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Case Studies in Environmental Medicine

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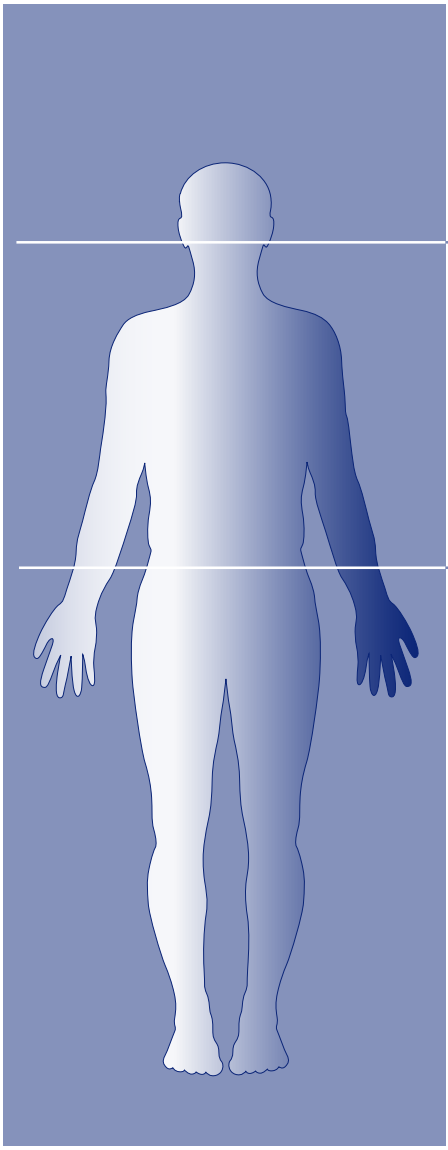

CHROMIUM TOXICITY

Environmental Alert

- Chromium (III) is an essential nutrient that can be toxic in large doses.
- The toxicity of chromium compounds depends on the oxidation state of the metal.
- Occupational exposure to chromium (VI) has been associated with increased incidence of lung cancer.
- The efficacy of chelation therapy in chromium poisoning has not been proven.

This monograph is one in a series of self-instructional publications designed to increase the primary care provider's knowledge of hazardous substances in the environment and to aid in the evaluation of potentially exposed patients. This course is also available on the ATSDR Web site, www.atsdr.cdc.gov/HEC/CSEM/. See page 3 for more information about continuing medical education credits, continuing nursing education units, and continuing education units.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Agency for Toxic Substances and Disease Registry
Division of Toxicology and Environmental Medicine

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Case Studies in Environmental Medicine (CSEM): Chromium Toxicity

Goals and Objectives

The goal of the CSEM is to increase the primary care provider's knowledge of hazardous substances in the environment and to aid in the evaluation of potentially exposed patients.

After completion of this educational activity, the reader should be able to discuss the major exposure route for chromium, describe two potential environmental and occupational sources of exposure to chromium, state two reasons why chromium is a health hazard, describe three factors contributing to chromium toxicity, identify evaluation and treatment protocols for persons exposed to chromium, and list sources of information on chromium.

Accreditation

Continuing Medical Education (CME)

The Centers for Disease Control and Prevention (CDC) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. CDC designates this educational activity for a maximum of 1.0 hour in category 1 credit toward the American Medical Association (AMA) Physician's Recognition Award. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

Continuing Nursing Education (CNE)

This activity for 1.1 contact hours is provided by CDC, which is accredited as a provider of continuing education in nursing by the American Nurses Credentialing Center's Commission on Accreditation.

Continuing Education Units (CEU)

CDC has been approved as an Authorized Provider of continuing education and training programs by the International Association for Continuing Education and Training and awards 0.1 continuing education units (CEUs).

Instructions

See page 4

The questionnaire and posttest must be completed and returned electronically, by fax, or by mail for eligibility to receive continuing education credit.

