Among the long list of man-made chemicals that we might inhale, those measured in the Metametrix Volatile Solvents Profile are most likely to be present in your blood. Compounds rarely present are not included to help keep costs down.

The compounds tested and their reference values from the large and ongoing U.S. National Health and Nutrition Examination Surveys (NHANES) are shown in Table 1. The values shown, listed in parts per billion (ppb), are averages of three reports that varied considerably in mean values, but had close agreement for 95th percentiles. Unfortunately, n-hexane, 2-, and 3-methylpentanes do not have published reference ranges.

<table>
<thead>
<tr>
<th>Volatile Organic Compound</th>
<th>Mean (ppb)</th>
<th>95th % (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td>0.104</td>
<td>0.50</td>
</tr>
<tr>
<td>Ethylbenzene</td>
<td>0.090</td>
<td>0.30</td>
</tr>
<tr>
<td>m,p-Xylene</td>
<td>0.23</td>
<td>0.80</td>
</tr>
<tr>
<td>o-Xylene</td>
<td>0.124</td>
<td>0.30</td>
</tr>
<tr>
<td>Styrene</td>
<td>0.06</td>
<td>0.20</td>
</tr>
<tr>
<td>Toluene</td>
<td>.043</td>
<td>1.50</td>
</tr>
</tbody>
</table>

Table 1. Levels of volatile solvents from NHANES surveys

The Significance of Elevated Levels

Living in modern society dictates exposure to solvent vapors. Since the pentanes shown in the report are major components of gasoline, filling your gas tank usually results in their inhalation. Absorption from the lungs into the blood is very efficient. Fortunately, the combined actions of the kidneys and liver should allow rapid elimination of the compounds, so the amount of these compounds found in blood from persons without occupational exposures (ie. painters, chemical workers, mechanics) should be low or non-detectable. Your biochemical individuality (produced by DNA alterations called single nucleotide polymorphisms – SNPs) determines the functioning of detoxification pathways. Some people have high volatile solvent blood levels because of a poor ability to clear the solvents. This insufficiency was demonstrated in a study of highly chemically sensitive persons. Although they carefully avoided chemical exposures, they had much higher levels of volatile solvents in their blood than persons who did not display the high sensitivity.4

Adverse Effects of Volatile Solvents

Many volatile solvents are neurotoxins that cause reduced neuronal functioning. Several of them are effective as anesthetics, used both medically and as recreational drugs. The neurotoxic action of solvents damps nerve transmission, disrupts axon function, and affects myelin. Levels of the solvents above the 95th percentile can produce neurobehavioral dysfunctions. Hexane can cause axon damage leading to paresthesias in the arms and legs. Adverse effects on the optic and ocular cranial nerves caused by benzene, toluene, styrene, and xylene produce myelin damage that affects vision.

The most common symptom of neurotoxicity from solvents is a decrease in cognitive function, referred to as chronic toxic encephalopathy. Symptoms are most common in solvent workers (painters, etc.), but can also appear in non-occupationally exposed persons who have genetic polymorphisms in their glutathione transferase system. These individuals may also have problems with balance.

Solvons can affect the functioning of the immune system, leading to a reduced ability to fight infections, and increased rates of allergy and autoimmunity. In bone marrow, solvent toxicity can lead to bone cancers and thrombocytopenia. Studies have found harmful effects on the endocrine system resulting in infertility and menstrual disorders in women and erectile dysfunction in men.
### Sources and adverse health effects of volatile solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Sources/Exposures</th>
<th>Adverse Health Effects</th>
</tr>
</thead>
</table>
| Benzene | • Made mostly from petroleum  
• One of the top 20 chemicals produced in the United States  
• Used to make other chemicals, such as styrene (for Styrofoam® and other plastics), cumene (for various resins), and cyclohexane (for nylon and synthetic fibers)  
• Used in the manufacture of drugs, pesticides, dyes, and other compounds  
• Most common non-occupational airborne exposures:  
  » The combustion of gasoline, pumping gas  
  » Cigarette smoke: The average smoker (32 cigarettes per day) takes in about 1.8 milligrams (mg) of benzene per day, 10 times the average daily intake of benzene by nonsmokers  
  » Indoor air fresheners  
  » Glues, paints, furniture wax, and detergents  
  » Well water can be contaminated with benzene from leaking gasoline storage tanks at gas stations. People with such contaminated water can be exposed from drinking it, eating foods prepared with it (especially coffee and tea), or inhalation during showering or bathing that can produce absorption of benzene through the skin.  
  » Houses with attached garages often have higher levels of benzene in the air. Levels of benzene and other solvents are also extremely high in the outside air around chemical and paint plants. These local sources of benzene emissions inside the United States can be located by visiting [www.scorecard.org](http://www.scorecard.org). | • Airborne exposure can result in reduced infection fighting  
• Problems in bone marrow such as:  
  » Increased risk of leukemia, breast cancer, multiple myeloma, Hodgkin’s lymphoma, and non-Hodgkin’s lymphoma (NHL)  
  » Cytopenia and thrombocytopenia, leucopenia, acute myeloid leukemia (AML), and aplastic anemia  
• Male infertility  
• Abnormally long menstrual cycles, female infertility, and increased rates of miscarriages  
• View benzene case studies at Agency for Toxic Substances and Disease Registry (ATSDR) [www.atsdr.cdc.gov/csem/benzene/](http://www.atsdr.cdc.gov/csem/benzene/) |
### Ethylbenzene

