the kidneys. These metabolites are thought to be largely responsible for the characteristic symptoms of methyl alcohol poisoning. Metabolism is much slower than for ethanol, which competitively inhibits the metabolism of methyl alcohol. Oxidation and excretion may continue for several days after ingestion. Elimination of unchanged methyl alcohol via the lungs and in the urine is a minor route of excretion.

Uses

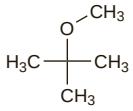
Methyl alcohol is used as a pharmaceutical and industrial solvent. It is also used as 'wood naphtha' to denature ethanol in the preparation of industrial methylated spirits. Methyl alcohol is also used as an extraction solvent in food processing.

Methyl *tert*-Butyl Ether

Éter metilterbutílico; Methyl Terbutyl Ether; Methyl Tertiary Butyl Ether; MTBE. 2-Methoxy-2-methylpropane.

Метил-трет-бутиловый Эфир

$C_5H_{12}O$ = 88.15.
CAS — 1634-04-4.



Description. Methyl *tert*-butyl ether is a volatile, flammable liquid. Wt per mL about 0.74 g. B.p. about 55°. Store in airtight containers.

Stability. Explosive peroxides may be generated by the atmospheric oxidation of methyl tert-butyl ether, but the risk is lower than with solvent ether.

Adverse Effects

Methyl *tert*-butyl ether is irritant and may cause CNS depression. Adverse effects that have been reported after use as a gallstone solvent are described under Uses and Administration, below.

Uses and Administration

Methyl *tert*-butyl ether is a solvent that has been used for the rapid dissolution of cholesterol gallstones.

Gallstones. An alternative to bile acid therapy in patients with gallstones (p.2409) who are not considered suitable for surgery is direct instillation of a solvent into the gallbladder.

Methyl *tert*-butyl ether has been used to dissolve cholesterol gallstones; stones rich in calcium or pigments are not dissolved.[1] Unfortunately incomplete dissolution and residual debris can lead to recurrence of stone formation.[2] The solvent is usually instilled via a percutaneous transhepatic catheter,[1,3] although other routes have been used.[4] Gallbladder stones were treated in 75 patients with continuous infusion and aspiration of methyl *tert*-butyl ether 4 to 6 times/minute for an average of 5 hours daily for 1 to 3 days.[1] At least 95% of the stone mass was dissolved in 72 patients. Gallbladder stones recurred in 4 patients between 6 and 16 months after the procedure; 7 of 51 patients with residual stone fragments had an episode of biliary colic during 6 to 42 months of follow-up. Nausea, sometimes with emesis, occurred in about one-third of patients. Overflow of solvent from the gallbladder can result in absorption from the gastrointestinal tract; methyl *tert*-butyl ether is detected on the breath and sedation can occur. One patient in whom overflow occurred developed ulcerative duodenitis and intravascular haemolysis. Coma and acute renal failure have also complicated treatment and have been attributed to leakage alongside the catheter rather than overflow of solvent.[5] Other workers[6,7] have obtained similar results for the dissolution of gallstones. One group[6] found that nausea and vomiting could be reduced if the treatment time was kept short and the perfusion volume was kept as low as possible; they also managed to prevent bile leakage and haemorrhage using a tissue adhesive or subcutaneous ceruletide to contract the gallbladder. Dissolution of gallbladder stones with methyl *tert*-butyl ether is likely to remain confined to specialist centres for use in patients unsuitable for surgical treatment.[1,8] A combination of litholytic modalities such as dissolution with solvents or bile acids, or lithotripsy may overcome some of the disadvantages of individual treatments.[9]

Methyl *tert*-butyl ether has been instilled via a nasobiliary catheter to dissolve stones in the common bile duct. Although effective in some cases,[10] further study has indicated disappointing overall results.[1,11]

Various combinations of drugs have been investigated to dissolve pigment-rich or mixed stones. For common bile-duct stones these include a cocktail of dimethyl sulfoxide 60%, methyl *tert*-butyl ether 20%, and sodium bicarbonate 20%, and a regimen of alternating infusions of pentyl ether and edetic acid-urea 10%.[12] A similar regimen of methyl hexyl ether and edetic acid-urea has been used successfully in 2 patients with calcified gallbladder stones.[13]

