Putting it into Practice: Pediatric Environmental Health Training Resource

Children and Solvents

Children's Environmental Health Network

Authors

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What is a solvent?

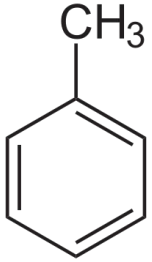
- Any substance that dissolves another substance to make a solution
  - Water is an example of a powerful solvent
  - Think about making lemonade by dissolving a powdered mix in water

Characterization of Solvents: Physical and Chemical Properties

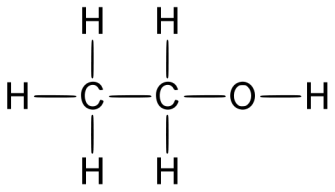
- Solubility & Polarity
- Flammability & Explosiveness
- Volatility
- Density
- Chemical structure (organic vs inorganic)

Classes of Solvents

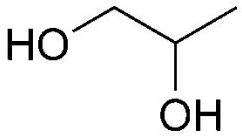
- 17 classes
- Examples
  - Aromatic (e.g. toluene)
  - Alcohols (e.g. ethanol, methanol)
  - Glycols (e.g. glycol ether, propylene glycol)
  - Ketones (e.g. methyl ethyl ketone)
  - Chlorinated hydrocarbons (e.g. trichloroethylene, perchloroethylene, tetrachloroethylene)



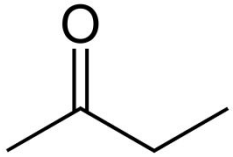
toluene



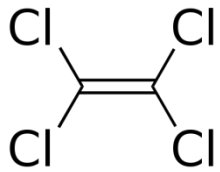
ethanol



propylene glycol



methyl ethyl ketone *aka* butanone



perchloroethylene

Why should we care about solvents outside chemistry class?

- 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 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.

Sources of Solvent Exposure
In the Household

Higher concentration of solvents in air inside the home than out

Source	Solvent (most common)
Household cleaners	Toluene *in 47% of all household products* in addition to xylenes, methyl ethyl ketone, acetone, methylene chloride, etc.
Recently dry cleaned clothing	Chlorinated Hydrocarbons (Perchloroethylene)
Cigarette smoke	Toluene *blood levels 3.5 X higher in smokers*
Vinyl shower curtains	Toluene, cyclohexanone, methyl isobutyl ketone, ethylbenzene degassing
Craft glue and paint/paint thinner	Toluene, xylene, etc.

ATSDR, 2000; Lin, Y.S. *J. Exposure Sci,* 2008; Lester, S. Center for Health, Environ. Justice, 2008.




Sources of Solvent Exposure
In Personal Care Products

Source	Solvent (most common)
Fingernail polish & remover	Toluene, butyl/ethyl acetate, acetone
Hand sanitizer	Isopropanol, ethanol, n-propanol
Mouthwash	Ethanol




Sources of Solvent Exposure

On the Job via Solvent Use

- Shoemakers
- Electronic assembly plants (printers)
- Rubber, paint & other chemical manufacturing plants
- Automobile repair shops & gas stations
- Nail & hair salons
- Laboratories
- Hospitals (hand sanitizer use)




Examples of Occupational Health and Safety Administration Limits

Substance	8 hr limit (ppm)	10 min limit (ppm)
Ethanol	1000	N/A
Perchloroethylene	100	300
Toluene	200	500
Xylene	100	200

Negative health effects can occur at air concentrations well below these limits.

Sources of Solvent Exposure

In the Environment

Source	Solvent
Gasoline and its exhaust	Ethanol, & BTEX (benzene, toluene, ethylbenzene, xylene)
Groundwater	Volatile organic solvents difficult to filter out
Air	Residences near dry cleaners, busy roadways, farms (pesticide use)

Aguilera, I. *Environ. Health Persp.*, 2009.




