

Vinyl Chloride

General information

Key Points

Fire

- Flammable
- Reactive under light, contact with air, oxidising agents or metals
- Emits toxic vapours of hydrogen chloride and phosgene when heated to decomposition
- In the event of a fire involving vinyl chloride, use fine water spray and normal fire kit with breathing apparatus

Health

- Toxic by all routes of exposure – inhalation, ingestion, skin contact
- Carcinogenic in humans
- Inhalation of vinyl chloride causes coughing, wheezing and breathlessness, headache, ataxia, drowsiness and coma
- Ingestion of vinyl chloride causes nausea, vomiting, diarrhoea, abdominal pain, and haematemesis may occur.
- Skin contact causes irritation, pain, burns and contact dermatitis. Rapid evaporation of compressed gas may produce local frostbite.
- Ocular exposure to the gas causes moderate irritation and pain. Exposure to liquid may possibly cause frostbite and corneal injury.

Environment

- Avoid release into the environment
- Inform Environment Agency of substantial incidents

Background

Vinyl chloride is a colourless, flammable gas, which has a slightly sweet odour. It is not known to occur naturally, but has been found at very low levels in landfill gas due to it being the breakdown product of various chlorinated hydrocarbons and in ground water. Vinyl chloride is also present in cigarette smoke.

The International Agency for Research on Cancer (IARC) has classified vinyl chloride as carcinogenic to humans.

The majority of the world production of vinyl chloride is used for the production of polyvinyl chloride (PVC). It is also used in the production of chlorinated solvents, primarily 1,1,1-trichloroethane. Vinyl chloride was previously used as a refrigerant and as a propellant in aerosol sprays for a variety of products, such as pesticides, drugs and cosmetics. These uses have been banned in many countries.

Vinyl chloride is only used as a chemical intermediate and exposure of the general public is unlikely. In the past there was significant occupational exposure but now it is only used in closed systems with minimal exposure of the workers.

Vinyl chloride is toxic to humans who are exposed to it either by inhalation, ingestion or skin contact. Exposure to vapours can cause coughing, wheezing and breathlessness, headache and drowsiness. Ingestion of vinyl chloride may cause sickness, diarrhoea and stomach pain. Contact of the skin or eyes with vinyl chloride liquid or vapour could cause irritation and dermatitis. Exposure to escaping gas from compressed (liquid) vinyl chloride may cause frostbite.

Repeated exposure to vinyl chloride may cause liver damage.

Children exposed to vinyl chloride are expected to show similar adverse health effects to those seen in exposed adults; such exposures are unlikely because it is not used in consumer products. There is no evidence to suggest that exposure to vinyl chloride during pregnancy may cause adverse effects to the unborn child.

Production and Uses

Key Points

- Vinyl chloride does not occur naturally in the environment
- It is a synthetic chemical obtained either by hydrochlorination of acetylene or by halogenation of ethylene
- Vinyl chloride undergoes exothermic polymerization in the presence of light, or air and heat, or a catalyst
- Approximately 95% of the world's vinyl chloride production is used for the production of PVC

Vinyl chloride does not occur naturally in the environment. It is produced for use as a chemical intermediate in the manufacture of other compounds, particularly PVC. Trace amounts of vinyl chloride may be formed unintentionally, for instance in land fills, as degradation products of chlorinated hydrocarbon solvents. The subsequent presence of vinyl chloride in emitted gas may give rise to traces levels also in ground water.

Approximately 95% of the world production of vinyl chloride is used for the production of PVC. The remainder is used for the production of chlorinated solvents, primarily 1,1,1-trichloroethane, via the more toxic 1,1,2-trichloroethane and 1,1,2-trichlorethane and 1,1-dichloroethane.

Vinyl chloride was previously used as a refrigerant and as a propellant in aerosols sprays for a variety of products, such as pesticides, drugs and cosmetics. These uses have been banned since 1974.

Frequently Asked Questions

What is Vinyl chloride?

Vinyl chloride is a colourless, flammable gas which is not stable at high temperatures. It has a mild, sweet odour. It does not occur naturally but is manufactured and used to make PVC, which is used in a variety of plastic products, including pipes, wire and cable coatings, and packaging materials. Very small amounts can be formed when other substances such as trichloroethane, trichloroethylene and tetrachlorethylene are broken down.

How does vinyl chloride get into the environment?

Vinyl chloride does not occur naturally in the environment. It is only used as an industrial intermediate under strictly controlled conditions, with minimal exposure of workers or to the environment. Trace amounts may be formed as degradation products of chlorinated solvents in landfills or hazardous waste sites but any exposure is likely to be minimal.

Liquid vinyl chloride evaporates easily in air, and in water and soil evaporates rapidly if it is near the surface. In the air it breaks down in a few days to other substances, which may be harmful. Small amounts of vinyl chloride can dissolve in water.