Instructions for Completing CSEM Online

1. Read this CSEM, *Chromium Toxicity*; all answers are in the text.
2. Link to the MMWR/ATSDR Continuing Education General Information page (www.cdc.gov/atsdr/index.html).
3. Once you access this page, select the Continuing Education Opportunities link.
4. Once you access the MMWR/ATSDR site online system, select the electronic file and/or register and test for a particular ATSDR course.
   a. Under the heading "Register and Take Exam," click on the test type desired.
   b. If you have registered in this system before, please use the same login and password. This will ensure an accurate transcript.
   c. If you have not previously registered in this system, please provide the registration information requested. This allows accurate tracking for credit purposes. Please review the CDC Privacy Notice (www.cdc.gov/privacy.htm).
   d. Once you have logged in/registered, select the test and take the posttest.
5. Answer the questions presented. To receive continuing education credit, you must answer all of the questions. Some questions have more than one answer. Questions with more than one answer will instruct you to "indicate all that are true."
6. Complete the course evaluation and posttest no later than **July 5, 2006**.
7. You will be able to immediately print your continuing education certificate from your personal transcript.

Instructions for Completing CSEM on Paper

1. Read this CSEM, *Chromium Toxicity*; all answers are in the text.
2. Complete the evaluation questionnaire and posttest, including your name, mailing address, phone number, and e-mail address, if available.
3. Circle your answers to the questions. To receive your continuing education credit, you must answer all of the questions.
4. Sign and date the posttest.
5. Return the evaluation questionnaire and posttest, no later than **June 6, 2006**, to CDC by mail or fax:

Mail
Continuing Education Coordinator
Division of Toxicology and
Environmental Medicine, ATSDR
1600 Clifton Road, NE (MS F-32)
Atlanta, GA 30333

or

Fax
770-488-4178
ATTN: Continuing Education Coordinator

6. You will receive an award certificate within 90 days of submitting your credit forms. No fees are charged for participating in this continuing education activity.

Case Study

A 35-year-old handyman has chronic skin ulcers and respiratory irritation

A 35-year-old man visits your family practice office near a large Midwestern city. He has complaints of "allergies" and sores on his hands and arms. Over the past 2 to 3 months, the patient has noticed the onset of "runny nose," "sinus drainage," dry cough, and occasional nosebleeds (both nares intermittently). No prior history of allergies exists. He has also had occasional nausea and is concerned because the sores and minor skin cuts on his hands do not seem to heal. The patient denies having fever, chills, dyspnea, or change in bowel or bladder habits, and he has not noticed excessive thirst or easy bruising. He recently began losing his appetite and losing weight without dieting.

With the exception of the complaints mentioned, review of systems is otherwise unremarkable. The patient has used various over-the-counter remedies for his respiratory problems without relief. He did, however, note significant improvement in symptoms when he visited his sister in Chicago for 5 weeks at the end of the summer.

Medical history reveals only usual childhood diseases. Other than over-the-counter (OTC) decongestants, he is taking no medications. He denies use of illicit drugs, but admits to occasional social use of alcohol. For the last 16 years, he has smoked 1 pack of low-tar cigarettes a day.

The patient has been employed as a mathematics teacher for 13 years; he usually works summers as a self-employed handyman. His hobbies include reading and tennis. Two years ago he moved into a ranch-style house several hundred yards from a small manufacturing plant; a small pond sits between his house and the plant. The house has central air conditioning and gas heat; it is supplied with well water and uses a septic sewage system. Four months ago, the patient began digging up the sewage system to make repairs. Shortly after he began digging, he first noticed the sores on his hands and forearms.

Physical examination reveals an alert white male with skin lesions on the exposed areas of the forearms and hands; edema of the hands is present. The dermal lesions include dermatitis and small circular areas with shallow ulcerated centers. Ear, nose, and throat examination is unremarkable, and chest examination reveals a few scattered rhonchi that clear with coughing. His liver is slightly enlarged and tender to palpation. Cardiovascular, genitourinary, rectal, and neurologic examinations are unremarkable.