Intentional Exposure

- Refers to the use/abuse of ethanol, toluene, and other solvents as well as the use of anesthetics
- Much of what we know about the health effects of solvents is based on individuals who are intentionally exposed or those occupationally exposed at high levels

Intentional Exposure

Alcohol Use/Abuse

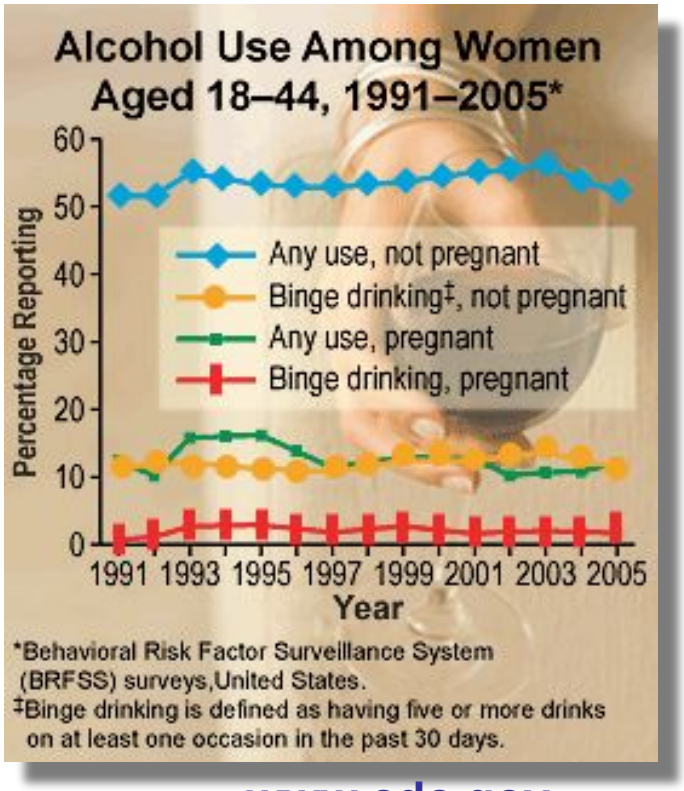
- In Adolescents
  - Roughly 75% of students have consumed alcohol by the end of high school & more than 1/3 have by 8th grade
  - About 50% of 12th graders have reported having been drunk at least once

Johnston, L.D. Institute for Social Research, 2012.

Intentional Exposure

Alcohol Use/Abuse

- In Pregnant women
  - 7.6% of pregnant women used alcohol & 1.4% binge drank
- Unplanned pregnancies and alcohol use
  - 52% of non-pregnant, childbearing-aged women reported alcohol use
  - 37% of pregnancies were unplanned during 1982-2010



www.cdc.gov

Mosher, W.D. *Natl.Health Stat. Report*, 2012.

Intentional Exposure

Solvent Inhalation Abuse

(100-15,000 ppm toluene in one sitting)

How?

- Occurs through sniffing or huffing glues/paints or solvent-soaked towels that contain combinations of solvents (i.e. toluene, benzene, xylene)

Why?

- A cheap and easily assessable recreational drug
- Imparts a temporary, instant feeling of euphoria, light headedness

Intentional Exposure
Solvent Inhalation Abuse

(100-15,000 ppm toluene in one sitting)

- >22 million Americans ≥ 12 yo have intentionally used inhalants
- Inhalant abuse among high school students has held steady between 4-9% since 2001
  - Low proportions of this cohort perceived inhalant abuse once or twice to be a “great risk”

SAMHSA 2007; Johnston, L.D. Institute for Social Research, 2012.

Intentional Exposure

In the Healthcare Setting

Anesthetics

- Vastly different chemical structures
- All are solvents
- Have same function




Pathways of Exposure

- **Chronic and Acute**
  - **Inhalation**
  - **Ingestion**
  - **Dermal absorption**
  - **Transplacental**

Health Effects in Children

- Little known about effects in children at any exposure level or type
- Children are not small adults
  - Unique physical risks
    - Changing locations, levels of mobility, food consumption
    - Lower breathing zones
    - Metabolic rate higher in children
    - Oxygen consumption relative to size of child higher
  - Unique biological risks
    - Differences in how children absorb, distribute, and/or metabolize chemicals

Bearer, C.F. *Environ. Health Persp.,* 1995.

