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ARSENIC PESTICIDES AND ENVIRONMENTAL POLLUTION: EXPOSURE, POISONING, HAZARDS AND RECOMMENDATIONS

By
MAMDOUH M. EL-BAHNASAWY[1], AMINA EL-HOSINI MOHAMMAD[1] AND TOSSON A. MORSY[3]
Military Medical Academy[1] and Department of Parasitology, Faculty of Medicine, Ain Shams University, Cairo 11566[2], Egypt

Abstract

Arsenic is a metalloid element. Acute high-dose exposure to arsenic can cause severe systemic toxicity and death. Lower dose chronic arsenic exposure can result in subacute toxicity that can include peripheral sensorimotor neuropathy, skin eruptions, and hepatotoxicity. Long-term effects of arsenic exposure include an in

Due to the physiologic effects of arsenic on all body systems, chronic arsenic-poisoned patient is a major nursing challenge. The critical care nurse provides valuable assessment and interventions that prevent major multisystem complications from arsenic toxicity.

Key words: Arsenic, Environmental hazards, Pathogenicity, Treatment, Nursing.

Review and Discussion

In Egypt, many authors dealt with arsenic toxicity in man and animal due to environmental pollution (el Nabawi *et al*, 1987; Hilmy *et al,* 1991; Sayed *et al,* 2005; El-Ghor *et al*, 2011)

Clinicians may need to consider arsenic exposure in the emergency care setting when treating those suspected of acute poisoning. In the office setting, clinicians also need to consider chronic arsenic exposure when determining causes of peripheral neuropathy or addressing patient concerns about arsenic found in drinking water and other environmental settings.

Sources of Exposure:

Arsenic is a naturally occurring element found in the earth's crust and within numerous ores. It is classed as a metalloid because it complexes with metals; it also reacts with other elements such as oxygen, hydrogen, chlorine, carbon, and sulfur. Elemental arsenic is rare, and the element exists more commonly as organic or inorganic compounds.

Arsenical compounds can be grouped as inorganic, organic, and arsine gas (AsH3), and they are further classified according to their valence states: elemental (0), arsenite (trivalent, +3), and arsenate (Pentavalent, +5). Trivalent Arsenic or arsenite compounds, both inorganic and organic, are considered the most toxic. Some fish and crustaceans contain large amounts of organic arsenic called "fish arsenic," consisting mostly of arsenobetaine (a trimethylated arsenic compound) and arsenocho-

line, which are thought to be of negligible toxicity (Yip and Dart, 2001).

Human exposures can occur from natural sources, such as volcanic eruptions, and arsenic leaching from soil and rocks into drinking water. Certain foods may contain potentially toxic levels of arsenic. Some analyses have found high levels of inorganic arsenic in hijiki (hiziki) seaweed (Rose *et al*, 2007).

Of note, arsenic is no longer produced in the United States; all of the arsenic used in the United States is imported (ATSDR, 2008). Man-made exposures derive from various sources including (Ford, 2002). Use and manufacture of arsenic-containing pesticides (arsenic trioxide, sodium arsenite, calcium arsenite, arsenic acid), ant poisons, and herbicides (Reigart and Roberts, 1999), Semiconductors (gallium arsenide) Fossil fuel combustion Smelting/refining Mining (Eisler, 2004), Metallurgy Decorative glass-making Use of medicines/contaminated drugs, as found in some Asian folk remedies, homeopathic remedies, and herbals (Saper *et al*, 2008). Some "moonshine" (illegally distilled alcohol) Contact with pressure-treated wood (e.g., treated with wood preservatives containing chromium-copper-arsenate [CCA] or other arsenic preservatives) Contaminated well water from industrial sources Ingestion of chicken that has been given feed supplements with arsenic (Lasky *et al*, 2004).

Arsenicals have been used in medications in past to treat syphilis (arsphenamine) and the skin conditions (Fowler's solution) and presently to treat the trypanosomiasis (melarsoprol) and acute promyelocytic leukemia as arsenic trioxide (Miller *et al*, 2002).

