

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 dysmorphism.^{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 solvents² 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

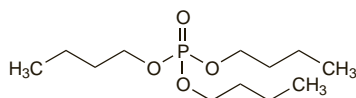
Toluene is widely used as an industrial solvent.

Tri-*n*-butyl Phosphate

Fosfato de tributilo; Tributyl Phosphate; Tributylfosfat; Tributylis Phosphas; Tri-*n*-butylis Phosphas; Tri(*n*-butyl)phosphate; Tri-*n*-butilto fosfat; Tri-*n*-butyle, phosphate de; Tri-*n*-butylfosfat; Tri-*n*-butylis phosphas; Tri-*n*-butylifosfaat. Phosphoric acid tributyl ester.

Три-*n*-бутилфосфат

C₁₂H₂₇O₄P = 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.

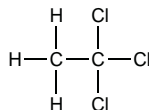
References.

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
C₂H₃Cl₃ = 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 report² 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 reported¹ 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 trichloroethylene and trichloroethane. *Acta Derm Venerol (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.

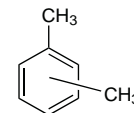
Xylene

Dimethylbenzene; Ksilen; Xileno; Xylo; Xylole.

Ксилол

C₈H₁₀ = 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.