

LESSON:

Three Is a Toxic Number

Summary: Students read a brief news article on a possible synergistic chemical exposure, then augment the article by researching the details of the studied chemicals' structure and toxicity, and identifying the current regulatory standards for each chemical. Lesson type: Extension Lesson—this lesson extends a topic in the *EHP* article.

EHP Article: "Triple Threat Activates Neurons," *EHP Student Edition*, September 2005, p. A372
<http://ehp.niehs.nih.gov/docs/2005/113-6/forum.html#trip>

Objectives: By the end of this lesson students should be able to:

1. describe the chemical structure and toxicity of bromoform, chloroform, and tetrachloroethylene by accessing the information on the ATSDR website;
2. cite the current regulatory standards for drinking water for the above contaminants;
3. generate their own hypotheses about why these chemicals might impact neurological development; and
4. describe the neurological disorder of autism.

Class Time: 1 hour (if students do individual research as homework)

Grade Level: 9–12

Subjects Addressed: Environmental Health, Biology, Health, Chemistry

►Prepping the Lesson (30 minutes)

INSTRUCTIONS:

1. Read the article "Triple Threat Activates Neurons" and review the Background Information and Student Instructions.
2. Visit the ATSDR website (<http://www.atsdr.cdc.gov>) to familiarize yourself with the structure of the site and the information provided. Determine the appropriate level of detail for students to add into their worksheet. Print out ToxFAQ sheets for each chemical if students will not be conducting their research using the Internet.
3. Prepare three large sheets of poster paper by cutting them into interlocking puzzle piece shapes. Label one sheet "BROMOFORM," another "CHLOROFORM," and the third "TETRACHLOROETHYLENE."
4. Gather markers and tape per group.

MATERIALS:

per student

- 1 copy of *EHP Student Edition*, September 2005, or 1 copy of the article "Triple Threat Activates Neurons."
- 1 copy of the Student Instructions
- Copies of ATSDR ToxFAQ sheets for each chemical or computers with Internet access (if students do not do research as homework)

per group:

- Information from the ATSDR website, if students will not access the Internet
- Poster paper cut into interlocking puzzle pieces
- Markers
- Tape

VOCABULARY:

- autism
- animal models
- bromoform
- CAMP-dependent protein kinase



- chloroform
- neurotoxicity
- polychlorinated biphenyls (PCBs)
- Superfund site
- synergistic effect
- tetrachloroethylene

BACKGROUND INFORMATION:

Autism is a neurological disorder that usually appears in early childhood and is characterized by unusual social and cognitive development. Children with autism can have mild to severe limitations in emotional, social, or communication skills and often exhibit repetitive behaviors like rocking, as well as avoiding eye contact and affection, and getting upset with changes in routines.

Researchers are attempting to understand what exact malfunction in the brain causes autism. It appears to be linked with a “speeding up” of neuronal activity; high-functioning people with autism, such as author Temple Grandin, have described having autism as being hypersensitive to stimuli that no one else even notices, such as a flashing light or the direct gaze of a stranger. These sensations can make it hard for autistic people to speak, carry on conversations, or understand others’ emotions. Some autistic people cope with these overwhelming stimuli by doing repetitive actions, by withdrawing from others, or by repeating phrases of familiar dialog for comfort. Autism can be devastating for families, and children with autism require intensive educational interventions to allow them to develop to their maximum potential and adapt successfully to family life.

Rates of autism seem to be rising in the population although some argue that the disorder is simply being more widely recognized now than in years past. The cause of autism is unknown at this time, although genetic factors combined with environmental triggers are hypothesized. One proposed cause of autism is exposure to mercury-containing vaccinations (the mercury is used in thimerosal, a preservative). This hypothesis is still unsubstantiated and controversial because of the concern that people will stop getting vaccinations, which are very important for disease prevention.

A recent article on the mercury-containing vaccination issue, called “Comparison of Blood and Brain Mercury Levels in Infant Monkeys Exposed to Methylmercury or Vaccines Containing Thimerosal,” was published in the August 2005 issue of *Environmental Health Perspectives*. According to this research, high levels of inorganic mercury are found in the brains of infant monkeys given vaccines with thimerosal. It was previously thought that thimerosal was “safe” because it was rapidly cleared from the blood. This research shows that although the mercury from thimerosal does clear quickly from the blood, it also accumulates in the brain. The study also found a significant increase in microglia in the infant monkey brains and a decrease in the number of astrocytes. The potential link of thimerosal to autism is that autistic patients have been shown to have “a marked activation of microglia” (Vargas et al. 2005).