The attention to chronic exposures of arsenic found in drinking water has grown (Soignet *et al*, 1998). In some locations, this contamination presents an enormous health hazard, as in the case of the ongoing epidemic of arsenic poisoning in West Bengal, India, and Bangladesh. High levels of arsenic leaching from natural underground sources have contaminated newly drilled wells, leading to more than one million people drinking arsenic-contaminated water with >50 mcg/L (NRC, 2001). Thousands of people living there were found having arsenic-related skin lesions, liver problems, and neuropathy.

Although less common, there have also been case reports of arsenic poisoning from contaminated well water in the United States (WHO, 2001). However, the greater focus of the United States and other countries has been on the potential long-term adverse health outcomes from exposures to much lower doses of arsenic in drinking water (below a level that causes clinical manifestations) that could lead to future increased risk of cancer. In the United States, drinking water generally contains an average of 2 mcg/L of arsenic, although 12% of water supplies from surface water sources in the North Central region of the country and 12% of supplies from ground water sources in the Western region have levels exceeded 20 mcg/L. People also eat small amounts of inorganic arsenic in their diet. US dietary intake of inor-

ganic arsenic has been estimated to range from 1-20 mcg/day.

Pressure-treated wood:

Wood has been preserved by pressure-treatment with pesticides including chromate copper arsenate (CCA), ammoniac copper arsenate (ACA), and ammoniac copper zinc arsenate (ACZA) in order to protect it from insect infestation, decay, and marine environments. In 2003, the United States manufacturers began a voluntary phase-out of arsenic containing wood preservatives for wood employed in some residential uses such as play structures, picnic tables, decks, and fencing. However, wood structures still exist that have CCA-treated elements.

Episodes of arsenic poisoning have been described in workers sawing the wood who were exposed to arsenic through inhalation or skin contact and in people burning the arsenical-treated wood that were exposed to the arsenic-contaminated smoke (Wadhwa *et al*, 2011).

Biological Basis of Disease:

Tasteless and odorless, arsenic compounds are well absorbed after ingestion or inhalation. For most trivalent and pentavalent arsenical compounds dissolved in water, gastrointestinal absorption exceeds 90 percent, whereas poorly soluble compounds such as arsenic trioxide are less well absorbed. Skin absorption is minimal. Arsenic can cross the placenta and accumulate in the fetus. Most information about adverse health effects of arsenic is derived from descriptions of accidental or intentional human exposures.

Arsenic is readily taken up by red blood cells and then quickly distributed to other tissues. Peak serum levels are reached about 30 to 60 minutes after a single oral dose. Kidney excretion occurs in three phases with half times estimated at: Phase-I, 1 to 2 hours (90% may be cleared); Phase-II, from the end of Phase-I to 8 to 30 hours; Phase-III, from the end of Phase-II to 8 to 10 days or more (Smith *et al*, 2000).

Primary target organs for toxicity are the gastrointestinal tract, skin, bone marrow, kidneys, and peripheral nervous system. There is some controversy as to how readily arsenic crosses the blood-brain barrier. Chronic ingestion of small amounts of arsenic results in the highest concentration in hair, nails, skin, and tissues rich in cysteine-containing proteins.

Trivalent arsenic (+3), the most toxic form, avidly binds to sulfhydryl groups (proteins, glutathione, cysteine) and interferes with numerous enzyme systems, such as those involving cellular respiration (inhibiting pyruvate dehydrogenase [PDH]), gluconeogenesis and glucose uptake, and glutathione metabolism. Pentavalent arsenic (+5) and arsine gas are converted to trivalent arsenic in vivo, but they may have some direct effect on uncoupling oxidative phosphorylation (Chakraborti *et al*, 2003).The majority of the trivalent arsenic is metabolized via methylation to form the monomethylarsonic acid (MMA) followed by dimethylarsinic acid (DMA) and excreted through the urine. Methylated arsenic compounds are less reactive to tissues, and they

increase the elimination rate from the body (Chowdhury *et al*, 2000).

