Putting it into Practice: Pediatric Environmental Health Training Resource

Children and Solvents

User Guide

Children's Environmental Health Network

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I. What are solvents?

A solvent is any substance that dissolves another substance to make a solution. Give the example of making lemonade by dissolving a powdered mix in water. In this case, water is the solvent, the powder is the solute, and the end solution is lemonade. Solvents can be characterized by their physical and chemical properties. There are 17 classes of solvents, including but not limited to aromatics, alcohols, glycols, ketones, and chlorinated hydrocarbons.

II. Main Topics

- Toxic solvents are ubiquitous.
- Children, fetuses, and others are at risk to solvent exposure.
- Adult symptoms related to solvent exposure are broad and well-known, but in children, symptoms are largely ill-defined.
- Alcohol (ethanol) and toluene transplacental exposure can lead to fetal alcohol spectrum disorder and fetal solvent syndrome, respectively.
- Trichloroethylene in maternal drinking water is associated with cardiac defects in offspring and pediatric cancer clusters.
- Simple measures as well as policy changes can prevent child and fetal solvent exposure.

III. Sources of Solvents: Inadvertent Exposure

Inadvertent exposure can occur in the household. A study conducted by the US Department of Health and Human Service, Agency for Toxic Substances and Disease Registry, showed that there are higher concentrations of solvents in air inside the home than out (2000).[1] Potential sources of solvents in the household include cleaning products, recently dry cleaned clothing, cigarette smoke, vinyl shower curtains, and craft glues and paints. Personal care products, like fingernail polish remover, hand sanitizer, and mouthwash, also contain and de-gas solvents. Another source of solvent exposure is on the job. A few prime examples are listed: shoemakers, electronic assembly plants (printers), rubber, paint & other chemical manufacturing plants, automobile repair shops & gas stations, nail & hair salons, laboratories, and hospitals (hand sanitizer use). (Slides 7-9)

In particular, electronic assembly plant workers had a blood toluene level up to 4 orders of magnitude higher than background, after being exposed to 34 ppm toluene for 8 hours.[2] (Brugnone et al. 1995) Another poignant example is hand sanitizer use in hospital settings. Use of hand sanitizers every 5 min for 10 hrs resulted in urinary ethanol biomarker levels that far exceed levels indicative of ethanol intentional consumption in adults.[3] (Reisfield et al. 2011)

Children and pregnant women should limit time spent in these environments or avoid them all together.

In addition, most research on the health effects of solvent exposure has focused on exposure in the industrial setting. Slide 10 provides Occupational Health and Safety Administration limits for 4 widely used solvents: ethanol, perchloroethylene, toluene, and xylene. Keep in mind that in the work place, exposures are often not averaged over an 8-hr shift. As a result, average exposures can be much higher or lower than reported.

Other sources of solvents are in the environment: (e.g. gasoline and its combustion products, groundwater contamination, and air near high solvent discharge areas, such as dry cleaners, busy roadways, or farms due to pesticide use).

IV. Sources of Solvents: Intentional Exposure

Not all solvent exposure is inadvertent. Intentional exposure (slides 12-17) in the pediatric population refers to the use/abuse of ethanol, toluene, and other solvents, as well as anesthetics by pregnant and nursing women and adolescents. Intentional exposure to solvents generally occurs at much higher concentrations than is found in the environment. Even so, we can use what we know about the outcome of individuals who abused solvents or who were exposed occupationally to high levels of solvents, to guide research efforts in determining the effect of environmental levels of solvents on children and fetuses. Likewise, information gleaned from intentionally exposed individuals can help us know what to look for clinically. Alcohol use in the adolescent population is high. Roughly 75% of students have consumed alcohol by the end of high school & more than 1/3 have by 8th grade. Likewise, about 50% of 12th graders have reported having been drunk at least once. Also sobering are the percentage of women who drink during pregnancy: 7.6% of pregnancy women report using alcohol, and 1.4% reported binge drinking in the United States. Fetal alcohol exposure many also occur before women are cognizant of being pregnant. 37% of pregnancies were unplanned, and 52% of non-pregnant child-bearing aged women reported alcohol use in 1982-2010. Probability alone suggests that maternal drinking may take place prior to the recognition of a new pregnancy.