Initial laboratory findings include evidence of 2+ proteinuria and hematuria, and slightly elevated bilirubin, aspartate aminotransferase ([AST]; known as serum glutamic-oxaloacetic transaminase [SGOT]), and alanine aminotransferase ([ALT]; known as serum glutamic-pyruvic transaminase [SGPT]). Scrapings of the dermal lesions, done with potassium hydroxide

Pretest

(a) Formulate an active problem list for this patient.

(b) What clues indicate that this case might have an environmental etiology?

(c) What further information will you seek before making a diagnosis?

(d) What treatment will you recommend?

preparation, show no fungal elements or signs of infestation on microscopic examination. A nasal smear for eosinophils is within normal limits.

Who's At Risk

- Workers in industries producing and using chromium are at greatest risk of its adverse effects.

Workers in industries that use chromium, especially stainless steel welding, chromate production, chrome plating, and chrome pigment industries, where exposure via inhalation of aerosols is primarily to hexavalent chromium (Cr [VI]), are at increased risk of chromium's effects. An estimated 175,000 workers might be exposed to Cr (VI) in the workplace on a regular basis; the number is much greater if exposure to other valence states of chromium is also considered. In many occupations, workers are exposed to both trivalent chromium (Cr [III]) and Cr (VI), as soluble and insoluble materials.

- Risk assessment is underway for residents living on landfill derived from chromium-containing solid wastes.

Residents near chromate production facilities might be exposed to higher-than-background levels of Cr (VI). There is also concern that residents whose homes have been built on landfill using slag from smelters or chromate-producing facilities might be exposed to chromium through inhalation and dermal contact. Groundwater contamination might increase exposure in persons using well water as a source of drinking water.

Coal and oil combustion contribute an estimated 1,723 metric tons of chromium per year in atmospheric emissions; however, only 0.2% of this chromium is Cr (VI). In contrast, chrome-plating sources are estimated to contribute 700 metric tons of chromium per year to atmospheric pollution, 100% of which is believed to be Cr (VI).

Challenge

(1) In addition to the patient, who in the case study might be at risk of chromium exposure?

Exposure Pathways

Chromium is a hard, steel-gray metal that is highly resistant to oxidation, even at high temperatures. It is the sixth most abundant element in the earth's crust, where it is combined with iron and oxygen in the form of chromite ore. Russia, South Africa, Albania, and Zimbabwe together account for 75% of world chromite production. Chromite ore has not been mined in the United States since 1961; by 1985 the United States was completely dependent on importation for its primary chromium supply.

Chromium is used in three basic industries: metallurgical, chemical, and refractory (heat-resistant applications), and these industries are the second largest source of ambient chromium. In the metallurgical industry, chromium

is an important component of stainless steels and various metal alloys. Metal joint prostheses made of chromium alloys are widely used in clinical orthopedics. In the chemical industry, chromium is used primarily in paint pigments (chromium compounds can be red, yellow, orange, and green), chrome plating, leather tanning, and wood treatment. Smaller amounts are used in drilling muds, water treatment, catalysts, safety matches, copy machine toner, corrosion inhibitors, photographic chemicals, and magnetic tapes. Refractory uses of chromium include magnesite-chrome firebrick for metallurgical furnace linings and granular chromite for various other heat-resistant applications.

- Chromium is released to air primarily by combustion processes and metallurgical industries.

Chromium exists in a series of oxidation states from -2 to +6 valence; the most important stable states are 0 (elemental metal), +3 (trivalent), and +6 (hexavalent). Chromium in chromite ore is in the trivalent state; industrial processes also produce the elemental metal and hexavalent chromium. The health effects of chromium are at least partially related to the valence state of the metal at the time of exposure. Trivalent (Cr [III]) and hexavalent (Cr [VI]) compounds are thought to be the most biologically significant. Cr (III) is an essential dietary mineral in low doses. Certain compounds of Cr (VI) appear to be carcinogenic, but insufficient evidence exists to determine whether Cr (III) or chromium metal can be human carcinogens. Cr (VI) is generally considered 1,000 times more toxic than Cr (III).