How could I be exposed to vinyl chloride?

As vinyl chloride is only used in the workplace under strictly controlled conditions, it is unlikely that you will be exposed to significant amounts unless you work with it.

Tobacco smoke however contains low levels of vinyl chloride.

If there is vinyl chloride in the environment will I have any adverse health effects?

The presence of vinyl chloride in the environment does not always lead to exposure. Clearly, in order for it to cause any adverse health effects you must come into contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact. Following exposure to any chemical, the adverse health effects you may encounter depend on several factors, including the amount to which you are exposed (dose), the way you are exposed, the duration of exposure, the form of the chemical and if you were exposed to any other chemicals.

Short-term exposure to vinyl chloride vapours can cause coughing, wheezing and breathlessness, headache and drowsiness. Ingestion of vinyl chloride may cause sickness, diarrhoea and stomach pain. Contact of the skin or eyes with vinyl chloride liquid or vapour could cause irritation and dermatitis. Exposure to escaping gas from compressed (liquid) vinyl chloride may cause frostbite. Repeated exposure to vinyl chloride may cause liver damage.

Can vinyl chloride cause cancer?

The International Agency for Research on Cancer (IARC) has classified vinyl chloride as being carcinogenic to humans.

Does vinyl chloride affect children or damage the unborn child?

Children exposed to vinyl chloride are expected to show similar adverse health effects to those seen in exposed adults. Experimental data indicates that no effect would be expected at exposure levels that are not markedly toxic to the mother.

What should I do if I am exposed to vinyl chloride?

It is very unlikely that the general population will be exposed to a level of vinyl chloride high enough to cause adverse health effects.

This document from the HPA Centre for Radiation, Chemical and Environmental Hazards reflects understanding and evaluation of the current scientific evidence as presented and referenced in this document.

Vinyl Chloride

Incident management

Key Points

Fire

- Flammable
- Reactive under light, contact with air, oxidising agents or metals
- Emits toxic vapours of hydrogen chloride and phosgene when heated to decomposition
- In the event of a fire involving vinyl chloride, use fine water spray and normal fire kit with breathing apparatus

Health

- Main route of exposure is likely to be via inhalation
- Inhalation can cause weakness, ataxia, inebriation, headache, fatigue, numbness, paraesthesiae, nausea, vomiting, epigastric pain, visual and auditory disturbances,
- Dermal exposure causes irritation, pain, burns and contact dermatitis. Rapid evaporation may produce local frostbite.
- Ocular exposure causes irritation, pain and possible frostbite and corneal injury.

Environment

- Avoid release into the environment
- Inform Environment Agency of substantial incidents

Hazard Identification

Standard (UK) Dangerous Goods Emergency Action Codes^(a)

UN	1086	Vinyl chloride, stabilized		
EAC	2YE	Use fine water spray. Wear normal fire kit in combination with breathing apparatus*. Can be violently or explosively reactive. Spillages and decontamination run-off should be prevented from entering drains and watercourses. There may be a public safety hazard outside the immediate area of the incident**.		
APP	-			
Hazards	Class	2.1	Flammable gas	
	Sub risks	-		
HIN	239	Flammable gas, which can spontaneously lead to violent reaction		

UN – United Nations number; EAC – Emergency Action Code; APP – Additional Personal Protection; HIN - Hazard Identification Number

*Normal fire fighting clothing i.e. fire kit (BS EN 469), gloves (BS EN 659) and boots (HO specification A29 and A30) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).

** People should stay indoors with windows and doors closed, ignition sources should be eliminated and ventilation stopped. Non-essential personnel should move at least 250 m away from the incident.

^a Dangerous Goods Emergency Action Code List 2011. National Chemical Emergency Centre (NCEC). The Stationary Office, London.

Chemical Hazard Information and Packaging for Supply Classification^(a)

Classification	F+	Extremely flammable	
	Carc. Cat 1	Category 1 carcinogen	
Risk phrases	R45	May cause cancer	
	R12	Extremely flammable	
Safety phrases	S53	Avoid exposure - obtain special instructions before use	
	S45	In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)	

^a Annex VI to Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures- Table 3.2.
<http://esis.jrc.ec.europa.eu/index.php?PGM=cla> (accessed 03/2012)

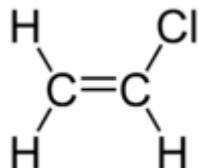
Globally Harmonised System of Classification and Labelling of Chemicals (GHS)^(a)

Hazard Class and Category	Press. Gas	Gas under pressure	
	Flam. Gas 1	Flammable gas, category 1	
	Carc. 1A	Carcinogenicity, category 1A	
Hazard Statement	H220	Extremely flammable gas	
	H350	May cause cancer	
Signal Words	DANGER		

Implemented in the EU on 20 January 2009.