- Found naturally in oil, and large amounts are produced in the United States
- Used to make styrene
- Also found in:
  - Gasoline
  - Paints and inks
  - Pesticides
  - Carpet glues
  - Varnishes and paints
  - Tobacco products
- Can be present in groundwater (both private wells and municipal aquifers) used in homes. Most of this contamination comes from leaking gas storage tanks (gas stations) as well as landfills.
- Dermal absorption in spray painters

### Adverse Health Effects
- The presence of ethylbenzene and xylene will prolong the time that toluene is present in the blood\(^\text{14}\)
- Neurotoxic “brain fog” (chronic or acute toxic encephalopathy)
- Bone marrow problems (see the list under “Benzene”)
- Hearing loss\(^\text{15}\)
- Increased chemical reactivity (MCS)\(^\text{16}\)
- The International Agency for Research on Cancer (IARC) has determined that ethylbenzene is a possible human carcinogen

### Xylenes

- One of the top 30 chemicals produced in the United States
- Three forms (isomers) of xylene (also known as dimethylbenzene) exist: meta-xylene, ortho-xylene, and para-xylene (m-, o-, and p-xylene)
- Mixed xylene is a mixture of the three isomers and usually also contains 6–15% ethylbenzene
- Used primarily as a “safe” replacement (non-cancer causing) for benzene in gasoline
- Used in the printing, rubber, and leather industries
- Widely used in cleaning agents, paints, paint thinners, and varnishes
- Majority of absorbed (mostly inhaled) xylene will have left the body within 18 hours, small amounts (4–10%) may be stored in fat and will take longer to exit the body
- Clearance of xylene from persons with more adipose tissue can take much longer
- Airborne exposures to xylene come mainly through:
  - Gasoline
  - Auto exhaust
  - Cigarette smoke
  - Paint and varnish fumes
- Dermal exposures mostly from direct contact with gasoline, paints, and furniture finishes.