- Chromium exists in three common stable valence states; in order of generally increasing toxicity, these states are chromium (0), (III), and (VI).

Cr (III) is an essential dietary nutrient. It is required to potentiate insulin and for normal glucose metabolism. Chromium deficiency has been associated with impaired glucose tolerance, fasting hyperglycemia, glucosuria, elevated percent body fat, decreased lean body mass, maturity-onset diabetes, cardiovascular disease, decreased sperm count, and impaired fertility.

The National Academy of Science has established a safe and adequate daily intake for chromium in adults of 50–200 micrograms per day (µg/day). Cr (III) is found in most fresh foods and drinking water. Dietary sources rich in chromium include breads, cereals, spices, fresh vegetables, meats, and fish. Other significant sources of chromium are mineral supplements, brewer's yeast, and beer. The daily dietary intake of chromium for a typical American adult is approximately half the minimum suggested safe and adequate daily intake of 50 µg/day.

Cr (III) and Cr (VI) are released to the environment primarily from stationary point sources resulting from human activities. Of the total atmospheric chromium emissions in the United States, approximately 64% are due to Cr (III) from fuel combustion (residential, commercial, and industrial) and from steel production; about 32% are due to Cr (VI) from chemical manufacture, chrome plating, and industrial cooling towers that used chromate chemicals as rust inhibitors in the past. A U.S. Environmental Protection Agency (EPA) report estimates that in the United States, about

2,840 metric tons of total chromium are emitted annually into the atmosphere (compared to approximately 110,000 tons of chromium metal produced each year).

- Nonoccupational sources of chromium include contaminated soil, air, and water.

Electroplating, leather tanning, and textile industries release relatively large amounts of chromium in surface waters. Leaching from topsoil and rocks is the most important natural source of chromium entry into bodies of water. Solid wastes from chromate-processing facilities, when disposed of improperly in landfills, can be sources of contamination for groundwater, where the chromium residence time might be several years. The content of chromium in tap water in U.S. households is from 0.4 to 8.0 micrograms per liter (µg/L). (EPA's maximum contaminant level for chromium in drinking water is 100 µg/L.)

In the 1960s and 1970s, chromium-containing slag was used as landfill in residential, commercial, and recreational settings in over 100 locations in Hudson County, New Jersey. This fill contained chromium in carcinogenic forms and in concentrations that are acutely toxic in certain circumstances. Community exposure from this fill occurred in a variety of ways. Wind erosion of the soil could have made slag particles airborne, increasing the opportunity for inhalation of chromium. Chromium compounds leached by rainwater could have migrated through cracks in soil, asphalt roadways, and masonry walls, forming high-content chromium crystals on their surfaces. In soil and roadways, these particles might have been eroded by wind and foot traffic and carried as chromium-laden dust into homes and workplaces. Children playing in areas where the slag was used as fill might also have been exposed through skin contact with chromium-contaminated dust, dirt, and puddles.

Other environmental sources of chromium include road dust contaminated by emissions of chromium-based catalytic converters or erosion products of asbestos brake linings, cement dust, tobacco smoke, and foodstuffs. Chromium picolinate is now heavily marketed as a dietary supplement, and dietary supplements are virtually unregulated by the Food and Drug Administration.

Cigarettes contain 0.24 to 14.6 milligrams (mg) chromium per kilogram (kg). It is plausible that cigarette smoking might constitute a significant source of chromium intake.