^a Annex VI to Regulation (EC) No 1272/2008 on Classification, Labelling and Packaging of Substances and Mixtures- Table 3.1.
<http://esis.jrc.ec.europa.eu/index.php?PGM=cla> (accessed 03/2012)

Physicochemical Properties

CAS number	75-01-4
Molecular weight	63
Empirical formula	C ₂ H ₃ Cl
Common synonyms	Chloroethylene; Chloroethene; Ethylene monochloride; Monochlorethene; VC
State at room temperature	Gas
Volatility	Vapour pressure 2530 mm Hg at 20°C. Heavier than air at 20°C
Specific gravity	2.2 at 20°C (air = 1)
Flammability	Flammable
Lower explosive limit	3.6%
Upper explosive limit	33.0%
Water solubility	Low solubility in water, 2.8 g L ⁻¹ at 25°C. Soluble in ethanol, diethyl ether, benzene and other organic solvents
Reactivity	Reactive. Vinyl chloride readily polymerises upon heating, under light or on contact with air, oxidising agents and metals, causing risk of fire or explosion
Reaction or degradation products	Decomposes on burning, emitting toxic vapours of hydrogen chloride and phosgene
Odour	Sweet
Structure	

References^(a,b,c)

^a Vinyl chloride (HAZARDTEXT[®] Hazard Management). In: Klasco RK (Ed): TOMES[®] System, Thomson Micromedex, Greenwood Village, Colorado, USA. (electronic version). RightAnswer.com, Inc., Midland, MI, USA, Available at: <http://www.rightanswerknowledge.com/data/dt/dt499.htm> (accessed 03/2012).

^b The Merck Index (14th Edition). Entry 9994: Vinyl Chloride, 2006.

^c The Dictionary of Substances and their Effects. Ed. S Gangolli. Second Edition, Volume 7, 1999.

Threshold Toxicity Values

EXPOSURE VIA INHALATION			
ppm	mg m⁻³	SIGNS AND SYMPTOMS	REFERENCES
8000 - 20000	20449 - 51124	CNS depression including headache, dizziness, nausea, light-headedness, ataxia, euphoria, visual disturbances, numbness, drowsiness and tingling of extremities	a
70000 - 100000	178937 - 255624	Narcotic	a
120000	306748	Cardiac arrhythmias and potentially fatal	a

^a International Programme on Chemical Safety, Poisons Information Monograph 558: Vinyl chloride.

Published Emergency Response Guidelines

Emergency Response Planning Guideline (ERPG) Values^(a)

	Listed value (ppm)	Calculated value (mg m ⁻³)
ERPG-1*	500	1278
ERPG-2**	5000	12781
ERPG-3***	20000	51124

* Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odour.

** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.

*** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing life-threatening health effects.

Interim Acute Exposure Guideline Levels (AEGs)^(b)

	ppm				
	10 min	30 min	60 min	4 hr	8 hr
AEGL-1[†]	450	310	250	140	70
AEGL-2^{††}	2800	1600	1200	820	820
AEGL-3^{†††}	12000 [◇]	6800 [◇]	4800 [◇]	3400	3400

[†] The level of the chemical in air at or above which the general population could experience notable discomfort.

^{††} The level of the chemical in air at or above which there may be irreversible or other serious long-lasting effects or impaired ability to escape.

^{†††} The level of the chemical in air at or above which the general population could experience life-threatening health effects or death.

Lower Explosive Limit (LEL) = 38000 to 293000 ppm

◇ ≥ 10 % LEL

^a American Industrial Hygiene Association (AIHA). 2011 Emergency Response Planning Guideline Values.

http://www.aiha.org/insideaiha/GuidelineDevelopment/ERPG/Documents/2011erpgweelhandbook_table-only.pdf (accessed 03/2012).

^b U.S. Environmental Protection Agency. Acute Exposure Guideline Levels, <http://www.epa.gov/oppt/aegl/pubs/chemlist.htm> (accessed 03/2012).

Exposure Standards, Guidelines or Regulations

Occupational Standards

WEL ^(a) http://www.hse.gov.uk/	LTEL(8 hour reference period): 3 ppm (7.8 mg m ⁻³)
	STEL(15 min reference period): No guideline value specified

Public Health Guidelines

DRINKING WATER QUALITY GUIDELINES AND REGULATIONS http://www.who.int/en/ http://dwi.defra.gov.uk/	0.3 µg L ⁻¹ (b) 0.5 µg L ⁻¹ (c)
AIR QUALITY GUIDELINE ^(d) http://www.who.int/en/	1 µg m ⁻³ equates to an estimate of lifetime risk 1 × 10 ⁻⁶
SOIL GUIDELINE VALUE	Data not available
HEALTH CRITERIA VALUES ^(e) http://www.environment-agency.gov.uk/	Index dose _{oral} 0.014 µg kg ⁻¹ bw day ⁻¹
	Index dose _{inhalation} 0.3 µg kg ⁻¹ bw day ⁻¹

WEL – Workplace exposure limit; LTEL - Long-term exposure limit; STEL – Short-term exposure limit

^a EH40/2005 Workplace Exposure Limits (second edition, published 2011).