Clinical Presentation:

Acute arsenic poisoning can occur after ingestions or, in workers, from acute inhalation exposure to high levels of arsenic dusts or fumes. Symptoms following acute, large exposures to inorganic arsenic may develop within minutes or hours. Acute toxicity typically starts in the gastrointestinal system and includes nausea, vomiting, abdominal pain, and diarrhea. There may be a garlic odor of the breath and stool in severely poisoned patients. These symptoms are soon followed by the dehydration, hypotension, irregular pulse and cardiac instability and in severe cases by shock, acute respiratory distress syndrome, and sometimes death (Franzblau and Lilis, 1989). In some cases, acute encephalopathy can develop and progress over several days, with delirium, coma, and seizures. Renal injury can lead to proteinuria, hematuria, and acute tubular necrosis (Windebank, 2000).

The severity of the toxicity depends upon the form and dose of the arsenic compounds. Acute oral exposure to inorganic arsenic at doses of 600 mcg per kg body weight per day or higher has resulted in death. If poisoned individuals survive the initial illness, they usually develop hepatitis and pancytopenia within a week, and then may experience a sensorimotor peripheral neuropathy one to three weeks after the exposure. This has been described as beginning with distal paresthesias, followed rapidly by an ascending sensory loss and weakness, which can sometimes mimic Guillain-Barré syndrome (Feldman, 1999).

The blood changes are usually reversible once exposure ceases. Partial recovery from peripheral neuropathy can occur in some cases, especially in the more mild cases of poisoning (Lauwerys and Hoet, 2000).

Other symptoms that can develop after severe acute poisoning include dermatologic lesions (patchy alopecia, diffuse pruritic macular rash, herpetic-like ulcers in the mouth), respiratory symptoms (dry hacking cough), and/or Mees lines; horizontal 1- to 2- mm white lines on nails, also called transverse leukonychia (Reynolds, 1991).

Less severely acutely poisoned patients may experience persistent gastroenteritis and mild hypotension necessitating intravenous fluids, along with a metallic taste and irritated mucous membranes that can mimic pharyngitis (Trapp *et al*, 2013).

Chronic toxicity:

Chronic effects can occur as the sequelae of acute poisoning (as discussed above) or as the result of chronic longer-term exposure to lower levels of arsenic. Chronic exposure to arsenical compounds has occurred at work, usually through inhalation of arsenic-containing vapors or dusts, or through non-work environmental exposures, such as drinking arsenic-contaminated water. The clinical effects of chronic toxicity can have an insidious onset and thus be more difficult to diagnose. In chronic poisoning, the peripheral neurologic complaints and skin manifestation are usually more prominent

than the gastrointestinal symptoms.

Skin lesions:

Different types of arsenic-related skin lesions have been described in the West Bengal and Bangladesh poisonings. Hyperpigmentation or hypopigmentation can be an early manifestation. Hyperkeratoses and scaling, particularly diffusely on the palms and soles, also are quite characteristic. Eczematous lesions have also been described (Chhuttani *et al*, 1967).

Skin carcinomas and Bowen's disease (squamous cell carcinoma in situ are associated with latent effects of arsenic poisoning. A cohort study from Bangladesh found a dose-response relationship between exposure to arsenic in drinking water and the risk of the premalignant lesions; compared with exposure to well water with a concentration of arsenic below 8.1 mcg/L the adjusted odds ratio for premalignant skin lesions was 5.4 in people exposed to water with a concentration between 175.1 and 864 mcg/L (Mees, 1919).

Peripheral vascular disease with associated gangrene, called "Blackfoot" disease, has been described in relationship to chronic arsenic poisoning (Ahsan *et al*, 2006).

Neurologic manifestations:

The symmetrical sensorimotor polyneuropathy is one of the most prominent symptoms of arsenic poisoning and can develop one to three weeks after acute poisoning or insidiously from chronic exposures.