Health Effects in Adolescents

Inhalation Exposure

- Source of information on acute and chronic high dosage, airborne exposure from:
  - Occupationally exposed adults
  - Adult and adolescent solvent abusers
- Little known about symptoms related to acute or chronic exposure at low dosage

Health Effects in Adolescents

Short-term/acute Inhalation Exposure

- Headache
- Respiratory irritation
  - Nose, throat, eye irritation
- Central nervous system depression (CNSD)
  - Light-headedness
  - Vertigo
  - Loss of consciousness
  - Fatigue
- Decreased manual dexterity
- Death
  - CNSD, cardiac arrhythmias, renal and hepatic failure, asphyxia

Health Effects in Adolescents

Long-term/chronic Inhalation Exposure

- CNSD
- Peripheral neuropathies
- Cancer
- Liver toxicity
- Bone marrow suppression
- Renal toxicity
- Cardiac toxicity

Health Effects in Children
Long-term/chronic Inhalation Exposure

Perchloroethylene (perc) used in dry cleaning

- Environmental perc exposure at a mean level of 4,980 µg/m^3 (median = 1,360 µg/m^3) alters neurobehavioral functions in residents living near dry-cleaning facilities
- Visual contrast sensitivity scores of exposed children ranked less than the 12th percentile of control scores
  - These children also displayed color discrimination deficiencies
- Higher rates of kidney cancer in residents living near perc-using dry cleaners

Schreiber, J.S. *Environ Health Persp,* 2002;
Ma, J. *J Environ. Public Health,* 2009.

Organic Dry Cleaning

Not a regulated term, but applies to dry cleaning methods that do not use perc

- Patented GreenEarth Cleaning
  - Nontoxic, inert, silicon-based solvent that decomposes into silica, water, & CO_2
- Hydrocarbon cleaning
  - Less hazardous than perc, but similar chemical structure
- CO_2 cleaning
  - Converts CO_2 from gas to liquid to clean clothing

Cowles, C. *NY Sun,* 2008.

Health Effects
Oral Exposure

- Little known, excluding ethanol consumption
- Death occurred at 60 mL adult consumption of toluene
  - Renal failure
  - Necrosis of myocardial fibers
  - Lung congestion and hemorrhage
- 6 yo male consumed 12-16 g tetrachloroethylene
  - Drowsiness, vertigo, agitation, hallucinations before coma, with recovery and no follow-up
- Consumption of breast milk from solvent-exposed mothers
  - Higher levels than in maternal blood b/c of high levels of fats in breast milk

Ameno, K. *Foresnic Sci Int,* 1989; ATSDR, 2012;
Koppel, *J.Toxciol Clin Toxicol,* 1985.

Health Effects
Dermal Exposure

- Solvents remove skin lipids
- Dermatitis
- Genotoxic effects

Health Effects *in Utero*
Transplacental Exposure

- Maternal Alcohol Exposure/Consumption
  - Fetal alcohol spectrum disorder
  - Severe end of FASD = fetal alcohol syndrome
  - Birth defects (eyes, heart, brain)
- Maternal Toluene Inhalation
  - Heavy inhalant abuse = fetal solvent syndrome
  - Currently, no established fetal solvent spectrum disorder.
  - Birth defects (again eyes, heart, brain)
- Maternal Exposure to Anesthetics

What is Fetal Alcohol Spectrum Disorder (FASD)?

"Behold, thou shalt conceive and bear a son; and now, drink no wine or strong drink…"
(Judges 13:7)

- A group of disorders caused by maternal exposure to alcohol
- Diagnosis encompasses the more subtle effects of prenatal alcohol exposure at all levels

What is Fetal Alcohol Syndrome (FAS)?

FAS is on the severe end of Fetal Alcohol Spectrum Disorder (FASD). The greater the ethanol intake, the more severe the outcome.

Initial Studies

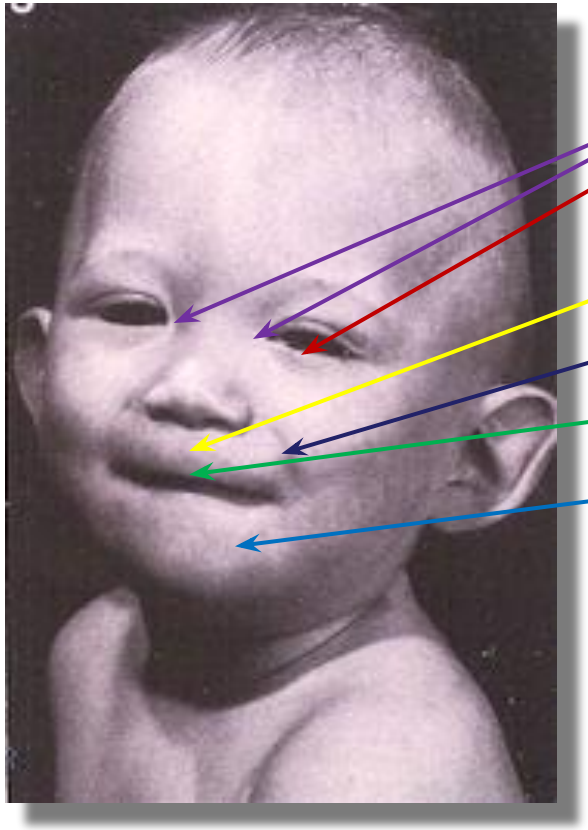
- France, 1968
  - 127 children born to alcoholics
  - common phenotype
- Seattle, WA, 1973
  - 7 children born to alcoholics
  - common phenotype

