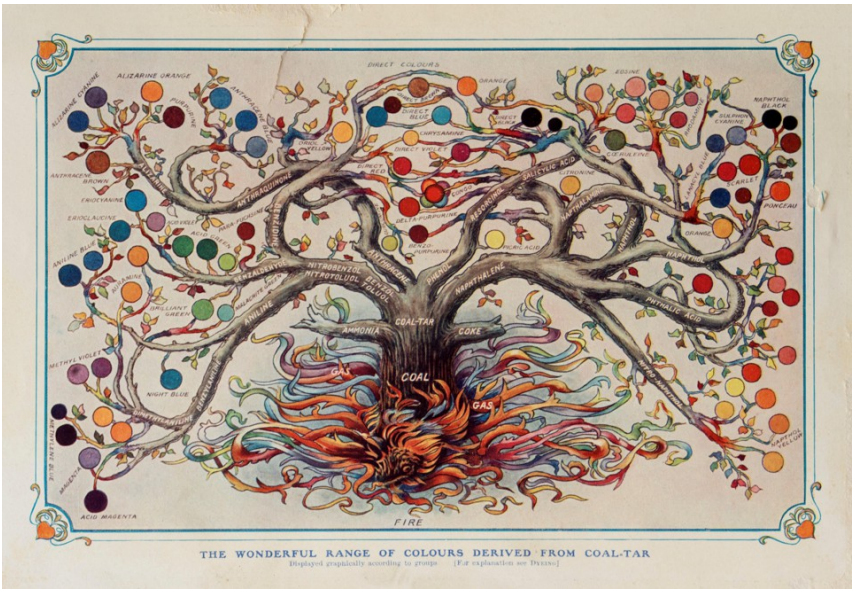
A Small Dose of Solvents
Or
An Introduction to the Health Effects of Solvents



Benzene Tree

Dossier

Name: Solvent (broad class of chemicals)
Use: varied – recreational (alcohol) to industrial (gasoline, degreasers)
Source: synthetic chemistry, petroleum products; plant oils
Recommended daily intake: none (not essential)
Absorption: intestine, inhalation (major), skin
Sensitive individuals: fetus, children
Toxicity/symptoms: nervous system, reproductive system, and death
General facts: long history of use (alcohol), highly volatility of solvent results in inhalation exposure of vapors
Environmental: volatile organic compounds react with sunlight to produce smog
Recommendations: avoid, use proper workplace protection

Case Studies

Anesthetic Agents

> "I also attended on two occasions the operating theatre in the hospital at Edinburgh, and saw two very bad operations, one on a child, but I rushed away before they were completed. Nor did I ever attend again, for hardly any inducement would have been strong enough to make me do so; this being long before the blessed days of chloroform. The two cases fairly haunted me for many a long year."
> - Charles Darwin, Autobiography (1993)

An effective anesthetic agent must be easy to use, quickly render the patient unconscious and not produce any toxicity. Dr. William T.G. Morton first publicly demonstrated the use of ether as an effective anesthetic agent at the Massachusetts General Hospital on October 16, 1846 before a crowd of skeptical physicians. Raymundus Lullius, a Spanish chemist, discovered ether $(CH_3CH_2)_2O$ in 1275. Its hypnotic effects were soon appreciated (and enjoyed by some), but for many decades ether was only used to treat the occasional medical ailments. Even with ether, the success of surgical procedures did not improve until the introduction of anapestic procedure and infection control some 20 years latter. Ether was replaced by cyclopropane in 1929, which was replace by halothane 1956. While anesthetic agents are desirable for the patient, exposure to hospital staff is highly undesirable and an important occupational consideration.

n-Hexane

n-Hexane is a simple and common hydrocarbon found in solvents, degreasing agents, glues, spray paints, gasoline, silicones and other common substances. A common workplace exposure to n-hexane is from degreasing agents, which usually contain a mixture of solvents. In 1997 a 24-year-old male automotive technician went to his doctor complaining of numbness and tingling of the toes and fingers. Further neurological evaluation revealed a reduced sensation in the forearms and diminished reflexes. For the previous 22 months this worker had used, on a daily basis, aerosol cans of brake cleaner that contained 50-60% hexane (composed of 20%-80% n-hexane), 20-30% toluene, and 1-10% methyl ethyl ketone. He used this degreasing agent to clean brakes, small tools, and even car engines. He commonly used latex gloves while at work. His condition improved when exposure to the cleaning agent was stopped. 2,5-hexanedione, a urinary metabolite of n-hexane and thought to be the toxic agent responsible for the nervous system effects, can be measured and used to estimate exposure to n-hexane. A subsequent study found that automotive technicians were indeed exposed to n-hexane. Degreasing

products typically contain a mixture of solvents that are readily absorbed when inhaled or allowed to pass through the skin. The latex gloves used by this worker offered little protection. More information on this case study can be found at MMWR (2001).

