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.

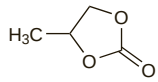
Propylene Carbonate

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.

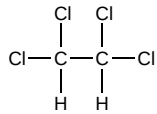
Tetrachloroethane

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.

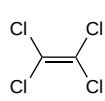
Tetrachloroethylene

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.

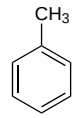
Toluene

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

CNS disease have also occurred after occupational exposure to toluene.

Some studies have noted an excess mortality from motor neurone diseases among leather workers,[4] although this has not been confirmed by others.[5] Occupational exposure to solvents has been postulated as the cause.[4] Of the many agents currently used in leather work, those with known or probable neurotoxic effects are *n*-hexane, methyl butyl ketone, toluene, and methyl ethyl ketone. Ethyl acetate is commonly used but has no recognised neurological adverse effects.[4] A Swedish study of workers in a range of occupations has found some support for an increased risk of amyotrophic lateral sclerosis after occupational exposure to solvents, probably toluene and petrol.[6] Another Swedish study found an association between multiple sclerosis and occupational exposure to solvents, especially white spirit and petrol.[6]

1. Marjot R, McLeod AA. Chronic non-neurological toxicity from volatile substance abuse. *Hum Toxicol* 1989; **8:** 301–6.
2. Lolin Y. Chronic neurological toxicity associated with exposure to volatile substances. *Hum Toxicol* 1989; **8:** 293–300.
3. Filley CM, *et al.* The effects of toluene on the central nervous system. *J Neuropathol Exp Neurol* 2004; **63:** 1–12.
4. Hawkes CH, *et al.* Motoneuron disease: a disorder secondary to solvent exposure? *Lancet* 1989; **i:** 73–6.
5. Martyn CN. Motoneuron disease and exposure to solvents. *Lancet* 1989; **i:** 394.
6. Gunnarsson L-G, Lindberg G. Amyotrophic lateral sclerosis in Sweden 1970-83 and solvent exposure. *Lancet* 1989; **i:** 958.

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

Pregnancy. Retrospective surveys of pregnancies in mothers with a history of solvent abuse suggested that toluene abuse during pregnancy can cause preterm delivery and perinatal death. It was suggested that toluene may be teratogenic as intra-uterine exposure was associated with prenatal and postnatal growth retardation, microcephaly, impairment of mental development, and facial dysmorphia.[1-3] It is uncertain if these results can be extrapolated to cover occupational exposure. Although some studies of occupational exposure to solvents during pregnancy have suggested an association,[4,5] exposure is usually to a number of solvents[5] and there is little consistent evidence to link exposure to any particular one with spontaneous abortion, retarded fetal development, still-birth, or congenital malformation.[6]

1. Wilkins-Haug L, Gabow PA. Toluene abuse during pregnancy: obstetric complications and perinatal outcomes. *Obstet Gynecol* 1991; **77:** 504–9.
2. Pearson MA, *et al.* Toluene embryopathy: delineation of the phenotype and comparison with fetal alcohol syndrome. *Pediatrics* 1994; **93:** 211–15.
3. Arnold GL, *et al.* Toluene embryopathy: clinical delineation and developmental follow-up. *Pediatrics* 1994; **93:** 216–20.
4. McDonald JC, *et al.* Chemical exposures at work in early pregnancy and congenital defect: a case-referent study. *Br J Ind Med* 1987; **44:** 527–33.
5. Khattak S, *et al.* Pregnancy outcome following gestational exposure to organic solvents: a prospective controlled study. *JAMA* 1999; **281:** 1106–9.
6. Scott A. *BMJ* 1992; **304:** 369.

Pharmacokinetics

Toluene is absorbed after inhalation and ingestion, and to some extent through the skin. It is rapidly metabolised mainly by oxidation to benzoic acid which is excreted in the urine largely as the glycine conjugate hippuric acid; *o*-, *m*-, and *p*-cresol are minor urinary metabolites. Some unchanged toluene is excreted through the lungs.

Uses

Toluene is widely used as an industrial solvent.

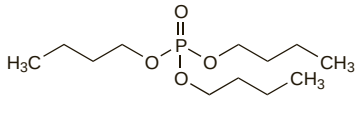
Tri-*n*-butyl Phosphate

Fosfato de tributilo; Tributyl Phosphate; Tributyl-fosfát; Tributylis Phosphas; Tri-*n*-butylis Phosphas; Tri(*n*-butyl)phosphate; Tri-n-butilo fosfatas; Tri-n-butyle, phosphate de; Tri-n-butylfosfat; Tri-n-butylis phosphas; Tri-n-butyylifosfaatti. Phosphoric acid tributyl ester.