Sensory symptoms tend to present first and to predominate, starting with numbness and tingling particularly in the soles of the feet and then later in the hands as well. These may be the only symptoms in milder forms of arsenic polyneuropathy.

In more severe forms, the pain is more intense, particularly with even light touch, so that affected persons are unable to walk because of intense burning pain in the soles. Cramping in the calves is another common symptom. An early sign on physical examination is diminished vibratory sense.

Progressive symptoms may then develop in a stocking/glove distribution with decreased pain, decreased sensation of touch and temperature, and symmetrical weakness, along with decreased deep tendon reflexes. Electrophysiological findings of arsenic neuropathy typically suggest a distal motor and sensory axonopathy.

Neurologic findings may also occur with chronic exposure. A study of 43 smelter workers exposed to inorganic arsenic dust for 13 to 45 years found moderate clinical symptoms and nerve conduction velocities that were significantly lower in two peripheral nerves as compared with matching referents. There was a significant negative correlation between cumulative absorption of arsenic and nerve conduction velocities (Yu *et al*, 2002). In one of the more recent descriptive case series studies examining the health consequences of drinking arsenic-contaminated water in India, a sample of 21 of 40 individuals with skin lesions and elevated arsenic in biological samples were diagnosed with clinical neuropathy. Most of the cases presented with

distal paresthesias and distal hypesthesias in stocking and glove distribution, followed by limb pains and diminished or absent deep tendon reflexes in those most affected.

In chronic arsenic exposure, peripheral nerve manifestations may also be subclinical. A blinded study of copper smelting factory workers exposed to arsenic trioxide found that the incidence of both subclinical (reduced the conduction velocity and amplitude measurements on nerve conduction studies without signs or symptoms of clinical neuropathy) and clinical neuropathy was greater in arsenic-exposed workers than in controls (Tseng, 1977). Although peripheral neuropathy has been the predominant neurologic manifestation of chronic arsenic poisoning, there have also been case reports of encephalopathy, described as cognitive impairment, disorientation, hallucinations, agitations, and memory problems (Lin and Huang, 1997). It is not clear from these case reports, however, how much of the symptoms can be attributed to arsenic and how much to other potential work exposures or psychiatric problems (Morton and Caron, 1989).

Cancer:

There are many epidemiological studies and case reports showing an association between arsenic exposure and cancer. This link has been the basis for regulatory actions. Cancers that have been associated with arsenic exposure include cancers of the skin, bladder, and lung, kidney, nasal, liver, and prostate.

Ingestion of inorganic arsenic increases the risk of developing skin cancers. Lesions commonly described are multiple squamous cell carcinomas, arising from the arsenic hyperkeratosis warts, as well as basal cell carcinomas arising from cells not associated with hyper keratinization (Rodriguez *et al*, 2003).

There has also been considerable epidemiologic evidence to support the association between exposure to inorganic arsenic and bladder cancer. A cohort study from Taiwan found that, compared with people drinking water with an arsenic concentration of $\leq$ 10 mcg/L, the adjusted relative risks of bladder cancer in people exposed to well water containing arsenic in concentrations of 10.1 to 50, 50.1 to 100, and >100 mcg/L were 1.9, 8.2, and 15.3, respectively (Cuzick *et al*, 1992).

Similarly, the report from Chile showed a dose-response relationship between the risk of lung cancer and exposure to arsenic in drinking water; the adjusted relative risk was 8.9 for drinking water with arsenic concentrations of 200- 400 mcg/L (Chiou *et al*, 1995). Both this study and another from Taiwan found evidence of synergy between arsenic and smoking on the risk of lung cancer. Others have shown a decline in mortality rates from lung cancer following the elimination of the arsenic from drinking water (Marshall *et al*, 2007).

A region of Chile that experienced a sudden rise and then fall of arsenic levels in drinking water developed an increase in lung and bladder cancer mor-

tality rate ratios about ten years after the start of the high arsenic exposures.