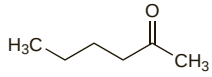
1. Bouchier IAD. Gall stones. *BMJ* 1990; **300:** 592–7.
2. Maudgal DP, Northfield TC. A practical guide to the nonsurgical treatment of gallstones. *Drugs* 1991; **41:** 185–92.
3. Thistle JL, *et al.* Dissolution of cholesterol gallbladder stones by methyl *tert*-butyl ether administered by percutaneous transhepatic catheter. *N Engl J Med* 1989; **320:** 633–9.
4. Foerster E-Ch, *et al.* Direct dissolution of gallbladder stones. *Lancet* 1989; **i:** 954.
5. Ponchon T, *et al.* Renal failure during dissolution of gallstones by methyl-*tert*-butyl ether. *Lancet* 1988; **ii:** 276–7.
6. Hellstern A, *et al.* Gall stone dissolution with methyl tert-butyl ether: how to avoid complications. *Gut* 1990; **31:** 922–5.
7. McNulty J, *et al.* Dissolution of cholesterol gall stones using methyltertbutyl ether: a safe effective treatment. *Gut* 1991; **32:** 1550–3.
8. Hetzer FH, *et al.* Kontaktlitholyse von Gallensteinen mit Methyltertbutyläther bei Risikopatienten—eine Fallbeschreibung. *Swiss Surg* 2001; **7:** 39–42.
9. Salen G, Tint GS. Nonsurgical treatment of gallstones. *N Engl J Med* 1989; **320:** 665–6.
10. Murray WR, *et al.* Choledocholithiasis—in vivo stone dissolution using methyl tertiary butyl ether (MTBE). *Gut* 1988; **29:** 143–5.
11. Neoptolemos JP, *et al.* How good is methyl tert-butyl (MTBE) for common bile duct (CBD) stone dissolution? *Gut* 1989; **30:** A736–7.
12. Anonymous. Gallstones, bile acids, and the liver. *Lancet* 1989; **ii:** 249–51.
13. Swobodnik W, *et al.* Dissolution of calcified gallbladder stones by treatment with methyl-hexyl ether and urea-EDTA. *Lancet* 1988; **ii:** 216.

Methyl Butyl Ketone

2-Hexanone; Methyl *n*-Butyl Ketone; Metilbutilcetona; Propylacetone. Hexan-2-one.

Метилбутилкетон

$C_6H_{12}O$ = 100.2.
CAS — 591-78-6.



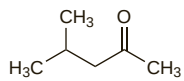
Description. Methyl butyl ketone is a colourless, volatile liquid. Wt per mL about 0.82 g. B.p. about 127°. Store in airtight containers.

Methyl Isobutyl Ketone

Hexone; Isobutilmetilcetona; Isopropylacetone; Metilisobutilcetona; MIBK. 4-Methylpentan-2-one.

Метилизобутилкетон

$C_6H_{12}O$ = 100.2.
CAS — 108-10-1.



Pharmacopoeias. In *USNF.*

USNF 26 (Methyl Isobutyl Ketone). A transparent, colourless, mobile, volatile liquid having a faint ketonic and camphoraceous odour. Sp. gr. not more than 0.799. Distilling range 114° to 117°. Slightly soluble in water; miscible with alcohol, with ether, and with benzene. Store in airtight containers.

Adverse Effects and Precautions

Methyl butyl ketone and methyl isobutyl ketone may depress the CNS in high concentrations. Their vapours are irritating to mucous membranes. Methyl isobutyl ketone may be implicated in volatile substance abuse (p.2019).

◊ References.

1. WHO. Methyl isobutyl ketone. *Environmental Health Criteria 117*. Geneva: WHO, 1990. Available at: http://www.inchem.org/documents/ehc/ehc/ehc117.htm (accessed 30/06/04)
2. WHO. Methyl isobutyl ketone health and safety guide. *IPCS Health and Safety Guide 58*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/hsg/hsg/hsg058.htm (accessed 30/06/04)

Effects on the nervous system. Peripheral neuropathy[1] has occurred after occupational exposure to methyl butyl ketone, particularly an outbreak of neuropathy in a printing plant after the replacement of methyl isobutyl ketone by methyl butyl ketone in a solvent mixture with methyl ethyl ketone. Methyl ethyl ketone may have potentiated the neurotoxicity induced by methyl butyl ketone.

For further discussion of neurotoxicity after occupational exposure to solvents including methyl butyl ketone, see under Toluene, p.2026.

1. Lolin Y. Chronic neurological toxicity associated with exposure to volatile substances. *Hum Toxicol* 1989; **8:** 293–300.

Handling. Suitable precautions should be taken to avoid skin contact with methyl butyl ketone or methyl isobutyl ketone as they can penetrate skin and produce systemic toxicity.