Introduction and History

Solvents are a broad class of compounds that we are commonly exposed to when we pump gas at the gas station, change the car oil, paint the house, glue something back together, drink alcohol, or as an anesthetic when we undergo surgery. Solvents are highly volatile in air and are readily absorbed by the lung when the vapors are inhaled. The small molecular weight of most solvents and their high fat solubility means they are easily absorbed across the skin. Occupational exposure to solvents is common, with an estimated 10 million workers in the United States exposed either though inhalation or skin contact. Acute exposure can result in loss of coordination, reduced speed of response, and general feeling of drunkenness. Long-term exposure can result in decreased learning and memory, reduced ability to concentrate, changes in personality, and even structural changes in the nervous system.

Robert Hinckley's (1880's) "The First Operation with Ether"

Some people find the effects of solvents on the nervous system desirable and purposely inhale (sniff) solvents to induce a form of intoxication. In the United States approximately 15% of high school students have tried solvent inhalation at least once. Solvents available for inhalation and abuse are common in the home. Home products that may contain solvents included paints, paint remover, varnishes, adhesives, glues, degreasing and cleaning agents, dyes, marker pens, printer inks, floor and shoe polishes, waxes, pesticides, drugs, cosmetics, and fuels, just to name a few.

In general there few benefits to solvent exposure and it should be avoided. The one important exception is the use of solvents to induce unconsciousness prior to surgery. As mentioned above, the solvent ether was discovered centuries ago but not used in surgery until the 1840s. Some physicians and dentists first became aware of effects of ether during "ether frolics" while attending school. Nitrous oxide was also experimented with around the same time but was not widely adopted by dentists and surgeons until the 1860s. Despite its liver toxicity, chloroform was also used as an anesthetic particularly in England and Scotland starting in the late 1840s. Anesthetic agents changed little until the accidental discovery of cyclopropane in 1929. With the increased use of electronic equipment in the surgery area, the flammability of the anesthetic agents became an important issue. In 1956, halothane was discovered by researchers in England, ushering in a new era in anesthesiology.

The use of solvents greatly expanded with the industrial revolution, which resulted in their widespread release into the environmental. Solvents, such as volatile organic compounds (VOCs), readily evaporate into air, for example, when oil-based paint dries. Industrial release also occurs during manufacture or spills. Solvent contamination of drinking water is not uncommon and is a public health issue. VOCs that enter the groundwater become trapped until released during use. Human exposure occurs from drinking water or from exposure during bathing. Solvents such as benzene and trichloroethylene are commonly found at hazardous waste sites and may endanger nearby groundwater.

Biological Properties

From a biological perspective the most important properties of solvents are their volatility, high fat solubility (lipophilicity) and small molecule size. Solvents with these characteristics are termed volatile organic compounds (VOCs). Under normal working conditions solvents readily evaporate into the air, from which they enter the lungs. The high lipid solubility and small size means they are quickly absorbed across lung membranes and enter the blood supply. Blood from the lung moves directly to the brain and other body organs before reaching the liver, where metabolism of the solvent occurs. With ongoing exposure equilibrium is reached between body burden and concentration of the solvent in the air.

Solvents are well absorbed following oral or skin exposure. Most solvents are quickly absorbed from the gut, although the presence of food may delay absorption. Alcohol is a good example of a solvent typically consumed orally. The skin offers little barrier to solvents. Skin exposure to solvents can result in local irritation and increased blood levels of the solvent.

Solvents are eliminated from the body by metabolism or exhalation. The more volatile and fat-soluble the solvent, the greater its concentration in exhaled air. Exhaled air can be used to estimate solvent concentration in the blood, as in breath analysis for alcohol exposure. Metabolism of solvents occurs primarily in the liver by P450 enzymes. In most cases the metabolism results in reduced toxicity and increased elimination of the resulting products. The toxicity of toluene is reduced when liver enzymes change the compound so that it does not readily cross cell membranes. On the other hand, the toxicity of benzene is increased when it is changed to a compound that can attack the blood forming cells of the bone marrow causing leukemia. There is considerable variability from one person to another in their ability to metabolize solvents. Subtle genetic difference can increase or decrease an individual's ability to metabolize certain solvents, resulting in more or less toxicity. The liver is also prone to damage by some solvents, for example, carbon tetrachloride (CCl_4). This damage can actually be made worse by prior exposure to alcohol.