Another avenue of intentional solvent exposure is through solvent inhalation abuse, which occurs through sniffing or huffing glues/paints or solvent-soaked towels that contain combinations of solvents (i.e. toluene, benzene, xylene). Solvent abuse is a cheap and easily assessable recreational drug and imparts a temporary, instant feeling of euphoria, light headedness.

Intentional solvent exposure may occur in the healthcare setting through the use of anesthetics. Anesthetics can have vastly different chemical structures, although all are solvents. They function to put one to sleep, and allow the user to wake without any permanent neurological damage.

V. Pathways of Exposure Overview

Solvents are present in many different environments: the outdoors, the household, in industry, and even in hospital settings. Unfortunately, little is known about the effects of solvents in children at any exposure level or type, although we know that adolescent solvent abusers show similar outcomes as in adults. Children are not small adults, however; they face unique physical and biological risks. Children are in various environments on a day to day basis (day care, car, home, school, etc.) have various levels of mobility, and consume different foods than adults. They have lower breathing zones, where denser vapors may settle in the air. Children also have higher metabolic rates and consume more oxygen relative to their size. Further research is necessary to understand the child response to solvent exposure of various types and levels. Most known health effects related to solvent inhalation exposure have been observed within occupationally exposed adults as well as adult and adolescent solvent abusers (Slides 21-22). As a result, research on health effects related to solvent exposure is limited to mainly acute or chronic use at high inhalant levels. Other modes of exposure include ingestion, dermal absorption, and transplacental. Discussion of each of these four modes follows:

Inhalation Exposure

Adolescents exposed to solvent via inhalation have a range of symptoms, including headache, respiratory irritation, central nervous system depression (CNSD), light-headedness, vertigo, loss of consciousness, fatigue, decreased manual dexterity, death from CNSD, cardiac arrhythmias, renal and hepatic failure, and asphyxia.

Schreiber et al. evaluated the health effects related to perchloroethylene exposure in residents who lived near dry-cleaning facilities. In general, they found that exposure alters neurobehavioral function, but in children, they also saw marked decreases in visual contrast sensitivity, a measure of vision.[4] (Schreiber 2002)

Organic dry cleaning has recently been getting public attention. Organic dry cleaning is an unregulated term, but generally applies to dry cleaning methods that do not use perchloroethylene. Three types of organic dry cleaning are the patented method GreenEarth Cleaning, hydrocarbon cleaning, and CO2 cleaning.

Oral and Dermal Exposure

There is little known about the health effects related to oral exposure to solvents other than ethanol. Slide 25 lists two examples of solvent consumption: an adult who consumed toluene, and a child who consumed tetrachloroethylene related to a dry cleaning accident. Furthermore, nursing infants can consume solvents via breast milk of exposed mothers. The Agency for Toxic Substances and Disease Registry showed that exposed mothers can display higher solvent concentrations in their breast milk than in their blood. The health effects on the nursing infant are unknown, however.

Solvents can also cause damage if children are exposed through their skin. Solvents can often remove skin lipids, cause dermatitis, and can even impart genotoxic damage to the skin.

Transplacental Exposure

An additional area of concern when discussing solvent exposure is the effect on fetuses via maternal exposure. One of the most publicized solvents related to birth defects is ethanol, which was well known even in biblical times. Occasional to heavy ethanol exposure *in utero* can lead to fetal alcohol spectrum disorder. In addition to maternal drinking, exposure to alcohol *in utero* can occur in other settings, including inhalation in the work place or hospital. While small amounts of ethanol can cause fetal alcohol spectrum disorder, which is primarily an insult to the brain, fetal alcohol syndrome (FAS) occurs from heavy prenatal ethanol consumption. Fetal alcohol syndrome occupies the most severe end of the spectrum. Ethanol exposure at any level during pregnancy, however, can result in birth defects of the eyes, heart, and brain.