Uses

Methyl isobutyl ketone is used as an industrial and pharmaceutical solvent and also as an alcohol denaturant. Methyl butyl ketone is used as an industrial solvent.

Methyl Chloride

Cloruro de metilo; Monochloromethane. Chloromethane.

Метилхлорид

CH_3Cl = 50.49.
CAS — 74-87-3.

Description. Methyl chloride is a colourless gas compressed to a colourless liquid with an ethereal odour. B.p. about –24°. Store in airtight containers.

Adverse Effects and Treatment

Symptoms of methyl chloride intoxication often appear after a latent period of several hours and are similar after acute or chronic exposure to the vapour. Symptoms include gastrointestinal disturbances such as nausea, vomiting, and abdominal pain, and signs of CNS depression including headache, weakness, drowsiness, confusion, visual disturbances, and incoordination progressing to convulsions, coma, and death from respiratory depression in severe cases. There have been a few reports of hepatic and renal damage.

Treatment consists of removal from exposure and supportive and symptomatic measures. Neurological effects may persist for many months.

◊ References to the toxicity of methyl chloride.

1. Repko JD, Lasley SM. Behavioral, neurological, and toxic effects of methyl chloride: a review of the literature. *CRC Crit Rev Toxicol* 1979; **6:** 283–302.

Uses

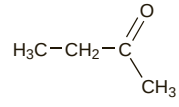
Methyl chloride is used as an industrial solvent. It has been used as an aerosol propellant and refrigerant and was formerly used as a local anaesthetic.

Methyl Ethyl Ketone

Ethyl Methyl Ketone; Etylometyloketon; MEK; Metiletilcetona; Metyloetyloketon. Butan-2-one.

Метилэтилкетон

C_4H_8O = 72.11.
CAS — 78-93-3.



Description. Methyl ethyl ketone is a colourless flammable liquid with an acetone-like odour. Wt per mL about 0.81 g. B.p. 79° to 81°. Soluble in water; miscible with alcohol and with ether. Store in airtight containers.

Adverse Effects

Methyl ethyl ketone is irritant. Inhalation may result in mild CNS effects including headache and dizziness; nausea and vomiting may also occur.

Methyl ethyl ketone may be implicated in volatile substance abuse (p.2019).

◊ References.

1. WHO. Methyl ethyl ketone. *Environmental Health Criteria 143*. Geneva: WHO, 1992. Available at: http://www.inchem.org/documents/ehc/ehc/ehc143.htm (accessed 30/06/04)

Effects on the nervous system. There are isolated reports of neurotoxicity produced by methyl ethyl ketone alone.[1] These include 1 of retrobulbar neuritis and 1 of peripheral neuropathy. It has been suggested, however, that methyl ethyl ketone potentiates the peripheral neuropathy induced by methyl butyl ketone and *n*-hexane.

For further discussion of neurotoxicity after occupational exposure to solvents including methyl ethyl ketone, see under Toluene, p.2026.

1. Lolin Y. Chronic neurological toxicity associated with exposure to volatile substances. *Hum Toxicol* 1989; **8:** 293–300.

Uses
Methyl ethyl ketone is used as an industrial solvent and as an extraction solvent in food processing.

Octyldodecanol

Octildodecanol; Octyldodécanol; Octyldodecanolum; Oktildodekanol; Oktildodekanolis; Oktyldodekanol; Oktylododekanol; Oktyylidodekanoli.

Октилдодеканол

$C_{20}H_{42}O$ = 298.5.

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

Ph. Eur. 6.2 (Octyldodecanol). A condensation product of saturated liquid fatty alcohols. It contains not less than 90% of (*RS*)-2-octyldodecan-1-ol, the remainder consisting mainly of related alcohols. A clear, colourless to yellowish, oily liquid. Relative density 0.830 to 0.850. Practically insoluble in water; miscible with alcohol. Protect from light.

USNF 26 (Octyldodecanol). It contains not less than 90% of 2-octyldodecanol, the remainder consisting chiefly of related alcohols. A clear, water-white, free-flowing liquid. Insoluble in water; soluble in alcohol and in ether. Store in airtight containers.

Profile
Octyldodecanol is used as a pharmaceutical solvent.

Pentane

Amyl Hydride; Pentan; *n*-Pentane.

Пентан

C_5H_{12} = 72.15.

CAS — 109-66-0.

Profile
Pentane is used as a solvent and as a fuel. It is highly volatile and has also been used topically for its cooling effects.

◊ References.

1. McKee R, *et al.* Toxicology of n-pentane (CAS no. 109-66-0). *J Appl Toxicol* 1998; **18:** 431–42.

Petroleum Spirit

Benzyna; Éter de petróleo; Light Petroleum; Petroleum Benzin; Petroleum Ether; Solvent Hexane.