Table 11.1 Products that contain solvents

Products that are mostly solvent	Partially solvent based
Gasoline	Glues
Diesel fuel	Adhesives
Charcoal lighter fluid	Oil based paints
Lantern fuel	Furniture polishes
Grease	Floor polishes and waxes
Lubricating oils	Spot removers
Degreasing agents	Metal and wood cleaners
Paint strippers	Correction fluid
Paint thinner	Computer disk cleaner
Turpentine	Varnishes and shellacs
Nail polish remover	Wood and concrete stains
Rubbing alcohol	

Health Effects

The majority of us are exposed to low levels of solvents every day. Millions of workers around the world are exposed to high levels of solvents on a daily basis that can adversely affect health. Workers often come in contact with more than one solvent during a day's work. Health hazards from solvent exposure range from mild to life threatening

depending on the compound involved and the level and duration of exposure. It should also not be forgotten that many solvents are highly flammable and that fire is also a significant health hazard.

Acute effects often involve the central nervous system because of the rapid absorption of the solvent from the lungs and direct distribution to the brain. The immediate effects may result in drowsiness or mild impairment of judgment . In most situations these effects are not serious and will end quickly once exposure stops. In some circumstances a slight lapse of judgment could be disastrous. A person responding to a hazardous materials spill or perhaps a fire must take appropriate precautions to limit exposure to any solvents that could impair their judgment and thus increase risk of injury.

Chronic exposure to solvents can result in a range of organ-system effects. Damage to the peripheral nervous system results in tingling sensation and loss of feeling in the hands and feet, increased reaction time, and decreased coordination. Reproductive effects included decreased and damaged sperm causing a loss in fertility. Liver and kidney damage is possible from a range of solvents. Cancer is also caused by a number of different solvents such as benzene and carbon tetrachloride.

There is no doubt that repeated exposure to high levels of solvent can result in permanent damage to the nervous system. These changes may result in impaired learning and memory, decreased attention span and other psychological effects. There is also considerable data to indicating that chronic low-level exposure to solvents can result in a cluster of symptoms variously referred to as painter's syndrome, organic solvent syndrome or chronic solvent encephalophathy. The painter's syndrome was first described in Scandinavia in the late 1970s and became a recognized occupational disease in these countries. The cluster of symptoms includes headache, fatigue, sleep disorders, personality changes, emotional liability, progressing to impaired intellectual function and ultimately dementia. Early symptoms are often reversible if exposure is stopped.

Table 11.2 Health Effects of Solvents

Effects of Solvents	**Examples**
Reproductive hazard	methoxyethanol, 2-ethoxyethanol, methyl chloride
Developmental hazard	alcohol (ethanol)
Liver or kidney damage	toluene, and carbon tetrachloride, 1,1,2-2-tetrachloroethane, chloroform
Nervous system damage	n-hexane, perchloroethylene, n-butyl mercaptan
Cause cancer	carbon tetrachloride, trichloroethylene, 1,1,2,2-tetrachloroethane, perchloroethylene, methylene chloride, benzene

Visual system	methanol

The easy availability of solvents in commercial and household products combined with the rapid onset of nervous systems effects encourages the use of solvents as an intoxicating drug. The recreational inhalation of solvents can produce euphoria, visual and auditory hallucinations and sedation. As mentioned above, repeated exposure to high levels of solvents results in permanent brain damage. Beyond purposeful inhalation for the direct nervous system effects there is accidental exposure. Children that accidentally drink furniture polish or other solvent based household products are vulnerable to nervous system effects and possibly pneumonitis.

Reducing Exposure

From a health perspective there are few redeeming features of solvents except when used as anesthetics. Clearly the simple recommendation is to avoid exposure unless administered for some medical reason. In the workplace, appropriate ventilation and personal safety equipment should be in place at all times. There are numerous national and international regulations on solvent exposure in the workplace. Substitution of less-toxic solvents in processes and products can reduce the risk of injury.

Regulatory Standards

In workplaces, standards and exposure recommendation are complex because they must address both level and duration of exposure. Below are some of the common terms used in establishing exposure recommendations.