REFERENCES:

Burbacher TM, Shen DD, Liberato N, Grant KS, Cernichiari E, Clarkson T. 2005. Comparison of blood and brain mercury levels in infant monkeys exposed to methylmercury or vaccines containing thimerosal. *Environ Health Perspect* 113:1015–1018. Available: <http://ehp.niehs.nih.gov/members/2005/7712/7712.pdf>.

Vargas DL, Nascimbene C, Zimmerman AW, Pardo CA. 2005. Neurological activation and neuroinflammation in the brain of patients with autism. *Ann Neurol* 57:67–68.

RESOURCES:

This exercise is designed to be used with the Agency for Toxic Substances and Disease Registry (ATSDR) (<http://www.atsdr.cdc.gov>) website

ATSDR, ToxFAQ Bromoform, <http://www.atsdr.cdc.gov/tfacts130.html>

ATSDR, ToxFAQ Chloroform, <http://www.atsdr.cdc.gov/tfacts6.html>

ATSDR, ToxFAQ Tetrachloroethylene, <http://www.atsdr.cdc.gov/tfacts18.html>

CDC, Autism Spectrum Disorders Fact Sheet, <http://www.cdc.gov/ncbddd/autism/actearly/autism.html>

CNN News, “U.S. Officials investigate ‘Cluster’ of Autism in New Jersey Town,” <http://cnnstudentnews.cnn.com/HEALTH/9902/01/autism.cluster>

Implementing the Lesson**INSTRUCTIONS**

1. Have the students read the article “Triple Threat Activates Neurons.”



- Using the provided Background Information, have a brief classroom discussion defining autism, its symptoms, and its physiology.
- Break students into three groups and assign a contaminant to each group (bromoform, chloroform, and tetrachloroethylene).
- Hand out the Student Instructions and “Three Is a Toxic Number—Notes” worksheet (one per student). Specify the level of detail expected by directing students to specific documents on the ATSDR website (see Notes & Helpful Hints below). Allow one evening or class for research on the Internet or provide copies of the ATSDR ToxFAQ sheets or other support materials from the ATSDR website for the students to use.
- The following day, give each group their poster paper puzzle piece to fill in with their research findings. Students may illustrate their puzzle piece if desired, possibly using stock images or magazine cutouts.
- Each group should present their puzzle piece to the class, then tape the puzzle piece on the wall or board so that it interlocks with the other puzzle pieces.
- Inform the students that as they listen to the presentations they should complete the table on the “Three Is a Toxic Number—Notes” worksheet.
- After each group has presented, students should individually generate a hypothesis about why the combination of these chemicals causes defects in nerve cell development. Students should also write a description of how people can protect themselves, their fetuses, and the public from these chemicals.
- Conclude with a class discussion on why these three chemicals might have a combined effect on autism rates and how drinking water standards and/or waste disposal practices might be changed in light of research such as that described in the *EHP Student Edition* article.

NOTES & HELPFUL HINTS:

- Adjust the level of difficulty/detail to the students’ level by utilizing different documents available on the ATSDR website. For a general discussion, the ToxFAQ for each chemical provides sufficient information. For a chemistry class, direct students to also view the Toxicological Profile “Chemical and Physical Information” PDF file for each contaminant. For a health class, refer students to the “Public Health Statement” for each chemical, which provides enhanced information on toxicity levels and known health effects.
- More advanced students could research neuron development and common stages where that development can be impeded and result in birth defects. This research can be incorporated into the development of their hypothesis.

▶Aligning with Standards**SKILLS USED OR DEVELOPED:**

- Communication (note taking, oral, written—including summarization)
- Comprehension (listening, reading)
- Critical thinking and response
- Research

SPECIFIC CONTENT ADDRESSED:**Unifying Concepts and Processes Standard**

- Evidence, models, and explanation
- Form and function

Science As Inquiry Standard

- Abilities necessary to do scientific inquiry
- Understanding about scientific inquiry

Science in Personal and Social Perspectives Standard

- Personal and community health
- Environmental quality
- Natural and human-induced hazards

▶Assessing the Lesson

Step 5: Students will most likely find the information in the ATSDR website easy to understand. They should display 3–4 sentences or bulleted points for each of the sections on the “Three Is a Toxic Number—Notes” worksheet:



1. Physical and Chemical Description—if utilizing the more detailed chemical information, students should note the chemical symbol and structure of the chemical as well as the molecular weight.
2. Known Health Effects—students should differentiate between health effects documented in humans versus those seen in animal studies, as well as health effects from low and high doses.
3. Sources and Uses—students should focus on the sources and uses that are most relevant to the case study described in the *EHP Student Edition* article.
4. EPA Drinking Water Standards—Students should list the EPA drinking water standards provided on the ATSDR ToxFAQ for each chemical they research. Note that when very small concentrations of a substance are dissolved in water $1 \text{ mg/L} = 1 \text{ ppm}$ and $1 \text{ } \mu\text{g/L} = 1 \text{ ppb}$.