Sources of Chromium Exposure

Environmental and occupational sources of chromium exposure include the following:

Environmental

- Airborne emissions from chemical plants and incineration facilities
- Effluents from chemical plants
- Contaminated landfill
- Cement dust
- Road dust from catalytic converter erosion and asbestos brake lining erosion
- Tobacco smoke
- Topsoil and rocks

Occupational

- Welding of alloys or steel
- Leather tanning (soluble Cr [III])
- Chrome electroplating (soluble Cr [VI])
- Chrome alloy production
- Textile manufacturing
- Paints/pigments (insoluble Cr [VI])
- Photoengraving
- Copier servicing
- Antifreeze
- Antialgae agents
- Production of high-fidelity magnetic audio tapes
- Tattooing
- Wood preservatives
- Agricultural antifungicides
- Porcelain and ceramics manufacturing
- Glassmaking

Challenge

On further questioning, the patient described in the case study relates that when he had reached several feet in depth while digging to repair the sewage system, he noticed an oozing from the ground of sometimes yellowish, sometimes greenish, water; this persisted throughout the several weeks of digging. The nearby pond, which is murky, also has a generally yellow tint, at times with small areas of greenish color. Suspecting an environmental link, you contact the local health department. Levels of chromium are found in the pond water that exceed corresponding health screening values, and the investigators inform you that the nearby plant is electroplating auto parts with chromium.

(2) Discuss all sources and pathways by which this patient might be exposed to chromium.

Biologic Fate

The entry routes of chromium into the human body are inhalation, ingestion, and dermal absorption. Occupational exposure generally occurs through inhalation and dermal contact, whereas the general population is exposed most often by ingestion through chromium content in soil, food, and water.

- Cr (VI) is better absorbed from the lungs, gut, and skin than is Cr (III).

Rates of chromium uptake from the gastrointestinal tract are relatively low and depend on a number of factors, including valence state (with Cr [VI] more readily absorbed than Cr [III]), the chemical form (with organic chromium more readily absorbed than inorganic chromium), the water solubility of the compound, and gastrointestinal transit time. In humans and animals, less than 1% of inorganic Cr (III) and about 10% of inorganic Cr (VI) are absorbed from the gut; the latter amount is slightly higher in a fasting state.

- After absorption, Cr (VI) is reduced to Cr (III).

The percentage of chromium absorption from the lungs cannot be estimated. Within the bronchial tree, epithelium lining fluids directly reduce Cr (VI) to Cr (III). Data from a few animal experiments indicate that with equal solubility, Cr (VI) compounds are absorbed more readily than Cr (III) compounds, probably because Cr (VI) readily penetrates cell membranes. Data from volunteers and indirect evidence from occupational studies indicate that absorption of certain Cr (VI) compounds can occur through intact skin.

- The difference in bioavailability and bioactivity between Cr (III) and Cr (VI) might account for the differences in toxicity.

After entering the body from an exogenous source, Cr (III) does not readily cross cell membranes, but binds directly to transferrin, an iron-transporting protein in the plasma. In contrast, Cr (VI) is rapidly taken up by erythrocytes after absorption and reduced to Cr (III) inside the cell. Regardless of the source, Cr (III) is widely distributed in the body and accounts for most of the chromium in plasma or tissues. The greatest uptake of Cr (III) as a protein complex is via bone marrow, lungs, lymph nodes, spleen, kidney, and liver. Autopsies reveal that chromium levels in the lungs are consistently higher than levels in other organs.

- Only Cr (III) is excreted, primarily in the urine.

Excretion of chromium occurs primarily via urine, with no major retention in organs. In humans, the kidney excretes about 60% of an absorbed Cr (VI) dose in the form of Cr (III) within 8 hours of ingestion. Approximately 10% of an absorbed dose is eliminated by biliary excretion, with smaller amounts excreted in hair, nails, milk, and sweat. Clearance from plasma is generally rapid (within hours), whereas elimination from tissues is slower (with a half-life of several days). Doses of Cr (VI) administered to volunteers were more rapidly eliminated than doses of Cr (III).

Challenge

(3) Analysis of blood and urine specimens from the patient described in the case study reveals elevated Cr (III) serum and urine concentrations. Assuming that the patient was exposed only to Cr (VI), explain the presence of Cr (III) in each of these body fluids.