STEL – Short term exposure limits (15 minute exposure) – protect on acute effects --- protect against loss of consciousness or loss of performance – allow need for short term exposure in emergency situation
TLV – Threshold Limit Value
TWA – Time Waited Average (acceptable for 8 hr day, 40 hr week)
TLV-C – Threshold Limit Value-C (ceiling not to be exceeded)

Recommendation and Conclusions

Solvents are common around the home and workplace. As with most toxic substances, the best policy is to substitute less-toxic products whenever possible, and reduce exposure via ventilation or protective equipment if substitutes are not available. Inhalation of solvents is particularly dangerous because of the rapid exchange in the lungs and quick access to the nervous system. Solvent inhalation produces predictable short-term effects but the long effects of repeated solvent exposure are not well characterized.

More Information and References

Slide Presentation

- A Small Dose of Solvents presentation material and references online: www.asmalldoseoftoxicology.org
  Web site contains presentation material related to the health effects of solvents.

Specific solvents

For information on specific solvents, the Agency for Toxic Substances and Disease Registry (ATSDR) provides the following fact sheets:

- Benzene (258 KB, PDF)
- Acetone (140 KB, PDF)
- Tetrachloroethylene (PCE or PERC) (259 KB, PDF)
- Trichloroethylene (TCE) (259 KB, PDF)
- Xylenes (72 KB, PDF)

European, Asian, and International Agencies

- United Nations Office on Drugs and Crime (UNODC). Online: http://www.unodc.org/ (search for "solvent abuse) (accessed: 3 October 2020).

North American Agencies

- US Department of Labor – Occupational Safety & Health Administration (OSHA). Online: < https://www.osha.gov/solvents/> (accessed: 3 October 2020).
  This site has extensive information on solvents in the workplace. Millions of workers are exposed to solvents on a daily basis.

- US Agency for Toxic Substance Disease Registry (ATSDR). Online: <http://www.atsdr.cdc.gov/> (accessed: 3 October 2020).
  Site contains fact sheets and case studies on many common solvents.

- US National Institute on Drug Abuse (NIDA). Online: https://www.drugabuse.gov/publications/drugfacts/inhalants or https://www.drugabuse.gov/drug-topics/inhalants. Inhalants DrugFacts (accessed: 3 October 2020).
  Site contains information on inhalants and solvents as drugs of abuse.

- Cabezas*, H C., P F. Harten*, AND M. R. Green. DESIGNING GREENER SOLVENTS. Shanley, A.M. (ed.), CHEMICAL ENGINEERING. Chemical Week Associates, 107(3):107-109, (2000).

- Risk Evaluation for Trichloroethylene (TCE) - https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-evaluation-trichloroethylene-tce#:~:text=Trichloroethylene%20%28TCE%29%20is%20currently%20undergoing%20risk%20evaluation%20under,Chemical%20Assessments%3B%20TCE%20is%20on%20the%20Work%20Plan.

- US National Library of Medicine. Tox Town – Solvents. Online: Discontinued. (accessed: 3 October 2020).

- US National Institute for Occupational Safety and Health (NIOSH). Organic Solvents. Online: http://www.cdc.gov/niosh/topics/organsolv/. (accessed: 3 October 2020).
  Excellent information on a wide range of solvents.

- US Department of Veterans Affairs - Health effects of exposure to solvents Online: https://www.publichealth.va.gov/exposures/solvents/index.asp#:~:text=Health%20effects%20of%20exposure%20to%20solvents%201%20Inhaled,Ingested%3A%20Although%20rare%2C%20this%20can%20cause%20serious%20illness. (accessed: 3 October 2020).

Non-Government Organizations

- Anesthesia Nursing & Medicine. Online: https://nurse.org/resources/nurse-anesthetist/ (accessed: 3 October 2020).
  Site has in-depth information on the history and current practice of anesthesia.

- American Lung Association. Toxic Air Pollutants. Online: https://www.lung.org/clean-air/outdoors/what-makes-air-unhealthy/toxic-air-pollutants (accessed: 3 October 2020).
  General information on the health effects of toxic air pollutants.

- The Wood Library-Museum of Anesthesiology. Online: < http://www.woodlibrarymuseum.org/ > (accessed: 3 October 2020).
  The objective of the Wood Library-Museum of Anesthesiology is to collect and preserve literature and equipment pertaining to anesthesiology and to make available to the anesthesiology community, others in the medical profession and the public the most comprehensive educational, scientific and archival resources in anesthesiology

Wikipedia

Solvent - https://en.wikipedia.org/wiki/Solvent
Chronic solvent-induced encephalopathy - https://en.wikipedia.org/wiki/Chronic_solvent-induced_encephalopathy
Inhalant - https://en.wikipedia.org/wiki/Inhalant

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