Arsenic exposure is believed to increase the risk of hepatic angiosarcomas, but it does not appear to be associated with hepatocellular carcinoma (Chiou *et al*, 2001).

Cardiovascular:

Studies have found that arsenic exposure increases the risk of developing hypertension (Ferreccio *et al*, 2000). As an example, a prevalence study of hypertension in Bangladesh found a dose-effect relationship between levels of arsenic in drinking water and the prevalence of hypertension; for a 50 mcg/L concentration of arsenic in water, the risk of hypertension was doubled when compared with unexposed individuals. This relationship is reminiscent of that seen with exposure to the heavy metal lead, which has also been associated with the development of hypertension.

Some studies have found an association between arsenic exposure and the risk of cardiovascular outcomes such as the coronary heart disease and stroke; however, other studies have not found such an association and evidence is inconclusive (Guo, 2003).

Liver:

Arsenic exposure has been associated with hepatic angiosarcoma. A study in Mexico found evidence of increased bilirubin and alkaline phosphatase concentrations in people exposed to arsenic in drinking water. A study of 248 people in India with evidence of chronic arsenic toxicity found that hepatomegaly was present in 77%; among a subset who underwent liver biopsy, noncirrhotic portal fibrosis was the predominant lesion (Rahman, 2002).

Endocrine:

Arsenic exposure appears to be associated with the development of type II diabetes mellitus. Incidence and prevalence studies have found a dose-response relationship between exposure to arsenic in drinking water and the risk of diabetes (Navas-Acien *et al*, 2004).

Respiratory:

A study from West Bengal found higher rates of respiratory symptoms and reduced lung function in men, but not women, with arsenic exposure. This association needs to be confirmed in other studies (Santra *et al*, 1999).

Reproductive and developmental:

Since the inorganic arsenic has been found to cross the placenta, there is a potential for adverse reproductive and developmental outcomes. Some studies have found evidence suggesting the marked increased on the infant mortality, spontaneous abortions, stillbirths, neonatal death, and preterm births associated with arsenic exposure. A 2001 review found that evidence was not conclusive, since the various studies suffered from limitations such as lack of information about lifestyle and other exposures (Navas-Acien, 2008).

However, the subsequent study of 29,134 pregnancies in Bangladesh addressed some of these concerns with better information on individual exposures and other risk factors (Rahman *et al*, 1998). This study found that the pregnant women drinking water from the sources with arsenic concentrations

above 50 mcg/L experienced significant increases in fetal loss (relative risk [RR] 1.14) and infant death (RR 1.17).

Nursing Role:

Limited data suggest that arsenic levels in the breast milk are low even in women exposed to high levels of environmental arsenic. This has potentially important implications for protecting infants from arsenic toxicity in regions where there are high concentrations of arsenic in the drinking water **(**von Ehrenstein *et al*, 2005). However, very little arsenic is excreted in breast milk, even in women with high exposure from drinking water. Thus, exclusive breast-feeding protects the infant from exposure to arsenic (Fängström *et al*, 2008). Nevertheless, shellfish contamination from seawater offers a rather low risk to the general French population, because shellfish do not constitute a major contributor to dietary exposure of chemical contaminants. Notwithstanding, consumer vigilance is necessary among regular shellfish consumers, and especially for those residing in fishing communities, for pregnant and breast-feeding women, and for very young children (Guéguen *et al*, 2011).

Children and Arsenic:

Children, in general, are more susceptible to toxicants, such as arsenic, for a variety of reasons including: more opportunities for exposure from increased hand-to-mouth behavior and breathing closer to the ground, differences in metabolism, and greater sensitivity of the developing nervous system to toxic insults. Children are less able than adults to internally detoxify inorganic arsenic through the methylation (Rahman *et al*, 2007).

Children can develop arsenic poisoning from playing on soil contaminated with arsenic from nearby mining or smelting or in hazardous waste sites. Another potential source of exposure is through contact with "pressure treated wood" through playing on it, chewing it, or being in the vicinity when it is burned.