<http://www.hse.gov.uk/pubns/priced/eh40.pdf> (accessed 03/2012).

^b Guidelines for Drinking-Water Quality, Fourth Edition. WHO, Geneva. 2011.

^c The Water Supply (Water Quality) Regulations 2000 (England) and the Water Supply (Water Quality) Regulations 2001 (Wales).

^d Air Quality Guidelines for Europe. World Health Organization Regional Office for Europe, Copenhagen WHO Regional Publications, European Series, No. 91, Second Edition, 2000.

^e Department for Environment, Food and Rural Affairs (DEFRA). Contaminants in Soil; Collation of Toxicological Data and Intake Values for Humans. Vinyl Chloride. 2004.

Health Effects

Major Route of Exposure^(a)

- Liquid vinyl chloride evaporates quickly when not under high pressure therefore poisoning is likely to be by inhalation only.

Immediate Signs or Symptoms of Acute Exposure^(b)

- Following inhalation features include weakness, ataxia, inebriation, headache, fatigue, numbness, paraesthesiae, nausea, vomiting, epigastric pain, visual and auditory disturbances, narcosis and death.
- Dermal exposure causes irritation, pain and burns. Rapid evaporation may produce local frostbite.
- Ocular exposure causes irritation, pain, possible frostbite and corneal injury.

TOXBASE - <http://www.toxbase.org> (accessed 03/2012)

^a TOXBASE: Vinyl chloride, 2012.

^b TOXBASE: Vinyl chloride – features and management, 2012.

Decontamination and First Aid

Important Notes

- Ambulance staff, paramedics and emergency department staff treating chemically-contaminated casualties should be equipped with Department of Health approved, gas-tight (Respirex) decontamination suits based on EN466:1995, EN12941:1998 and prEN943-1:2001, where appropriate.
- Decontamination should be performed using local protocols in designated areas such as a decontamination cubicle with adequate ventilation.
- Flammability warning: prevent exposure to all sources of ignition such as naked flames, electrical equipment, oxidising chemicals and the smoking of tobacco products.

Dermal Exposure^(a)

- Remove patient from exposure.
- If frostbite has occurred remove clothing carefully, soaking with tepid water or surgery may be necessary.
- If no frostbite, remove contaminated clothing and irrigate with copious amounts of water; treat as a thermal burn.
- Other measures as indicated by the patient's clinical condition.

Ocular Exposure^(b)

- Remove patient from exposure.
- Remove contact lenses if present and immediately irrigate the affected eye thoroughly with water or 0.9% saline for at least 10-15 minutes. Continue until the conjunctival sac pH is normal (7.5 - 8.0), retest after 20 minutes and use further irrigation if necessary.
- Any particles lodged in the conjunctival recesses should be removed
- Patients with corneal damage or those whose symptoms do not resolve rapidly should be referred for urgent ophthalmological assessment.
- Other measures as indicated by the patient's clinical condition.

Inhalation^(a)

- Maintain a clear airway and ensure adequate ventilation.
- Ensure a clear airway and adequate ventilation.
- Remove from exposure if appropriate and give oxygen.
- Perform a 12 lead ECG and measure the QRS duration and QT interval.
- Other measures as indicated by the patient's clinical condition.

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TOXBASE - <http://www.toxbase.org> (accessed 03/2012)

^a TOXBASE: Vinyl chloride – features and management, 2012.

Vinyl chloride

Toxicological overview

Key Points

Kinetics and metabolism

- Vinyl chloride is readily and rapidly absorbed via inhalation, ingestion and through the skin
- At room temperature vinyl chloride is a gas, so inhalation is the major route exposure
- Following absorption, it is distributed through the body, with the highest concentrations found in the liver and kidneys, followed by the lungs and spleen
- Vinyl chloride is mainly metabolised in the liver into reactive metabolites
- Vinyl chloride is mainly excreted in the urine as thiodiglycolic acid

Health effects of acute exposure

- Acute inhalation of vinyl chloride may cause nausea, headache, dizziness and drowsiness; central nervous system depression and cardiac arrhythmias
- Vinyl chloride can cause irritation to the eyes, mucous membranes and respiratory tract
- Compressed gas or liquid can cause frostbite or irritation of the skin and eyes

Health effects of chronic exposure

- Repeated exposure to vinyl chloride may cause liver toxicity, neurological and behavioural symptoms
- Vinyl chloride is considered to be a human carcinogen

Toxicological Overview

Summary of Health Effects

Vinyl chloride is rapidly and well absorbed after inhalation or following oral exposure (as a solution in an organic solvent). The primary route of exposure to vinyl chloride is inhalation, approximately 40% of inspired vinyl chloride is absorbed after exposure by inhalation. Although no there are no human studies, animal studies showed absorption of more than 95% after oral exposure. Dermal absorption of vinyl chloride in the gaseous state is not significant [1-3].