Receiving less attention but still a public health concern is maternal toluene exposure. There is currently no established fetal solvent spectrum disorder; however, heavy toluene-inhalant abuse can result in fetal solvent syndrome (FSS), which (similar to ethanol) affects development of eyes, heart, and brain. Patients with FSS share many phenotypic similarities with FAS-affected patients, but also have several unique characteristics, which are listed on Slide 34. Slides 31 and 35 offer images and descriptions of the facial features of children with FAS and FSS, respectively.

The eye is a shared target for both toluene and ethanol toxicity, manifesting as micropthalmia, retinal defects, dysfunction of rods, and optic nerve hypoplasia. Till et al. showed that pregnant women exposed occupationally to toluene had offspring with reduced visual function. One potential mechanism for the eye as a target is its high lipid content, which solvents, such as ethanol and toluene, may solubilize.[5] (Till 2005)

In utero exposure to solvents may even occur in controlled environments, such as the hospital. Between 0.5-2% of pregnant women receive surgery that requires anesthetics. Sylvester et al. has shown that fetal exposure to general anesthesia during the 1st trimester was associated with hydrocephalus and eye malformations.[6] (Sylvester 1994)

VI. Pediatric Cancer Clusters

Slides 38-39 focus on two childhood cancer clusters associated with maternal drinking water that had been contaminated with trichloroethylene. Exposure to solvents caused cancer clusters to develop in these two geographic areas. A cancer cluster is defined as the occurrence of a greater than expected number of cancer cases within a given geographic area. In particular, Woburn, MA, and Tom's River, NJ, are known for greater than expected numbers of childhood cancer due to contaminated drinking water.

In the Woburn cancer cluster, 21 cases of childhood leukemia from 1969-1989 occurred; in contrast, normal projected frequency of pediatric leukemia during this time was only 5.5 cases.

Jonathan Harr's 1996 novel *A Civil Action* and subsequent movie starring Jon Travolta (1998) has increased awareness of this tragic event.

Another cancer cluster due to water contaminated with trichloroethylene and other solvents occurred in New Jersey, where 90 cases of childhood cancer have been documented between 1975 and 1995, with only 10 cases having been expected.

In addition to the aforementioned cancer clusters, trichloroethylene is strongly associated with congenital heart defects, shown in both epidemiologic and animal model studies. Slide 44 lists four example studies that utilized animal models to link maternal TCE exposure to congenital heart defects. The studies have shown that maternal TCE exposure can disrupt gene expression in myocytes.

VII. Diagnostic Tests and Treatment

There are several biomarkers that can be measured in blood, expelled air, and urine. Many drawbacks to relying on this test exist, however. The biomarkers are unique to the solvent, and the half-lives of solvents and their byproducts are very short.

The treatment for solvent exposure mainly focuses on removing the patient from the source and/or removing the solvent from the patient. Unfortunately, there is no simple antidote. Treatments do vary across mode of exposure and type of solvent. For inhalation, remove the patient from the source, reduce his/her physical activity, and provide oxygen therapy. For ingestion of aromatic hydrocarbons, such as toluene, benzene, and xylene, activated charcoal and lavage can be used. A risk is aspiration, however. Also, increase fluid consumption to increase excretion. For dermal exposure, remove affected clothing and wash exposed area with soap and water. If eyes are affected, flush eyes for 10-15 minutes.