### Adverse Health Effects
- Neurotoxic “brain fog” (chronic or acute toxic encephalopathy)
- Fatigue
- Headache, depression, mood changes
- Adversely effects learning, behavior, and memory in offspring exposed in utero\(^\text{17}\)
- Studies have found xylene can cause changes to liver, heart, kidneys, lungs, and nervous system\(^\text{17}\)
<table>
<thead>
<tr>
<th>Solvent</th>
<th>Sources/Exposures</th>
<th>Adverse Health Effects</th>
</tr>
</thead>
</table>
| **Styrene** | • A high production chemical (over 13 billion pounds of styrene was produced in the United States in 2006)  
• Primarily used in the production of polystyrene plastics and resins used principally for insulation and for making fiberglass  
• Airborne exposures for styrene:  » Cigarette smoke  
• Auto exhaust  
• Photocopies  
• Workers in the polyester plastic and fiberglass industries  
• Ingestion exposures for styrene:  » Food that has been heated in Styrofoam containers  
• Food that has been stored in Styrofoam containers | • The presence of toluene and trichloroethylene reduces the metabolism of styrene. A combination of acetone and styrene causes a reduction in free glutathione in the liver.  
• Impaires reaction time and vestibular function  
• Reduces MAO-B activity in platelets$^{18}$  
• Cognitive disorders including short-term verbal memory impairment, decreased verbal learning, and impaired logical memory  
• The most frequent symptoms include headache, dizziness, light-headedness, fatigue, irritability, memory loss, and feeling “drunk”$^{18}$  
• Impaired color vision$^{19}$ |
| **Toluene** | • Produced in the process of making gasoline and other fuels from crude oil, in making coke from coal, and as a by-product in the manufacture of styrene  
• Used in making paints, paint thinners, fingernail polish, lacquers, adhesives, and rubber; Also used in some printing and leather tanning processes  
• Half life in the blood is about 6 hours  
• Airborne exposures to toluene come from:  » Fumes of paints, glues, solvents, gasoline  
• Working in places where these compounds are used regularly (painters, acrylic nail salons, etc.)  
• Nail polish, stain removers, carburetor cleaners, cigarette smoke, auto exhaust  
• Higher levels are found in smokers, persons who drink alcohol regularly, and in those who are exposed to paint and lacquer thinners  
• Gasoline is 5-7% toluene and the primary source of population exposure | • Aspirin blocks the clearance of toluene and increases the blood toluene levels, as do benzene and alcohol  
• Most common symptoms:  » fatigue, impaired memory, impaired concentration, irritability, headaches, labile mood, depression, neurotic behavior, dizziness, OCD symptoms and insomnia$^{20, 21}$  
• Psychomotor coordination problems$^{22}$  
• Can be psychologically addictive  
• View toluene case studies at ATSDR www.atsdr.cdc.gov/substances/toxsubstance.asp?toxid=29 |
### Table 2. Sources and adverse health effects of volatile solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Sources/Exposures</th>
<th>Adverse Health Effects</th>
</tr>
</thead>
</table>
| n-Hexane                    | • Hexane, a commonly used solvent, consists of n-Hexane and its isomers of 2-methylpentane and 3-methylpentane  
• Used in glues, adhesives, and paints, and is present in gasoline and jet fuel  
• The only published study on the level of n-hexane gives the 95th percentile level for the presence of this solvent in the blood as a range of 403-812 ppb, methylpentane levels not measured²³  
• Levels of hexane found in farmers had a 95th percentile of only 270 ppb²³  
• Drivers who were regularly exposed to exhaust fumes had a 95th percentile level of 468 ppb²³  
• Exposure sources  
  » Gasoline and automobile exhaust  
  » Quick-drying glues  
  » Jet fuel and jet exhaust  
  » The presence of the methylpentanes without n-Hexane typically indicate that the exposure is neither recent nor ongoing. | • Acute exposure causes CNS disturbances  
  » Headache, mental irritability, paresthesias²⁴  
• Chronic exposure - peripheral neuropathy - muscle weakness, loss of sensation, impaired gait  
• Can lead to demyelination and nerve fiber degeneration  
• Balance problems and classic toxic encephalopathy²⁵ |
| 2-methyl-pentane            |                                                                                                                                                                                                                 |                                                                                                                                                                                                                        |
| 3-methyl-pentane (Aliphatic Hydrocarbons) |                                                                                                                                                                                                                 |                                                                                                                                                                                                                        |
| Iso-octane                  | • A component of gasoline  
• An octane isomer which defines the 100 point on the octane rating scale  
• Produced on a massive scale in the petroleum industry usually as a mixture with related hydrocarbons. | • Inhaled isoctane can cause confusion, dizziness, headaches, nausea, and severe vomiting.  
• Contact with skin can cause dryness and redness of the skin, and can be extremely painful.²⁶  
• Bioaccumulation potential is high.  
• No chronic studies are available that assess carcinogenic effects.²⁷ |

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Patterns of multiple solvents

A pattern of simultaneous positive results for benzene, ethylbenzene, xylene, and toluene may be traced to an exhaust leak in your primary vehicle. Such a chronic source of exposure presents a particularly high risk of health effects. The most common problem involving solvents (individually and in combination) is toxic encephalopathy. This problem will manifest itself with balance disorders (typically not recognized unless tested), headache, depression, reduced cognition, reduced memory and reasoning ability, and reduced attention and reaction time. It will also be present in neuropsychiatric symptoms such as mood changes and neurotic behavior and will often be accompanied by headache and fatigue.

Guidelines for Lowering Toxicant Levels

Avoidance

Identify the exposure source and take steps to avoid further exposures. Sometimes this means discontinuing the use of household cleaning products or personal hygiene preparations, and sometimes other lifestyle changes are needed such as seeking ways to avoid vapors in the home or work environments.

Stimulation of detoxification pathways

The majority of these compounds are cleared from the body after going through oxidation, followed by a variety of conjugation reactions with substrates like glucuronic acid, glycine, or glutathione. Some compounds frequently used as dietary supplements to support or stimulate the detoxification pathways are:

- Taurine
- Glycine
- Glutamine
- N-Acetyl cysteine

Volatile solvent detoxification products that have been passed into the gut may be broken down by bacterial enzymes and released for absorption back into the blood. D-Glucaric acid (as calcium D-glucarate, for example) may be used to reduce this process, and steps to improve the intestinal bacterial balance can help to restore healthy elimination of toxins.

Cleansing

Enhance the clearance of persistent toxins from the body with cleansing protocols. Colonic irrigation, a procedure for removing waste and toxins from the bowel, has been used to rapidly reduce the level of circulating toxins in the body.28,29

Retesting

If initial levels are found extremely high, then retesting may be done in weekly intervals to ensure that effective steps are being taken to remove the high risk of adverse health effects. For moderate or mild elevations, intervals of 4-6 months or more are commonly employed to give assurance of improvements and to detect any new exposures that may occur.

References


27. USEPA Integrative Risk Information System, 2,2,4-Trimethylpentane (CASRN 540-84-1), [www.epa.gov/iris/subst/0614.htm](http://www.epa.gov/iris/subst/0614.htm). Agency Completion Date — 07/31/2007