Acute exposure to vinyl chloride can cause dizziness, drowsiness, unconsciousness, and at extremely high levels can cause death. Vinyl chloride is a respiratory irritant producing coughing, wheezing and breathlessness. Other effects include headache, ataxia and coma [3, 4].

Dermal exposure to vinyl chloride may cause irritation, pain and burns. Rapid evaporation may produce local frostbite. Contact dermatitis has been reported. Vinyl chloride is not readily absorbed dermally. Ocular exposure may cause irritation, pain and possible frostbite and corneal injury [5].

In the past, long term occupational exposure to concentrations of 1000 ppm or more produced a distinctive syndrome ('vinyl chloride illness'). This includes peripheral circulatory changes typical of Raynaud's Disease (numbness, tingling and blanching of the fingers on exposure to cold), and sclerosis-like changes in the fingers with subsequent bony changes in the tips of the fingers (acro-osteolysis), chronic exposure can also cause liver damage [1-4]. Currently all manufacturing processes using vinyl chloride use completely enclosed systems hence any exposure of workers is unlikely [3].

According to the International Agency for Research on Cancer (IARC), vinyl chloride is a recognised human carcinogen. There is much data to substantiate a causal association between exposure to vinyl chloride and a distinctive form of liver cancer (angiosarcoma). Several studies also confirm that exposure to vinyl chloride causes other forms of cancer i.e. hepatocellular cancer, brain tumours, lung tumours and malignancies of the lymphatic and haematopoietic system [2].

Kinetics and metabolism

Vinyl chloride is readily and rapidly absorbed via inhalation, ingestion, and minimally through the skin. It is a gas at room temperature, and thus inhalation is the major route of exposure.

In various studies of human volunteers exposed to vinyl chloride by inhalation, retention (the difference between the inhaled and exhaled concentrations) in the lung was estimated to be 27 to 42% [4, 6]. Concentrations reached a maximum within 15 minutes, declined rapidly after 30 minutes and increased to a constant value [6].

Uptake of vinyl chloride when given as a solution in organic solvent via the oral route is more than 95%. Any vinyl chloride not metabolised during first pass through the liver will be expired. Thus the net dose may be less than the uptake, especially at high doses resulting in saturation of metabolising enzymes [3]. After an acute oral exposure in rats, peak levels of vinyl chloride in brain, liver, kidney and lung were measured 5 minutes after dosing, indicating rapid absorption from gastrointestinal tract [3].

No data were available regarding skin absorption in humans. Animal studies in which rhesus monkeys were exposed to vinyl chloride vapour showed that very little was absorbed through the skin [3, 6].

Vinyl chloride is rapidly distributed through the body, with the highest concentrations found in the liver and kidneys, followed by the lungs and spleen [4, 7]. Placental transfer of vinyl chloride has been shown to occur rapidly in rats.

The main route of metabolism of vinyl chloride is in the liver by cytochrome P450 enzymes. It is first metabolised to chloroethylene oxide, a highly reactive, short-lived epoxide that rapidly rearranges to form chloroacetaldehyde. These reactive metabolites are detoxified via conjugation with glutathione [3, 4]. The rapid metabolism and excretion limits the accumulation of vinyl chloride in the body [6].

In humans, at low doses vinyl chloride is largely excreted in the urine as thiodiglycolic acid, its excretion increasing with exposure to the parent compound [4]. At higher doses when metabolism is saturated, the major route of excretion is exhalation of unchanged vinyl chloride. Excretion via faeces is only a minor route [3].

Sources and route of exposure

The major source of exposure to vinyl chloride is from occupational exposure, since its principal use is in industrial processes, such as during the production of PVC [4, 6]. However, currently all manufacturing processes using vinyl chloride use completely enclosed systems hence any exposure of workers is unlikely [3].

Vinyl chloride is unlikely to be present in significant quantities in domestic situations and does not occur naturally, although it has been found in landfill gas and groundwater as a degradation product of chlorinated hydrocarbons deposited [3].

There is very little exposure of the generally population to vinyl chloride. WHO estimated that the majority of the population would inhale 2 – 10 $\mu\text{g day}^{-1}$ vinyl chloride, assuming a daily inhalation rate of 20 m^3 . Vinyl chloride may be present in the environment close to industrial locations where it is manufactured or used, or near waste disposal sites. Calculation of daily inhalation rates for populations living in the immediate vicinity of some vinyl chloride plants

indicates the population could inhale 4 - 100 $\mu\text{g day}^{-1}$ [4]. However, concentrations present at such locations would be expected to be many times lower than those observed during occupational exposure [3, 8]. Exposure to vinyl chloride may also be higher in situations where large amounts of vinyl chloride are accidentally released to the environment, such as during a spillage during transportation.

