Toxic Topics: Arsenic *by: Michael Ichniowski, MD*

"I probably should have told you this before, but, you see… well… insanity runs in my family – it practically gallops!"
Mortimer Brewster in "Arsenic and Old Lace" by Frank Kesselring

Mortimer, the character played by Cary Grant in the film version of this dark comedy, was referring to his two brothers, one a psychopathic criminal and one who believes himself to be Teddy Roosevelt, and his two maiden aunts, Abby and Martha. His aunts were quite familiar with the effectiveness of arsenic as a poison, but to say any more would spoil the film for those who have not yet seen it.

Arsenic (As), a heavy metal with an atomic weight of 33, has been used for centuries, both as a substance of benefit to man and as a potent poison, toxic to most animal life. It has been used as an alloy to strengthen metals, in semi-conductors for electronics, and in antibiotics (among the earliest treatments for syphilis), pesticides and herbicides. As more has been learned about the toxicity of arsenic, many of these products have been replaced by less toxic alternatives. Arsenic has been called the King of Poisons and the Poison of Kings, well known for its potent toxicity, and used by rulers to eliminate rivals and other undesirables. It has also been used in chemical weapons, including lewisite, a volatile liquid harmful to skin and lungs, for which the antidote BAL (British Anti-Lewisite or dimercaprol) was developed.

Arsenic is found in the earth's crust in both organic and inorganic forms. In contrast to mercury, which is made more toxic by organification, arsenic in naturally occurring organic forms is considered non-toxic. However, synthetic organic arsenicals, many developed as pesticides, are highly toxic. The inorganic compounds occur in trivalent (+3) and pentavalent (+5) forms, with the trivalent being more toxic and carcinogenic.

Exposure to arsenic occurs by inhalation or ingestion of both man-made and naturally occurring compounds, and human exposure can be quite substantial from these many sources. Groundwater and well water can be contaminated by proximity to arsenic deposits in soil and rock, and by runoff from farms and fields where arsenic-containing pesticides have been used. Soil can also be contaminated

by these pesticides, which can persist for many years. Plants grown in such soil can absorb arsenic and contaminate foods produced from these plants. Recent reports of arsenic found in fruit juices and organic brown rice syrup (used in certain toddler formulas and other food products) may well have occurred from such contamination.

Another arsenic product of current concern is Roxarsone, an organic form which is added to chicken feed to promote growth and prevent coccidiosis in poultry. A recent FDA study found higher levels of toxic inorganic arsenic in the livers of chickens fed this product compared to non-exposed poultry. Researchers have also found inorganic arsenic in the waste of exposed poultry, which adds to arsenic in fields where the poultry are raised. A bill currently under consideration by Maryland's legislature would ban the use of this product, which is also under review by the FDA.

Until 2003, pressure-treated wood for outdoor use was impregnated with chromated copper arsenate (CCA), a pesticide designed to prevent damage by termites and other insects. With time and weathering, arsenic would leach out of treated wood onto its surface and into the soil, posing a particular risk to young children playing near decks and playgrounds where CCA treated wood was used. The increased hand-to-mouth activity of children increases the risk of toxicity. The regular use of wood sealants reduces the leaching of arsenic from CCA-treated wood. Caution is required when treated lumber is cut, and such wood should never be burned as this releases arsenic that may be inhaled. There has been a case report of mild arsenic poisoning among a family exposed to these fumes.

Arsenic is well absorbed when ingested or inhaled and is distributed throughout the body. It acts as an antimetabolite affecting all organs. Its half-life in blood is 10 hours, and it is excreted largely by the kidneys (90% in urine, 10% in bile). Because of the relatively short time in the circulation

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and the renal excretion, a timed urinary collection is the diagnostic test of choice; further analysis to distinguish inorganic from organic arsenic is also necessary. Detoxification by methylation transforms a small amount of absorbed arsenic, a process that is less effective in children than adults.

Acute high-dose ingestion rapidly causes gastrointestinal injury, with nausea, vomiting, hematemesis, and cramping and diarrhea. Later effects include myocardial depression, conduction disturbances, bone marrow suppression, hepatic dysfunction and peripheral neuropathy. The neuropathy is sensorimotor and ascending, mimicking Guillain-Barre syndrome, and may cause permanent dysfunction. A characteristic sign of acute arsenic exposure is the appearance of Mees' lines on the fingernails, white transverse creases that appear several weeks after the poisoning.

Chronic arsenic exposure can produce fatigue and malaise and an increased risk of infection, especially pneumonia. Early exposure to arsenic-contaminated water has also been linked to an increased risk of bronchiectasis in adulthood. Skin changes caused by arsenic include hyperkeratosis, dyskeratosis and eczematoid eruptions; alopecia may also occur. Arsenic crosses the placenta readily, leading to an increased risk of spontaneous abortion, stillbirth and preterm birth. Fetal and childhood exposure can also affect children's development and intellectual function.

Arsenic is listed as a known carcinogen, and chronic exposure is associated with an increased risk of bladder, lung and skin cancers that rises with increased levels of exposure. Other forms of cancer that have been linked to arsenic exposure include those of liver and kidney; the risk of acute myelogenous leukemia and aplastic anemia is also increased.

Treatment of arsenic poisoning from a confirmed significant exposure can be done with chelation, in consultation with a medical toxicologist. Chelators that have been found to be effective in increasing the elimination of arsenic include dimercaprol (BAL), d-penicillamine and succimer.

As with all toxic exposures, prevention is of prime importance, and there has been a steady decline in the use of arsenic-containing products, with a nearly complete ban on previously used arsenical pesticides. Drinking water standards currently stand at 10 parts per billion (ppb), though even at this level, there is an increase in the risk of cancer. Testing of well water is of particular importance due to the many potential sources of groundwater contamination. Boiling and charcoal filtering of water will not remove arsenic.

References: Etzel, RA and Balk, SJ (eds.). *Pediatric Environmental Health, 3rd edition.* Elk Grove Village, IL: AAP; 2012; 329-337.
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Discussion on Drug Shortage in Maryland

(from left to right) Dr. Jonathan Gottlieb, Dr. Renee Ellen Fox, Congressman Elijah Cummings, Senator Barbara Mikulski, Jeffrey Rivest.

On Wednesday, April 4, 2012, Senator Barbara Mikulski hosted a roundtable discussion on drug shortages in Maryland. The event, at the University of Maryland Medical Center was attended by Congressman Elijah Cummings and Hospital President Jeffrey Rivest. Speaking on behalf of the AAP and its Committee on Federal Government Affairs, Maryland Chapter member Dr. Renee Ellen Fox brought the AAP perspective to the Senator. In addition, a UMMC hospital patient, a 24 year old young man with osteosarcoma and his mother, talked of the great stress they are under with concerns about the scarcity of the medicine he needs to survive. Dr. Jonathan Gottlieb, Chief Medical Officer of UMMC, and Agnes Ann Feemster, a senior pharmacist, spoke of the continuing challenges faced by the shortages which have quadrupled in the last five years.

Senator Mikulski and Congressman Cummings pledged to work with their colleagues in the congress to enact legislation that would work to resolve these critical issues.