Diagnostic Evaluation:

The evaluation of an individual with potential arsenic toxicity involves taking a medical/environmental history. The history should identify potential sources of exposures and symptoms consistent with arsenic poisoning.

The physical examination should include examination for hyperkeratotic lesions and peripheral neuropathy.

Potential environmental/occupational exposures should be documented and measured. Soil, air, and water can be sampled, if indicated, and arsenic levels determined through reliable laboratories or government agencies. Biological monitoring evidence can also be obtained to confirm excessive arsenic exposure.

Acute exposure:

In the case of an acute ingestion, abdominal radiographs may demonstrate gastrointestinal radiopaque material soon after ingestion, although the absence of opaque material does not rule out exposure. In general, measurement of arsenic levels in urine is preferable to blood, since blood arsenic is cleared rapidly. In the emergent situation, spot

urine arsenic can be obtained prior to beginning chelation therapy. The urine creatinine in the spot sample should also be obtained to correct for urine concentration. During treatment, 24-hour urine arsenic monitoring is usually performed to follow the levels of arsenic excretion over time. In acutely symptomatic patients, urine arsenic levels are usually in the thousands of micrograms per liter. Because urine arsenic excretion can be intermittent, a definitive diagnosis usually is supported by finding a concentration greater than or equal to 50 mcg/L, or 100 mcg of arsenic (As) per gram creatinine in the absence of recent fish or shellfish intake. If there has been fish or shellfish intake within the last 48 hours, the nontoxic "fish arsenic" may lead to increased urine levels of total arsenic, and so the urine arsenic may need to be speciated in order to obtain assessment of inorganic arsenic levels. Speciating arsenic to obtain total arsenic and inorganic arsenic can usually be done by a clinical laboratory capable of measuring total arsenic; if little or no inorganic arsenic is detected, one can deduce that the arsenic found in the total measurement was the nontoxic organic form. It is very difficult to find clinical laboratories that can perform measurements of the individual components of inorganic arsenic such as the metabolites monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA), but this is normally not necessary in the usual clinical circumstances (Concha *et al*, 1998).

Chronic Exposure:

In evaluating a patient for chronic arsenic exposure, either a 24-hour urine arsenic or spot urine arsenic and creatinine can be obtained after advising the patient to eat no fish or shellfish for 48 to 72 hours. The 24-hour urine determination is more accurate but less convenient. Regular surveillance for arsenic exposure in workers (for instance, after shifts) is done with measurements of spot urine arsenic and creatinine.

A single meal of fish can increase total urine arsenic to more than 1000 mcg/L. In persons who do not have occupational exposures to inorganic arsenic and who have not recently eaten seafood, the total urine arsenic is generally less than 10 mcg per gram creatinine. There have been varying results from studies reporting the relationship between work-related air exposures and urinary arsenic measurements, but based upon more recent studies from copper smelters, 30 to 35 mcg As/g creatinine would be expected from exposure to air levels of arsenic averaging 10 mcg/m^3 (Heitland and Köster, 2008).

Since inorganic arsenic (to a much greater extent than organic arsenic) is taken up and bound in hair and fingernails, hair and nails could be good indicators for the amount of inorganic arsenic absorbed during the growth period (hair grows at 0.4 mm per day, while nails grow at a rate of 0.1 mm per day). However, in a setting in which air exposure is a consideration, as in an industrial environment, it is very difficult to remove exogenous arsenic from hair, and therefore to get a

reliable reading (Rivera-Reyna *et al*, 2013). Also contributing to the variability of results from hair and nail testing is lack of standardization for analyses. Commercial laboratory hair analyses for multiple elements including arsenic are highly inaccurate. Determination of arsenic in hair and nails has been most useful in epidemiological studies performed to evaluate environmental exposures of populations to inorganic arsenic; it is less useful in the evaluation of an individual patient. Laboratory testing to assess chronic toxicity, including laboratory parameters that could become abnormal days to weeks after an acute overexposure, should include a complete blood count, renal and liver function tests, and a urinalysis. If there are signs or symptoms of peripheral neuropathy, nerve conduction/EMG testing should be considered.