What is FAS?

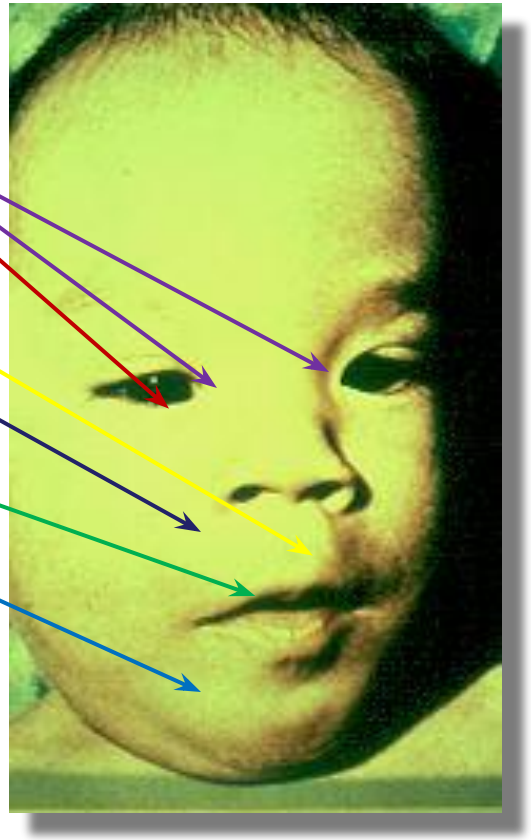
- Criteria made by a committee
- Must meet three criteria:
  - Evidence of growth retardation
  - Evidence of a characteristic pattern of facial anomalies
  - Evidence of CNS neurodevelopmental abnormalities

Kilegman, R.M. *Nelson Textbook of Pediatrics,* 2011.

The Face of FAS



Epicanthal folds
Short palpebral fissures
Smooth philtrum
Maxillary hypoplasia
Thin upper lip
Micrognathia



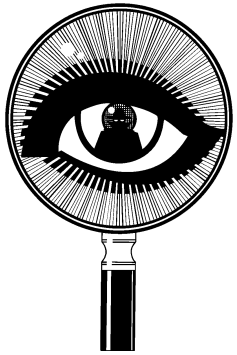
Ethanol is the Leading Known Cause of Mental Retardation in the USA

- 1% of all live births in the USA manifest FAS or **some** prenatal alcohol damage (FASD)
  - FASD can be manifested with exposure to any level of ethanol
  - However, little is known about the effect of small amounts of alcohol exposure on fetal life
- 1 in 3,000 live births with FAS
- FAS and FASD estimated to cost $75 million to $9.7 billion a year in the USA
- **It's preventable!**

www.cdc.gov/ncbddd/fasd/index.html

The Eye May Be a Sensitive Target for Ethanol

- Microphthalmia
- Retinal defects
- Dysfunction of rods
- Optic nerve hypoplasia



What is Fetal Solvent Syndrome (FSS)?