There is little information regarding vinyl chloride in drinking water. Due to its volatility and reactivity, it would not be expected to remain in drinking water in significant quantities [8]

Vinyl chloride is found in cigarette (1.3-1.6 ng cigarette⁻¹) and cigar (14-27 ng) smoke. Heavy smokers may therefore inhale up to 0.5 $\mu\text{g day}^{-1}$ [8].

Health Effects of Acute / Single Exposure

Human Data

Inhalation

The acute toxic effects following inhalation of vinyl chloride are summarised in table 1. The main effect of acute exposure to vinyl chloride is on the central nervous system causing headache, vertigo, drowsiness, disorientation, nausea, burning of extremities, dizziness, ataxia and narcotic effects at higher concentrations [4, 6, 9-11].

Acute inhalation of vinyl chloride may cause respiratory tract irritation, wheezing, chemical bronchitis and respiratory depression. Such effects are usually transient and resolve when exposure is removed. Exposure to vinyl chloride may also lead to Reactive Airway Dysfunction Syndrome (RADS), a chemical-induced type of asthma [4, 6, 9-11].

Exposure to higher concentrations for longer periods may result in death due to central nervous system and respiratory depression [11].

Exposure to vinyl chloride may predispose the person to cardiac arrhythmias [11].

Table 1. Summary of toxic effects following acute exposure to vinyl chloride by inhalation [4, 6, 9-11].

Dose (ppm)	Duration of exposure (min)	Signs and symptoms
8000 - 20000		Dizziness, nausea, headache
70000 – 100000		Narcotic, coma
120000		Cardiac arrhythmias, death
4000	5	Threshold of effect
8000	5	Dizziness
12000	5	Dizziness, headache, nausea and dulling of vision
1000	60	Drowsiness, faltering gait, visual disturbances and numbness and tingling in the extremities

There have been two fatalities reported from acute vinyl chloride exposure to airborne levels estimated to be greater than 100,000 ppm; deaths were from respiratory failure [4].

Ingestion

Ingestion of vinyl chloride is unlikely as it is a gas at room temperature. No data could be retrieved [4].

Dermal / ocular exposure

Vinyl chloride is stored under pressure as a liquid. Exposure to escaping vinyl chloride may cause frostbite to the exposed skin, with redness, blistering and scaling. A man whose hands were accidentally sprayed with vinyl chloride developed erythema and some second-degree burns which healed without complication [3, 11].

Ocular contact with vinyl chloride vapours is moderately irritating to the eye. Contact with escaping compressed gas may cause mechanical injury and frostbite [4, 11].

Delayed effects following an acute exposure

Individuals who are exposed to vinyl chloride may not experience immediate symptoms as there may be a latent period of 24 to 48 hours between exposure and CNS and respiratory depression and liver or kidney toxicity [11].

Animal and In-Vitro Data

Inhalation

Vinyl chloride appears to be of low toxicity when administered to various species by inhalation; the two hour LC50 value being 293000 – 595000 mg kg⁻¹ for a range of species [4]. At these high exposures congestion was seen in internal organs particularly the lung, liver and kidney as well as pulmonary oedema [3].

Following exposure of mice and rats to 10000 – 30000 ppm vinyl chloride for 30 minutes, narcosis was reported, as well as, pulmonary oedema, congestion of the lungs, liver and kidneys and pulmonary haemorrhage [3, 7]. In rats, mice and hamsters, exposed to high levels by inhalation, death was preceded by increased motor activity, twitching of extremities, tremor, ataxia, tonic-clonic convulsions and accelerated respiration [3].

Cardiovascular effects were also reported in-vivo. In dogs, severe cardiac arrhythmias (intermittent tachycardia, ventricular fibrillation, atrioventricular block) occurred under narcosis after inhalation of 260,000 mg m⁻³ of vinyl chloride, although the statistical significance of these were not reported [3, 7].

Studies have reported the effect of vinyl chloride on blood clotting. Guinea pigs exposed to 400000 ppm vinyl chloride for 30 minutes had a decrease in blood clotting [7].

Hepatic damage was observed in animals exposed to high concentrations of vinyl chloride. Acute exposure of guinea pigs and mice to 200000 - 300000 ppm had liver congestion, fatty degeneration and fatty infiltration, as well as centrilobular vacuolisation, although rats exposed to 60000 ppm for 6 hours showed no observable effects [4, 7].

Hepatic changes increase by ethanol or phenobarbitone pre-treatment have been observed following massive exposure in animals [4].

Ingestion

No studies reporting adverse effects following acute ingestion of vinyl chloride in animals were identified.