Treatment:

In cases of acute exposure, care should be taken to avoid contamination of medical personnel during the decontamination process.

Therapy of severe arsenic poisoning relies on provision of basic and advanced life support and usually chelation therapy. Consultation with a regional poison center and/or clinical toxicologist is recommended to assist with management of severely poisoned patient (Hasegawa, 2008).

Activated charcoal is sometimes used, but the efficacy is still not clear. In the absence of better data, some sources recommend its use. Careful attention must be paid to fluid and electrolyte balance. Agents that prolong the QTc, such as the class IA, IC, and III anti-dysrhythmic agents should be avoided.

The decision to use a chelating agent depends upon the clinical condition of the patient, the history of arsenic exposure, and laboratory results of arsenic exposure (if available). In a severely ill patient with known, or highly suspected, acute arsenic poisoning, chelation may need to be started before laboratory confirmation of arsenic levels is received (Sternowsky *et al*, 2002).

Decontamination:

Skin decontamination is particularly important in cases of poisoning from arsenical pesticides. Remove contaminated clothing, and wash the pesticide from the skin and hair taking care to avoid contaminating providers (Priha *et al*, 2001).

Gastrointestinal decontamination can be performed in cases of recent ingestion (typically within one hour). Do not administer cathartics since arsenic typically causes diarrhea. Use nasogastric suction, and administer activated charcoal. Fluids -Administer intravenous fluids to maintain adequate urine flow while carefully monitoring fluid and electrolyte balance. The monitoring-patients should have continuous cardiac monitoring. Chelation -Chelation therapy is usually indicated in patients with symptomatic arsenic poisoning (see below (Quang and Woolf, 2000).

Chelation:

Two chelating agents are available in the United States: dimercaprol (British anti-lewisite or BAL) and meso-2, 3-

dimercaptosuccinic acid (Succimer). A third drug, sodium 2, 3-dimercapto-1-propane sulfonate (DMPS), is marketed by a German pharmaceutical company under the trade name, Dimaval® (Heitland and Köster, 2009).

BAL can be administered intramuscularly (in peanut oil) to patients with reduced consciousness or decreased gastrointestinal motility. It has a narrow therapeutic: toxic ratio and a high rate of side effects. Although BAL helps to speed excretion of arsenic, it is not clear that administration can prevent the development of the peripheral neuropathy.

The regimen for administering intramuscular (IM) BAL is as follows: Severe poisoning - each injection should be 3 mg/kg BAL IM. Administer an injection every four hours for the first two days (12 total injections). Then administer an injection every six hours for one day (four total injections). Continue treatment with an injection every 12 hours. Discontinue treatment after 10 days or if there is recovery or if the 24-hour excretion falls below 50 mcg. Mild poisoning- each injection should be 2.5 mg/kg BAL IM. Administer an injection every six hours for two days (12 total injections). Then administer an injection every 12 hours for one day (two total injections). Continue treatment with an injection every day. Discontinue treatment after 10 days or if there is recovery or if the 24-hour excretion falls below 50 mcg. Children- the dosage schedule is the same as the mild poisoning regimen above, with dosages between 2.5 and 3.0 mg/kg per dose .

For treating subacute or chronic severe toxicity, succimer (an oral hydrophilic analogue of BAL) is the chelator of choice. The dose is 10 mg/kg (maximum 500 mg per dose is suggested) administered with food every eight hours for five days and then every 12 hours for an additional 14 days (Quang and Woolf, 2000). There are no controlled studies of outcome, but the hope is that chelation therapy will enhance excretion of arsenic while it is still chelatable in the tissues. DMPS is a water-soluble analogue of BAL that can be administered by oral, IV, or IM routes and may also be of benefit in treating chronic arsenic toxicity; it is not approved for use in the United States. When given IM, it is administered at 5 mg/kg per dose as a 5% solution; a typical regimen would be dosing every 6 to 8 hours on the first day, every 8 to 12 hours on the second day, and every 12 to 24 hours thereafter (Ford, 2002).