Три-н-бутилфосфат

$C_{12}H_{27}O_4P$ = 266.3.

CAS — 126-73-8.



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

Ph. Eur. 6.2 (Tri-*n*-butyl Phosphate; Tributyl Phosphate BP 2008). A clear, colourless to pale yellow liquid. Slightly soluble in water; miscible with alcohol. Protect from light.

Profile

Tri-*n*-butyl phosphate is an organophosphate that is used as a solvent and plasticiser.

◊ References.

1. WHO. Tri-*n*-butyl phosphate. *Environmental Health Criteria 112*. Geneva: WHO, 1991. Available at: http://www.inchem.org/documents/ehc/ehc/ehc112.htm (accessed 29/06/04)

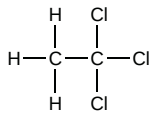
Trichloroethane

Methylchloroform; α-Trichloroethane; Tricloroetano. 1,1,1-Trichloroethane.

Трихлорэтан

$C_2H_3Cl_3$ = 133.4.

CAS — 71-55-6.



Description. Trichloroethane is a colourless, slightly hygroscopic liquid. Sp. gr. about 1.31. B.p. about 74°. Practically insoluble in water; miscible with alcohol, with chloroform, and with ether. Non-flammable. Store in airtight containers.

Adverse Effects and Treatment

Acute intoxication with trichloroethane may result in initial excitement followed by CNS depression with dizziness, drowsiness, headache, lightheadedness, and ataxia, progressing to coma and death from respiratory depression in severe cases. Death may also occur from ventricular arrhythmias. Fatalities have occurred after accidental exposure to high concentrations of trichloroethane in confined spaces. Trichloroethane is commonly used in dry cleaning, type correction fluids, and as a solvent for plaster removal and is frequently implicated in volatile substance abuse (p.2019).

Nausea, vomiting, and diarrhoea have been reported after ingestion. Trichloroethane is a mild irritant.

Treatment of adverse effects consists of removal from exposure and general supportive and symptomatic measures. Activated charcoal is unlikely to be of benefit after ingestion and gastric lavage is contra-indicated. Adrenaline and other sympathomimetics should be avoided because of the risk of precipitating cardiac arrhythmias.

◊ Reviews.

1. Health and Safety Executive. 1,1,1-Trichloroethane. *Toxicity Review 9*. London: HMSO, 1984.
2. WHO. 1,1,1-Trichloroethane. *Environmental Health Criteria 136*. Geneva: WHO, 1992. Available at: http://www.inchem.org/documents/ehc/ehc/ehc136.htm (accessed 30/06/04)

Effects on the heart. Effects on the heart of trichloroethane abuse were considered usually to be acute, and sudden death from ventricular arrhythmias had occurred in abusers. There have, however, been a few cases of chronic cardiac toxicity after both abuse and occupational exposure.[1]

1. Marjot R, McLeod AA. Chronic non-neurological toxicity from volatile substance abuse. *Hum Toxicol* 1989; **8:** 301–6.

Effects on the liver. According to a brief review of non-neurological toxicity from volatile substance abuse,[1] there were no reports of damage to the liver after the abuse of trichloroethane. There was a report of hepatotoxicity after acute occupational exposure, but this might have been a hypersensitivity reaction. There was another report[2] of fatty liver disease in 4 patients with a history of occupational exposure to trichloroethane although there has been some debate over the validity of the association for 2 of these cases.[3,4] Chronic active hepatitis associated with trichloroethane exposure has since been reported.[5]

1. Marjot R, McLeod AA. Chronic non-neurological toxicity from volatile substance abuse. *Hum Toxicol* 1989; **8:** 301–6.
2. Hodgson MJ, *et al.* Liver disease associated with exposure to 1,1,1-trichloroethane. *Arch Intern Med* 1989; **149:** 1793–8.
3. Guzelian PS. 1,1,1-Trichloroethane and the liver. *Arch Intern Med* 1991; **151:** 2321–2.
4. Hodgson MJ, Vanthiel DH. 1,1,1-Trichloroethane and the liver. *Arch Intern Med* 1991; **151:** 2322 and 2325–6.
5. Croquet V, *et al.* Hépatite chronique active probablement induite par le 1,1,1-trichloroéthane. *Gastroenterol Clin Biol* 2003; **27:** 120–2.