Dermal / ocular exposure

Few studies reporting toxicity following acute dermal or ocular exposure to vinyl chloride were identified. Guinea pigs exposed to up to 400000 ppm vinyl chloride for 30 minutes in an inhalation chamber did not show any adverse effects on skin or eyes [7]

Health Effects of Chronic / Repeated Exposure

Human Data

Inhalation

Prior to 1974, it was not uncommon for workers to be exposed to concentrations of vinyl chloride in the region of 2590 mg m^{-3} (1000 ppm) for periods ranging from 1 month to several years. Such exposure has been reported to cause a specific pathological syndrome called the “vinyl chloride illness” characterised by scleroderma-like changes in the fingers with subsequent bony changes in the tips of the fingers, acro-osteolysis and Raynaud’s phenomenon [3, 4]. Other symptoms described were earache and headache, dizziness, unclear vision, fatigue and lack of appetite, nausea, sleeplessness, breathlessness, stomach ache, pain in the liver/spleen area, pain and tingling sensation in the arms/legs, cold sensation at the extremities, loss of libido and weight loss [3]. Peripheral circulatory changes may also occur which correlate with length of exposure [10].

Chronic exposure to vinyl chloride may also result in liver toxicity, initially hepatomegaly, with hepatic fibrosis and portal hypertension occurring after several years [4].

Chronic inhalation of vinyl chloride may also cause respiratory effects, such as emphysema, decreased respiratory volume, decreased oxygen and carbon dioxide transfer, pulmonary fibrosis and dyspnoea, although cohort studies have reported an overall deficit in mortality from respiratory disease [10].

Ingestion

There are currently no data on the effects of chronic vinyl chloride ingestion in humans.

Dermal / ocular exposure

Occupational exposure to vinyl chloride has produced scleroderma-like skin changes on the hands of a small percentage of exposed workers in the past. The skin changes were characterized by a thickening of the skin, decreased elasticity and oedema, and were almost exclusively observed in exposed individuals who also suffered from Raynaud’s phenomenon. Skin biopsies revealed increased collagen bundles in the sub-epidermal layer of the skin [7].

Genotoxicity

Vinyl chloride has been demonstrated to be clastogenic in humans and is hence a mutagen. Frequencies of chromosomal aberrations, micronuclei and sister chromatid exchanges in the peripheral blood lymphocytes of workers exposed to high levels of vinyl chloride have been shown to be increased compared to controls [3, 7]. Although in many studies the exposure concentrations and duration of exposure were only estimated, a dose-response relationship and a normalisation of genotoxic effects with time after reduction of exposure can be seen [3].

Carcinogenicity

The International Agency for Research on Cancer (IARC) has classified vinyl chloride as being carcinogenic to humans (Group 1) [2].

A large number of epidemiological studies and case reports have substantiated the causal association between vinyl chloride and angiosarcoma of the liver as well as hepatocellular carcinoma, brain tumours, lung tumours and malignancies of the lymphatic and haematopoietic system. Slightly elevated risks for gastric and gastrointestinal cancer (other than liver cancer) were reported in some studies, but these were not confirmed in others [2].

Reproductive and developmental toxicity

Several epidemiological studies have reported an association between vinyl chloride exposure in pregnant women and an increased incidence of birth defects, while other studies have not reported similar findings [3, 4, 7]. However, those studies that reported an increased rate of birth defects among the children of parents residing nearby vinyl chloride production facilities failed to show a significant correlation between development toxicity and proximity to the facility or parental occupation [3, 4, 7].

Increased incidence and severity of preeclampsia during pregnancy was reported in exposed women compared to non-exposed women [7].

Several case reports suggest that male sexual performance such as impotence, loss of libido and decreased androgen secretion, may be affected by vinyl chloride. However, these studies are limited by lack of quantitative exposure information and possible co-exposure to other chemicals [3, 4, 7].

Epidemiological studies have suggested an association between paternal exposure to vinyl chloride and spontaneous abortion and/or birth defects although other studies have not supported these findings [3, 4, 7, 10].

In summary, epidemiological studies on the potential developmental toxicity of vinyl chloride or of effects on libido and potency have not produced conclusive results [6].

Animal and In-Vitro Data

Inhalation

Rats, mice and hamsters exposed to 260 mg m⁻³, 130 mg m⁻³ and 520 mg m⁻³ vinyl chloride, respectively for up to 24 months (rats) or 18 months (mice and hamsters) showed increased mortality. In most species the main target organ for vinyl chloride is the liver. A dose-related increase in liver weight has been reported in rats exposed to 26 – 7800 mg m⁻³, and degenerative effects on liver parenchyma occurred in rabbits (520 mg m⁻³), rats (1300 mg m⁻³) and mice (2600 mg m⁻³). Adverse effects on the testes in rats were also noted (26 – 7000 mg m⁻³), as well as kidney and lung in rats and mice at higher doses. Rats, mice and rabbits appear to be more sensitive than guinea pigs and dogs [3].