General Preventive Measures:

Efforts should be taken to reduce exposures to inorganic arsenic, to the extent feasible, from both naturally occurring and man-made sources. In the United States, the Occupational Safety and Health Administration regulate inorganic arsenic exposure in air in the workplace through a "permissible exposure limit" or PEL of 10mcg/m3 as a time-weighted average over an eight-hour work day. The National Institute of Occupational Safety and Health (NIOSH) is more conservative and advises minimizing exposures to a recommended exposure limit (REL) of 2 mcg/m3,15 minute exposure (Steindel and Howanitz, 2001).

The WHO (1993) reported that based on health criteria the guideline value for arsenic in drinking water should ideally be > 10 mcg/L, but given measurement limitations the WHO recommended a provisional guideline value of 10mcg/L (Reigart and Roberts, 2008).

In 2002, the US Environmental Protection Agency (EPA) lowered the maximum contaminant level for the amount of arsenic allowed in drinking water from 50 ppb to 10 ppb (10 mcg/L) based upon review of carcinogenic risks (NRC, 2008).

Most of the arsenical pesticides (including the common sodium arsenate ant killer, "Terro" were banned for use in the United States in 1991, but they may still be found in use in other countries. The Copper Chromium Arsenate (CCA) used as a wood preservative, was not included in the ban. The use of CCA in pressure-treated wood for residential uses in the United States was supposed to voluntarily cease by December 31, 2003. However, existing structures remain as potential sources of concern. Care should be taken never to burn pressure-treated wood in fireplaces or campfires (Peters *et al*, 1984).

Referral:

Practitioners involved in the care of patients with arsenic poisoning, or patients who have questions about arsenic exposures, may find it helpful to consult with occupational/environmental medicine clinicians who can assist in the diagnosis of arsenic poisoning, in the arrangement for the environmental/work site evaluations and interventions, and in evaluations for worker compensation. Occupational/ environmental/medicine clinicians can also help with the decision for chelation therapy and administration of appropriate therapy (Gensheimer *et al*, 2010).

Clinicians specializing in occupational and environmental medicine can be located by contacting the Association of Occupational and Environmental Clinics (AOEC), a group of occupational medicine clinics (frequently academically affiliated) with board-certified occupational medicine physicians (phone: 202-347-4976; website: www.aoec.org).

Recommendations

The primary target organs for arsenic toxicity are the gastrointestinal tract, skin, bone marrow, kidneys, and peripheral nervous system. Acute toxicity typically starts in the gastrointestinal system and includes nausea, vomiting, abdominal pain, and diarrhea. These symptoms are soon followed by dehydration, hypotension, irregular pulse and cardiac instability and in severe cases by shock, acute respiratory distress syndrome, and sometimes death. In chronic poisoning, the peripheral neurologic complaints and skin manifestations are usually more prominent than the gastrointestinal symptoms.

The arsenic is rapidly cleared from the blood, so measurement of urinary arsenic either on a 24-hour urine collection or in spot urine (along with a creatinine to correct for the concentration of the spot urine) is generally preferable. A concentration greater than or equal to 50mcg/L or 100 mcg of arse-

nic per gram creatinine in the absence of recent fish or shellfish intake strongly suggests arsenic poisoning. Treatment of acute poisoning involves decontamination of the skin and gastrointestinal tract as appropriate for the exposure, administration of fluids, cardiac monitoring, and usually chelation with BAL. DMPS is another option for treatment in countries where it is available. Some patients with chronic toxicity may also benefit from chelation with saucier. No doubt, the senior nurses should attend specific courses and know how to deal with arsenic exposure and poisoning, and emergency antidote for the treatment of ingested poisons is must.

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