Бензин; Петролейный Эфир

Description. Petroleum spirit is a purified distillate of petroleum, consisting of a mixture of the lower members of the paraffin series of hydrocarbons. It is a colourless, transparent, very volatile, highly flammable liquid with a characteristic odour. It is available in a variety of boiling ranges.

Pharmacopoeias. In *Ger.*, *Jpn.*, and *Pol*. Various boiling ranges are specified.

Swiss describes Benzinum Medicinale, consisting mainly of hexane and heptane.

◊ NOTE. The motor fuel termed 'petrol' in the UK and 'gasoline' in the USA is a mixture of volatile hydrocarbons of variable composition containing paraffins (alkanes), olefins (alkenes), cycloparaffins, and aromatic compounds.

Adverse Effects and Treatment
As for Kerosene, p.2024. Petroleum spirit and petrol, being more volatile and of lower viscosity than kerosene, are more likely to be inhaled and to cause aspiration pneumonitis. The toxicity of petrol varies with its composition; some adverse effects have been attributed to lead additives or to the content of *n*-hexane or benzene. Petrol may be implicated in volatile solvent abuse (p.2019).

◊ References to the toxicity of petroleum spirit.[1-3]

For discussion of neurotoxicity after occupational exposure to solvents including petrol, see under Toluene, p.2026.

1. WHO. Selected petroleum products. *Environmental Health Criteria 20*. Geneva: WHO, 1982. Available at: http://www.inchem.org/documents/ehc/ehc/ehc020.htm (accessed 30/06/04)
2. Daniels AM, Latcham RW. Petrol sniffing and schizophrenia in a Pacific island paradise. *Lancet* 1984; **i:** 389.
3. Eastwell HD. Elevated lead levels in petrol "sniffers". *Med J Aust* 1985; **143** (suppl): S63–4.

Uses
Petroleum spirit and other petroleum distillates are used as pharmaceutical solvents.

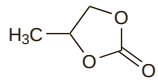
Propylene Carbonate

Carbonato de propileno. 4-Methyl-1,3-dioxolan-2-one.

Пропиленкарбонат

$C_4H_6O_3$ = 102.1.

CAS — 108-32-7.



Description. Propylene carbonate is a clear colourless mobile liquid. Freely soluble in water; miscible with alcohol and with chloroform; practically insoluble in petroleum spirit.

Pharmacopoeias. In *USNF*.

USNF 26 (Propylene Carbonate). Sp. gr. 1.203 to 1.210 at 20°. Store in airtight containers.

Profile
Propylene carbonate is used as a solvent in oral and topical pharmaceuticals and for cellulose-based polymers and plasticisers. It has been used as a nonvolatile, stabilising liquid carrier in hard gelatin capsules.

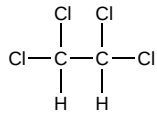
Tetrachloroethane

Acetylene Tetrachloride; Tetrachloroetan; Tetracloroetano. 1,1,2,2-Tetrachloroethane.

Тетрахлорэтан

$C_2H_2Cl_4$ = 167.8.

CAS — 79-34-5.



Description. Tetrachloroethane is a colourless liquid with a chloroform-like odour. B.p. about 146°. Wt per mL about 1.59 g. Store in airtight containers.

Adverse Effects and Treatment
As for Carbon Tetrachloride, p.2021. Tetrachloroethane is probably the most toxic of the chlorinated hydrocarbons. Poisoning can occur through percutaneous absorption as well as after ingestion or inhalation.

Handling. Suitable precautions should be taken to avoid skin contact with tetrachloroethane as it can penetrate skin and produce systemic toxicity.

Uses
Tetrachloroethane is used as an industrial solvent.

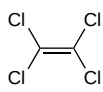
Tetrachloroethylene

Perchloroethylene; Tetrachloroethene; Tetrachloroethylenum; Tetracloroetileno.

Тетрахлорэтилен

C_2Cl_4 = 165.8.

CAS — 127-18-4.



Adverse Effects and Treatment
As for Carbon Tetrachloride, p.2021. Symptoms, especially after ingestion, are less severe with tetrachloroethylene than with carbon tetrachloride.

The vapour or liquid may be irritating to skin or mucous membranes.

Tetrachloroethylene may be implicated in volatile substance abuse (p.2019). Dependence may follow habitual inhalation of small quantities of tetrachloroethylene vapour.

◊ References to adverse effects of tetrachloroethylene.