Other studies reported that rats exposed to 130 mg m⁻³ showed reduced body weight and increased relative spleen weight, as well as hepatocellular lipid accumulation, mitochondrial swellings and proliferation of cells lining the liver sinusoids, rats exposed to 1300 mg m⁻³ showed reduced body weight, increased weight of heart, spleen, liver and kidney,

degeneration of the testis and myocardium and tubular necrosis and those exposed to 52000 mg m⁻³ showed reduced body weight, elevated weight of heart and spleen, liver, kidney and testis. Hepatotoxicity was observed at all doses [3].

Increases in relative heart weight was also reported in rats exposed to 10 ppm vinyl chloride for 6 months and 100 ppm for 3 months, whereas rats chronically exposed to 5000 ppm vinyl chloride for one year showed increases in areas of myodegeneration and arterial wall thickening, although statistical significance was not reported. Exposure of rats to 30000 ppm vinyl chloride for one year also caused thickening of arterial walls and consequently blockage of the lumen due to proliferation of the endothelium [7].

Exposure to 5000 ppm vinyl chloride for one year caused increased splenic haematopoiesis and decreased blood clotting time in rats, although statistical significance was not reported [7].

Following exposure to 20000 ppm vinyl chloride for 10 months no bone alterations in rats was reported, but 30000 ppm for 12 months cause osteochondrome, although again statistical significance was unreported [7].

Ingestion

The primary target organ of vinyl chloride in rats after long-term oral exposure is the liver. Female rats appeared to be more sensitive than males to the hepatotoxicity of vinyl chloride, with increased mortality in females at doses of 1.3 mg kg⁻¹ body weight⁻¹ day⁻¹ and above and in males at 5.0 mg kg⁻¹ body weight⁻¹ day⁻¹ and above. Increased relative liver weights were found at 14.1 mg kg⁻¹ body weight⁻¹ day⁻¹ after feeding periods of 6 or 12 months and blood clotting time was decreased [3]. Morphological alterations of the liver included extensive hepatocellular necrosis at doses of ≥5 mg kg⁻¹ body weight⁻¹ day⁻¹, foci of haematopoiesis at 14.1 mg kg⁻¹ body weight⁻¹ day⁻¹, and cysts and liver cell polymorphism at doses ≥ 1.3 mg kg⁻¹ body weight⁻¹ day⁻¹ [3, 7].

Dermal effects may also occur following ingestion of vinyl chloride. Exposure to 30 mg kg⁻¹ body weight⁻¹ day⁻¹ for two years caused skin fibrosis [7].

Genotoxicity

Vinyl chloride has been extensively studied in the Ames test. Positive results were consistently obtained in the presence of metabolic activation. Activity was seen against *Salmonella typhimurium* strains TA100, TA1530 and TA1535 but not in TA98, TA1537 and TA1538 indicating that the mutations are the result of base-pair substitutions (transversion and transition) rather than frameshift mutations [3]. Vinyl chloride has also been shown to give positive results in *in-vitro* tests for gene mutation in yeasts and for chromosome aberrations in mammalian cells in culture. *In-vitro* studies indicate it has mutagenic potential [7].

Vinyl chloride has also been extensively studied for mutagenic effects *in-vivo* in rodents. Studies to investigate clastogenicity following exposure by inhalation using either metaphase analysis or the micronucleus test have consistently given positive results [4].

Carcinogenicity

Various carcinogenicity studies in different animal species indicate that there is sufficient evidence that vinyl chloride is carcinogenic to animals [2].

Following oral and inhalation exposure, vinyl chloride was carcinogenic in rats, mice and hamsters, producing tumours in the mammary gland, lung, Zymbal gland, skin and angiosarcomas of the liver [2]. A combination of oral administration of ethanol and inhalation of vinyl chloride resulted in more liver tumours (including angiosarcomas) than after treatment with vinyl chloride alone [2].

Vinyl chloride was carcinogenic in rats following prenatal exposure. A dose-response effect has been demonstrated [1].

Reproductive and developmental toxicity

Inhalation studies in which rats or mice were exposed to vinyl chloride throughout pregnancy indicated developmental toxicity only occurred at doses above those causing maternal toxicity. Potential fetal toxicity was observed at 1300 mg m⁻³ in mice and 3900 mg m⁻³ in rats with no evidence of teratogenicity in either species [6].

In a 2-generation reproductive toxicity study in rats exposed to concentrations up to 2860 mg m⁻³ by inhalation, no adverse effects on embryo-fetal development or reproductive capacity at any dose level [7].

In a 12 month repeated dose inhalation toxicity study, signs of testicular toxicity (damage to seminiferous tubules) was observed at 260 mg m⁻³ and above, with a no observable adverse effect level (NOAEL) of 260 mg m⁻³ [6].

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