Chemical	Physical or Chemical Description	Known Health Effects	Sources and Uses	EPA Drinking Water Standards
Bromoform	Colorless to yellow, heavy, nonflammable, liquids with a sweet odor, somewhat soluble, readily evaporates	Sleepiness, brain activity slowed, in high concentrations causes unconsciousness or death, probable human carcinogen, liver or kidney damage in animals exposed to high concentrations, link to birth defects is unknown	Solvent, flame retardant, chlorination by-product, reagent	0.7 parts per million
Chloroform	Colorless liquid with a pleasant, nonirritating odor and a slightly sweet taste. Burns only when reaches very high temperatures, readily evaporates, breaks down slowly	Dizziness, fatigue, headaches, liver or kidney damage, reproductive and birth effects unknown, direct contact with skin can cause sores, possible human carcinogen, causes liver and kidney cancer in rats and mice	Chlorination by-product, used to make other chemicals	100 micrograms per liter
Tetrachloroethylene	Nonflammable at room temperature, easily evaporates, sharp, sweet odor	Dizziness, headaches, sleepiness, confusion, nausea, difficulty in speaking and walking, unconsciousness, death in high concentrations, women exposed occupationally may have menstrual problems and increased spontaneous abortions, liver and kidney damage in animals, behavior changes in rat offspring, toxic to unborn mice and rat pups, probable human carcinogen, liver tumors in mice and kidney tumors in male rats	Solvent used in dry-cleaning and metal degreasing	0.005 milligrams per liter (5 micrograms per liter)



Step 6: Check that student writing is grammatically correct, clear, and logical. Students' hypotheses may vary but they could discuss that all three chemicals are neurotoxicants (causing dizziness, sleepiness, unconsciousness). Since the brain is a target organ for these chemicals, it is logical that neurons may be a target in developing fetuses. Links to birth defects are unknown for chloroform and bromoform, but there is some evidence for adverse effects on fetuses for tetrachloroethylene because of the increased spontaneous abortions, although the physiological reason for these abortions is unknown. The combinations of these chemicals may combine and amplify the direct effects of the individual chemicals, or they may generate a whole new mechanism that alters the nerve cell development.

More advanced students may be able to discuss specific information about neuronal development and birth defect mechanisms.

Step 7: Students' recommendations for protecting humans from these chemicals should focus on personal protection (like using water filtration systems and reducing shower time) and safe disposal of industrial chemicals (perhaps by improving landfill containment or finding improved technology for neutralizing these chemicals before disposal) and protection of groundwater. Public notification of water contamination should also be stressed so pregnant women in particular have the option of taking additional steps to protect their fetuses against exposure to environmental contaminants.

► Authors and Reviewers

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STUDENT INSTRUCTIONS:

Three Is a Toxic Number

- Step 1:** Read the article “Triple Threat Activates Neurons,” *EHP Student Edition*, September 2005, p. A372.
- Step 2:** Your teacher will divide the class into three groups, one for each of the three chemicals examined in the study: bromoform, chloroform, and tetrachloroethylene.
- Step 3:** Each person in the group will visit the website for the Agency for Toxic Substances and Disease Registry (<http://www.atsdr.cdc.gov>) and search for information on their chemical (or use the ATSDR ToxFAQ handouts provided by your teacher).
- Focus on the following topics as you fill in the table on the worksheet titled “Three Is a Toxic Number—Notes”:
1. a physical/chemical description of the substance;
 2. health effects in humans, children, and animals at high and low doses, including descriptions of whether research has been done or is inconclusive for a specific health outcome (e.g., cancer);
 3. sources of the chemical and its uses; and
 4. EPA standards for the chemical’s presence in drinking water.
- Step 4:** Your teacher will provide your group with a poster paper “puzzle piece” for displaying your research findings. This poster may be illustrated, if desired. All information must be clearly organized.
- Step 5:** During the class presentations fill out the rest of the table on the “Three Is a Toxic Number—Notes” worksheet.
- Step 6:** Using the class findings and the information in the article “Triple Threat Activates Neurons,” write a clear, logical hypothesis about why the combination of bromoform, chloroform, and tetrachloroethylene has a different effect from the individual chemicals (for example, is there some characteristic shared by each of these chemicals that raises a red flag about neurodevelopment? Are there individual characteristics of these chemicals that raise a red flag about birth defects?).
- Step 7:** Write recommendations to protect individual, fetal, and public health from the possible combined effects of this toxic “triple threat.”



Three Is a Toxic Number—Notes

Chemical	Physical or Chemical Description	Known Health Effects	Sources and Uses	EPA Drinking Water Standards
Bromoform				
Chloroform				
Tetrachloroethylene				