Effects on the skin. Scleroderma has been reported[1] in 3 patients occupationally exposed to trichloroethylene and, in 2 cases, also to trichloroethane.

1. Flindt-Hansen H, Isager H. Scleroderma after occupational exposure to trichlorethylene and trichlorethane. *Acta Derm Venereol (Stockh)* 1987; **67:** 263–4.

Pharmacokinetics

Trichloroethane is absorbed after inhalation and ingestion, and through intact skin. Small amounts are metabolised to trichloroethanol and trichloroacetic acid and excreted in the urine, but it is largely excreted unchanged through the lungs over a period of days.

Uses

Trichloroethane has wide applications as an industrial solvent. It is commonly used in dry cleaning, typewriter correction fluids, and as a solvent for plaster removal.

White Spirit

Stoddard Solvent; Trementina.

Уайтспирит

CAS — 64742-82-1 (white spirit type 1); 64741-92-0 (white spirit type 2); 64742-48-9 (white spirit type 3); 64742-88-7 (white spirit type 0); 8052-41-3 (Stoddard solvent).

Description. White spirit is a mixture of hydrocarbons available as a colourless liquid. Store in airtight containers.

Adverse Effects and Treatment

As for Kerosene, p.2024.

◊ References to the toxicity of white spirit.[1]

For discussion of neurotoxicity after occupational exposure to solvents including white spirit, 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)

Uses

White spirit is used as an industrial solvent. It is available in various grades. One grade available in the USA is known as Stoddard solvent.

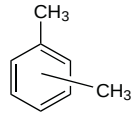
Xylene

Dimethylbenzene; Ksylen; Xileno; Xylol; Xylole.

Ксилол

C_8H_{10} = 106.2.

CAS — 1330-20-7; 108-38-3 (m-xylene); 95-47-6 (o-xylene); 106-42-3 (p-xylene).



Description. Xylene is a mixture of the *o*-, *m*-, and *p*-isomers in which the *m*-isomer predominates. It is a colourless, volatile, flammable liquid. Wt per mL about 0.86 g. B.p. about 138° to 142°. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

The acute toxicity of xylene is similar to that of benzene (p.2020) but is less marked. Adverse effects are treated similarly to benzene.

Xylene has been implicated in volatile substance abuse (p.2019). Commercial xylene may contain benzene, and this may perhaps influence the pattern of adverse effects.

Xylene should not be used to dissolve ear wax if the tympanic membrane is perforated.

◊ References.

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. Health and Safety Executive. Xylenes. *Toxicity Review 26*. London: HMSO, 1992.
3. WHO. Xylenes. *Environmental Health Criteria 190*. Geneva: WHO, 1997. Available at: http://www.inchem.org/documents/ehc/ehc/ehc190.htm (accessed 30/06/04)

Effects on the eyes. Eye injuries due to accidental contact with paints containing xylene have been reported.[1] The injuries resembled alkali burns and were treated in a similar manner. Xylene-induced keratopathy has been reviewed.[2]

1. Ansari EA. Ocular injury with xylene - a report of two cases. *Hum Exp Toxicol* 1997; **16:** 273–5.
2. Trujillo F, *et al.* Xylene keratopathy: a case report and review of the literature. *Cornea* 2003; **22:** 88–90.

Effects on the nervous system. References to the adverse effects of xylene on the nervous system.

1. Arthur LJH, Curnock DA. Xylene-induced epilepsy following innocent glue sniffing. *BMJ* 1982; **284:** 1787.
2. Roberts FP, *et al.* Near-pure xylene causing reversible neuropsychiatric disturbance. *Lancet* 1988; **ii:** 273.

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

Pharmacokinetics

Xylene is absorbed after inhalation, ingestion, and to some extent through the skin. It is rapidly metabolised by oxidation to the corresponding *o*-, *m*-, or *p*-methylbenzoic (toluic) acids and excreted in the urine largely as the glycine conjugate, methylhippuric acid (toluric acid). Xylenols are minor metabolites and are excreted in the urine as the glucuronide and sulfate conjugates. Some unchanged xylene is excreted through the lungs.

Uses

Xylene is used as an industrial and pharmaceutical solvent and in preparations to dissolve ear wax.