VIII. How to Reduce Solvent Exposure

One of the main purposes of this teaching module is to educate listeners about solvent exposure in order to prevent it. There are a number of easy fixes that we can implement to reduce solvent exposure and use:

- Air out recently dry cleaned clothes before bringing indoors
- Avoid solvent-heavy cleaners, glues, and paints or use with proper ventilation
- Properly store and/or lock up all household chemicals
- Avoid bringing children to nail salons
- Dispose of household chemicals properly
- Avoid using vinyl shower curtains

Please note that while employing "easy fixes" certainly reduces risk of exposure, it does not eliminate it, due to the ubiquity of solvents.

In addition to personal changes, we can also limit solvent exposure through policy. The Safe Chemicals Acts of 2013 is a pending policy change to the Toxic Substances Control Act of 1976. The changes would require EPA to identify the worst chemical offenders, require basic health and safety information for chemicals in market goods, update chemical safety assessment methods, and empower the EPA to restrict chemicals with risks to health and the environment.

In addition to national policy, work has been done at the state level to regulate children's exposure to toxic substances, such as solvents. In particular, Washington State has implemented the Child-Safe Products Act. Under this Act, lead, cadmium, and phthalates have been limited in children's products that can be sold in state. Also, the act demanded manufacturers to report particular chemicals that are used in their products. Such chemicals include but are not limited to toluene, xylene, and benzene.

IX. Communicating with Parents about Environmental Exposures

One of our many roles as pediatricians is to educate our patients. A few ways to approach conversations with parents are to:

- Identify risks that are specific to the parent and child (i.e. hobbies, occupation, drug abuse)
- Review preventative measures ("easy fixes" as listed on Slide 47) and discuss common sources of solvent exposure (personal care products, household cleaners, nail salons, job sites, etc.).
- Review health concerns and risks related to solvent exposure

These conversations can help heighten parental awareness and prevent first-time or repeat exposures.

X. Helpful Links

- Agency for Toxic Substances and Disease Registry: *www.atsdr.cdc.gov*
- Center for Disease Control: Fetal Alcohol Syndrome: *www.cdc.gov/ncbddd/fasd/index.html*
- Center for Health, Environment and Justice (Vinyl Shower Curtain Report): *http://watoxics.org/files/VolatileVinyl.pdf*
- Health Building Network: *http://healthybuilding.net/*
- List of Hazardous Arts and Crafts Material (2009): *www.oehha.org/education/pdf_zip/ArtOct2009.pdf*
- Occupational Safety and Health Administration: *www.osha.gov*
- Safe Chemicals Act: *http://www.saferchemicals.org/safe-chemicals-act/*
- Substance Abuse and Mental Health Services Administration: *www.oas.samhsa.gov*

CASE STUDY

A Case Study, taken directly from the Agency for Toxic Substances and Disease Registry website: A 28-year-old pregnant female comes with complaints of coughing spasms, chest tightness, and a sensation of being unable to breathe. These symptoms began about 6 hours earlier, while she was repainting a bicycle with an acrylic lacquer spray paint in a small, poorly ventilated basement area for 2 hrs. The patient also experienced nausea, headache, dizziness, and lightheadedness, which cleared within an hour after leaving the basement area. The chest and respiratory complaints, however, have persisted, prompting the office visit. She is concerned that her symptoms are related to the paint spraying and might affect her pregnancy.

1. *What further information and history would you attempt to elicit?*
2. *One of the ingredients in the spray paint is toluene. Could this be responsible for the patient's symptoms?*
3. *The patient is concerned about possible effects on the fetus. What advice would you offer?*
4. *How will you treat this patient?*

Related discussion material can be found in the handbook for the case study: http://www.atsdr.cdc.gov/csem/toluene/docs/toluene.pdf.

KEY RESOURCES FOR FURTHER READING

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Select Additional Resources

Sources of Solvent Exposure

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Inhalation Exposure

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Oral Exposure

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Cancer Clusters

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Treatment

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<u>Note:</u> This User Guide is intended to accompany the PowerPoint module of the same name. It elaborates on some studies which may require more in-depth information than what is provided on the slides. However, the contents of all slides in the module are equally important to present.

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