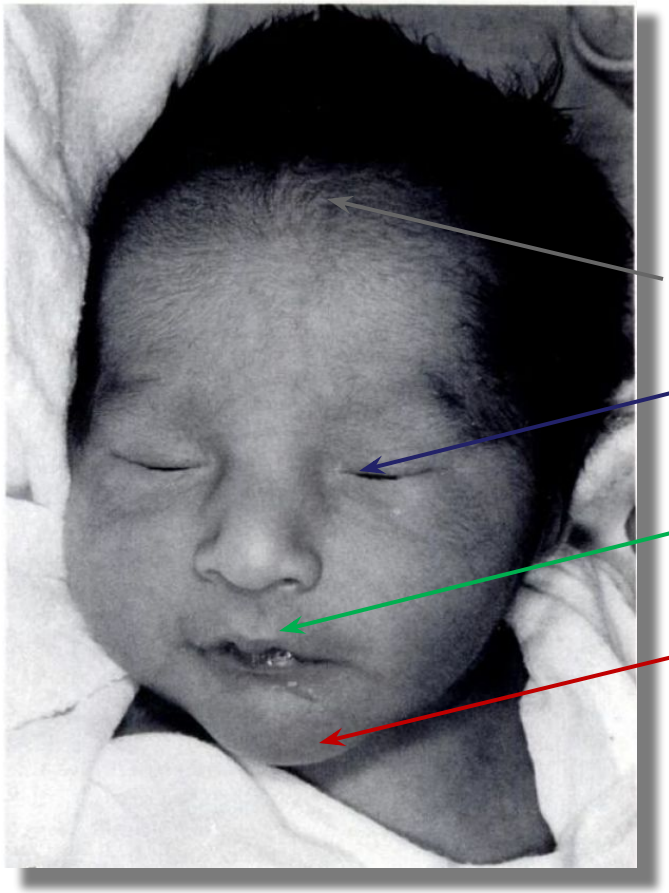
Initial study of toluene embryopathy born to heavy inhalant abusing woman in 1979

Shared phenotypes between FAS and FSS	Phenotypes more characteristic of FSS
Small palpebral fissure	Ear anomalies
Thin upper lip	A narrow bifrontal diameter
Mid-facial hypoplasia	Abnormal scalp hair patterning
Micrognathia (small jaw)	Down-turned corners of the mouth
	A large fontanelle

Pearson, M.A. *Pediatrics,* 1994;
Toutant, C.L. *Lancet,* 1979.

The Face of FSS

Newborn



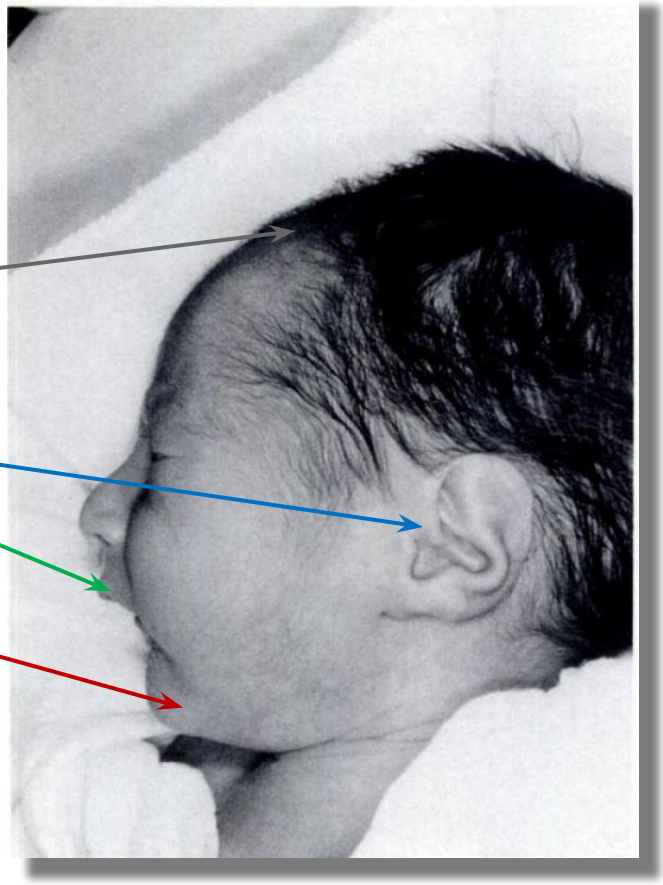
Abnormal scalp hair pattern

Small palpebral fissure

Ear anomalies

Thin upper lip

Micrognathia



Pearson et al. 1994

Eye as a Target Again

- Occupationally exposed pregnant women
  - Offspring had decreased visual function
    - Reduced contrast sensitivity and abnormal red–green vision
- Mechanism
  - The eye is full of lipids, which may be solubilized by solvents

Till, C. *Neurotoxicology,* 2005.