1. Bagnell PC, Ellenberger HA. Obstructive jaundice due to a chlorinated hydrocarbon in breast milk. *Can Med Assoc J* 1977; **117:** 1047–8.
2. WHO. Tetrachloroethylene. *Environmental Health Criteria 31*. Geneva: WHO, 1984. Available at: http://www.inchem.org/documents/ehc/ehc/ehc31.htm (accessed 30/06/04)
3. WHO. Tetrachloroethylene health and safety guide. *IPCS Health and Safety Guide 10*. Geneva: WHO, 1987. Available at: http://www.inchem.org/documents/hsg/hsg/hsg010.htm (accessed 30/06/04)
4. Health and Safety Executive. Tetrachloroethylene (tetrachloroethene, perchloroethylene). *Toxicity Review 17*. London: HMSO, 1987.
5. Mutti A, *et al.* Nephropathies and exposure to perchloroethylene in dry-cleaners. *Lancet* 1992; **340:** 189–93.

Pharmacokinetics
Tetrachloroethylene is slightly absorbed from the gastrointestinal tract; absorption is increased in the presence of alcohol and fats or oils. It is absorbed after inhalation and after direct contact with the skin. It is excreted unchanged in expired air; initial elimination is rapid but a proportion may be retained and excreted slowly.

Metabolites of tetrachloroethylene, mainly trichloroacetic acid, have been found in the urine.

Uses and Administration
Tetrachloroethylene is a chlorinated hydrocarbon widely used as a solvent in industry. It was formerly given orally as an anthelmintic, but has been superseded by equally effective and less toxic drugs.

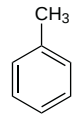
Toluene

Methylbenzene; Phenylmethane; Toluen; Tolueno; Toluol; Toluole.

Толуол

C_7H_8 = 92.14.

CAS — 108-88-3.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of toluene:
Tolley; Tolly; Tooly.

Description. Toluene is a colourless, volatile, flammable liquid with a characteristic odour. Wt per mL about 0.87 g. B.p. about 111°. Store in airtight containers.

Adverse Effects, Treatment, and Precautions
Toluene has similar acute toxicity to benzene (p.2020) but is a less serious industrial hazard. Adverse effects are treated similarly to benzene. It is a common constituent of adhesives and is frequently implicated in volatile substance abuse (p.2019). Commercial toluene may contain benzene, and this may perhaps influence the pattern of adverse effects. In addition to acute toxic effects, toluene abuse has been associated with damage to the nervous system, kidneys, liver, heart, and lungs (see below). Chronic poisoning caused by occupational exposure to toluene has resulted mainly in nervous system disorders.

◊ Reviews.

1. WHO. Recommended health-based limits in occupational exposure to selected organic solvents. *WHO Tech Rep Ser 664* 1981. Available at: http://libdoc.who.int/trs/WHO_TRS_664.pdf (accessed 03/09/08)
2. WHO. Toluene. *Environmental Health Criteria 52*. Geneva: WHO, 1985. Available at: http://www.inchem.org/documents/ehc/ehc/ehc52.htm (accessed 30/06/04)
3. Health and Safety Executive. Toluene. *Toxicity Review 20*. London: HMSO, 1989.

◊ The non-neurological toxicity after volatile substance abuse has been reviewed.[1] Chronic toluene abuse may result in damage to the *kidneys*; renal tubular acidosis and glomerulonephritis have been described, although evidence for the latter is only circumstantial. Renal tubular acidosis has been regarded as reversible; however, there are reports suggesting that damage to renal tubules is permanent.

The few reports linking chronic toluene abuse with *liver* damage cover hepatomegaly and hepatorenal failure. Effects on the *heart* are usually acute; sudden death has resulted from ventricular arrhythmias. Chronic myocarditis with fibrosis has been reported. Chronic toluene inhalation can cause damage to the *lungs.* Autopsies in a few patients have shown changes indicative of emphysema.

Nervous system toxicity has also been reviewed.[2,3] Cerebellar dysfunction has occurred after toluene abuse; an acute intoxication phase, which usually subsides within weeks of abstinence, is followed by a chronic phase which may be permanent. Diffuse CNS disease such as encephalopathy, dementia, and multifocal brain injury may also develop. An association between toluene abuse and peripheral neuropathy has not been confirmed; muscle weakness may be a result of electrolyte and fluid disturbances. Choreoathetosis, epilepsy, and optic atrophy with anosmia and deafness have been reported after toluene abuse. Some of these neurological effects, particularly cerebellar effects and diffuse