Anesthetics

- 0.5-2% of pregnant women receive surgery
- 1st trimester general anesthesia was associated with:
  - Hydrocephalus with eye malformations
    - OR = 39.6 (95%CI = 7.5 – 209.6)
  - Hydrocephalus with another defect
    - Odds Ratio = 9.6 (95% Confidence Interval = 3.8 – 24.6)

Kuczkowski, K.M. *Obstet Gynecol Sury,* 2004;
Sylvester, *Am J Public Health,* 1994.

Solvent Contaminated Drinking Water

Childhood Cancer Clusters

Trichloroethylene in maternal drinking water

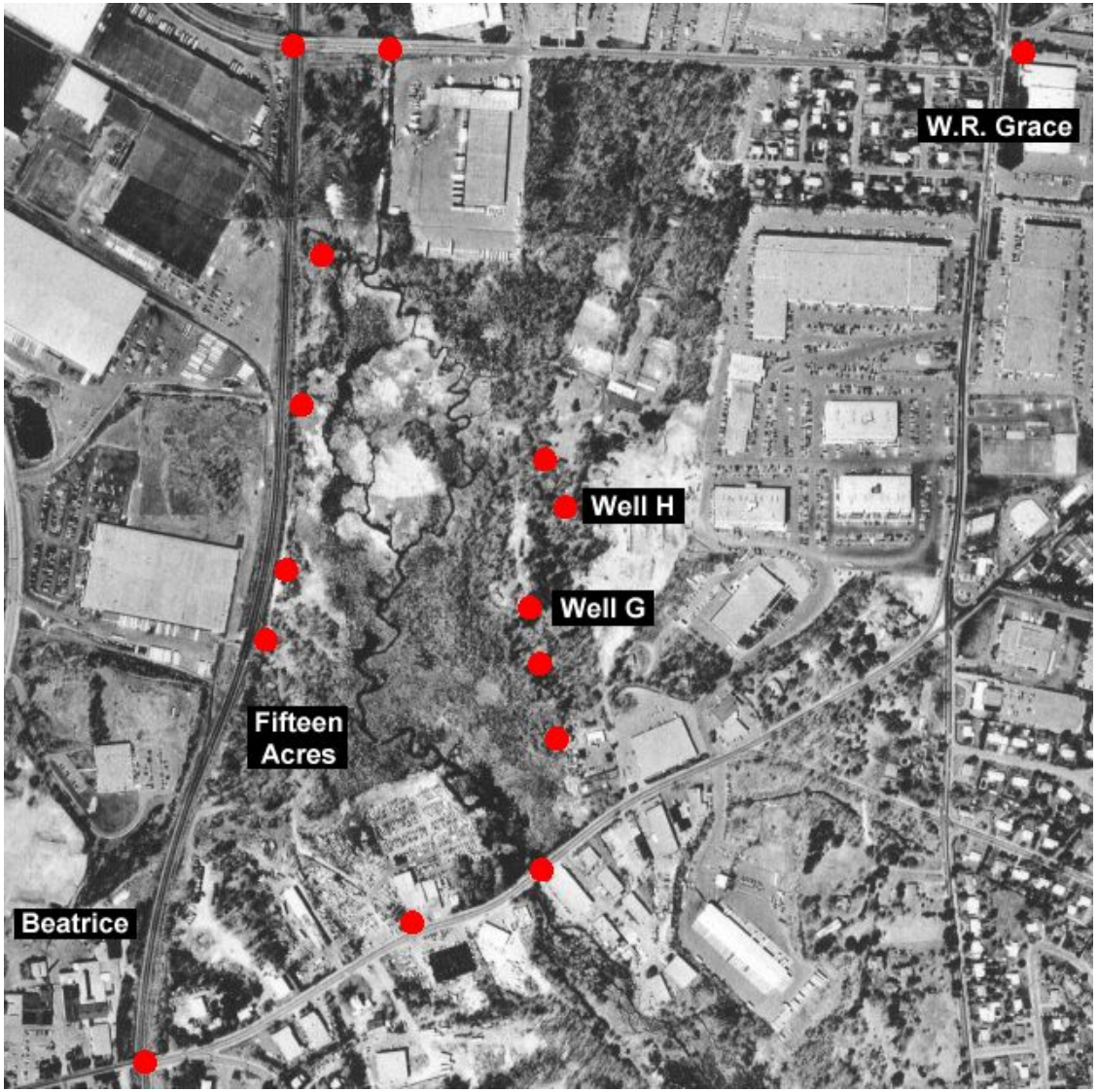
- Woburn, MA
- Tom's River, NJ

What is a cancer cluster?

Occur in a particular geographic area when a higher number of cancer cases are reported than expected

- Woburn, MA
  - 21 childhood leukemia cases from 1969-1986
  - Only 5.5 cases expected
- Tom's River, NJ
  - 90 childhood cancer cases from 1975-1995
  - Only 10 cases expected

Woburn, MA Cancer Cluster (1980s)



Rent the movie:
A Civil Action
with
John Travolta
1998

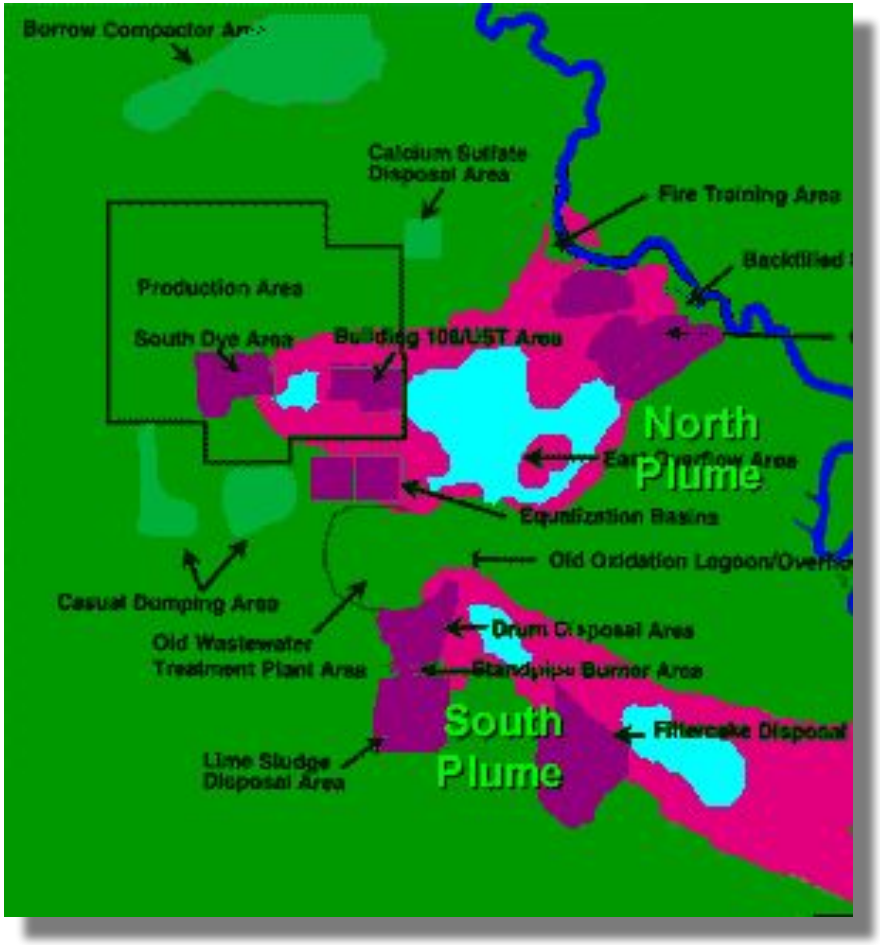
Read the book:
A Civil Action
by
Jonathan Harr
Non-fiction 1996

Woburn, MA

- Trichloroethylene and other solvents contaminated water supply
- 21 cases of childhood leukemia from 1969-1989
- Adjusted odds ratio of 8 for risk of leukemia in child if mother drank well water while pregnant
- Fortunately, since 1986, expected incidence of childhood leukemia returned to expected levels.

Costas, K. *Sci Total Environ,* 2002.

Dover Township, New Jersey
Tom's River Cancer Cluster

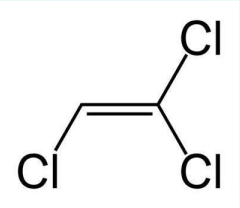


Tom's River Cancer Cluster

- Drinking water contaminated from 2 polluted sites
  - Trichloroethylene, tetrachloroethylene, & other chemicals from Reich Farm
- 90 cases of childhood cancer from 1975 – 1995
  - Leukemia (9 times higher than expected)
  - Brain and CNS cancer (11.5 times higher than expected)
- Association found between maternal consumption of water during pregnancy and childhood cancer

The New Jersey Department of Health and Senior Services, 2001

Trichloroethylene



- Epidemiologic association between trichloroethylene in maternal drinking water and congenital cardiac defects
- Animal model and cell line studies support association
  - Chick model: Reduced epithelial-to-mesenchymal transition of valve progenitors
  - Avian and rat models: Increase in cardiac malformations (i.e. absent coronary artery, aortic valve stenosis, septal defects, etc.)
  - Rat myocytes: Disruption of calcium flux control
  - Bovine endothelial cells: Alteration in endothelial and eNOS function

Boyer, A.S. *Toxciol Sci,* 2000; Johnson, P.D. *Environ. Health Persp,* 2003; Caldwell, P.T. *Toxciol Sci,* 2008; Ou, J. *Toxciol Sci,* 2003.

Biomarkers for Solvent Exposure

- Unmetabolized solvents and their biomarkers can often be found in blood, expelled air, and urine
- But, half-life of solvents and byproducts usually very short

Solvent	Urinary Biomarkers
Toluene	• Hippuric acid • Ortho-cresol • Unmetabolized toluene
Benzene	• t,t-muconic acid
Perchloroethylene Trichloroethylene	• Trichloroacetic acid • Umetabolized perchloroethylene • Unmetabolized trichloroethylene

Treatment

- No antidote
- For inhalation of solvents
  - Remove patient from source
  - Reduce physical activity
  - O_2 therapy, positive pressure ventilation
- For ingestion of solvents
  - Activated charcoal and lavage (risks aspiration)
  - Increase fluid consumption to increase excretion
- For dermal exposure
  - Remove affected clothing
  - Wash exposed area with soap and water
  - Flush eyes 10-15 min.

Rahill, A.A. *Aviat Space Envrion Med,* 1996.

Prevention is key

Remember that children are not small adults

Easy Fixes

- 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

Prevention is key

Long-term goals

- Reduce levels of solvents in occupational settings
- Undergo pre-emptive investigations of communities that may be vulnerable to contaminated groundwater or particulates
- Continue to educate solvent-abusing populations
- Increased research on fuel alternatives to gasoline

National Policy Changes

The Safe Chemicals Act (*pending*)

- Update to Toxic Substances Control Act (1976)
- Led by the late Senator Frank Lautenberg (D-NJ) and Senator Kirsten Gillibrand (D-NY)
- **Goals**
  - To require EPA to identify the worst chemical offenders
  - To require basic health and safety info for chemicals in market goods
  - To update chemical safety assessment methods
  - To empower the EPA to restrict chemicals with risks to health and the environment

State-level Policy Changes

Child-Safe Products Act, Washington State

- Part of WA Ecology's Reducing Toxic Threats Initiative
- Goals
  - To limit lead, cadmium, and phthalates in children's products
  - To develop a list of chemicals (>60 chemicals) that manufactures are required to report

DEPARTMENT OF ECOLOGY
State of Washington

Talking to parents

- Identify risks that are specific to the parent and child (i.e. hobbies, occupation, drug abuse)
- Review preventative measures (previous slides) and discuss common sources of solvent exposure
- Review health concerns and risks related to solvent exposure

Case Study *(directly from ATSDR)*

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.

www.atsdr.cdc.gov/csem/toluene/docs/toluene.pdf

Questions to Consider:

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?*

www.atsdr.cdc.gov/csem/toluene/docs/toluene.pdf

Recap

- Toxic solvents are ubiquitous: on the road, under the sink, in the shower, at work, at the nail salon, etc.
- Children, fetal life, and others are at risk to solvent exposure.
- More research on the health effects on children exposed to solvents is necessary.
- Alcohol, toluene, and TCE transplacental exposure can lead to FASD, FSS, and heart defects & cancer, respectively.
- Prevention is key, and in many cases, it can be easy.

Key Resources

- 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 of Health, Environment and Justice (Vinyl Shower Curtain Report)
  - *http://watoxics.org/files/VolatileVinyl.pdf*
- List of Hazardous Arts and Crafts Material (2009)
  - *www.oehha.org/education/pdf_zip/ArtOct2009.pdf*
- Healthy Building Network
  - *www.healthybuilding.net*
- 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*

Contact Information

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