Physiologic Effects

Chromium's nutritional role has not been thoroughly delineated, but it appears to potentiate insulin action, probably in the form of glucose tolerance factor (GTF). The estimated safe and adequate daily intake of chromium for adults is in the range of 50 to 200 µg/day, although data are insufficient to establish a recommended daily allowance.

- Cr (III) is an essential trace mineral in human nutrition.

Dietary chromium deficiency is reactively uncommon; most cases occur in persons with special problems such as total parenteral nutrition, diabetes, or malnutrition. Chromium deficiency is characterized by glucose intolerance, glycosuria, hypercholesterolemia, decreased longevity, decreased sperm counts, and impaired fertility. In one patient receiving total parenteral nutrition, a peripheral neuropathy was corrected after chromium supplementation.

- Because Cr (VI) is a powerful oxidizing agent, exposure can cause irritation and corrosion.

Major factors governing the toxicity of chromium compounds are oxidation state and solubility. Cr (VI) compounds, which are powerful oxidizing agents and thus tend to be irritating and corrosive, appear to be much more toxic systemically than Cr (III) compounds, given similar amounts and solubilities. Although mechanisms of biological interaction are uncertain, this variation in toxicity may be related to the ease with which Cr (VI) can pass through cell membranes and its subsequent intracellular reduction to reactive intermediates.

- The target organ of inhaled chromium is the lung; the kidneys, liver, skin, and immune system may also be affected. Cr (III), an essential dietary element, plays a role in maintaining normal metabolism of glucose, fat, and cholesterol.

Skin Effects

Chromic acid, dichromates, and other Cr (VI) compounds are not only powerful skin irritants, but they can also be corrosive. On broken skin, a penetrating round ulcer may develop. Common sites for these persistent ulcers ("chrome holes") include the nail root, knuckles and finger webs, backs of the hands, and forearms. The characteristic chrome sore begins as a papule, forming an ulcer with raised hard edges. Ulcers can penetrate deep into soft tissue or become the site of secondary infection, but are not known to lead to malignancy. The progression to ulceration is generally painless, suggesting toxicity to peripheral sensory nerves. The lesions heal slowly and can persist for months.

- Severe dermatitis and skin ulcers can result from contact with Cr (VI) salts.

At concentrations below those resulting in irritation, skin sensitivity is the most common effect after exposure to chromium compounds, especially

- Chromium compounds can be sensitizers as well as irritants.

Cr (VI) compounds. Up to 20% of chromium workers develop contact dermatitis (dermatitis toxicosis). Allergic dermatitis with eczema has been reported in printers, cement workers, metal workers, painters, and leather tanners. Data suggest that a Cr (III)-protein complex is responsible for the allergic reaction, with Cr (III) acting as the hapten.

Respiratory Tract Effects

- When inhaled, Cr (VI) is a respiratory tract irritant and can cause pulmonary sensitization.

Human occupational experience clearly indicates that, when inhaled, Cr (VI) is a respiratory tract irritant, resulting in airway irritation, airway obstruction, and possibly lung cancer. Dose, exposure duration, and the specific compound involved determine chromium's effects.

- Chronic chromium inhalation increases the risk of lung cancer.

Pulmonary irritant effects following prolonged inhalation of chromate (VI) dust can include chronic irritation, congestion and hyperemia, chronic rhinitis, polyps of the upper respiratory tract, tracheobronchitis, chronic pharyngitis, ulceration of the nasal mucosa with possible septal perforation, and chronic bronchitis. Radiograph abnormalities reflect enlargement of the hilar region and lymph nodes, increased peribronchial and perivascular lung markings, and adhesions of the diaphragm. Consistent associations have been found between employment in the primary chromium industries and higher risk for respiratory cancer (see Carcinogenic Effects).

Pulmonary sensitization resulting in an asthmatic response is more common in exposure to Cr (VI) than to Cr (III). A delayed anaphylactoid reaction was reported in a male worker occupationally exposed to chromium vapors from Cr (VI) trioxide baths and chromium fumes from steel welding. A subsequent inhalation challenge with sodium chromate resulted in a reaction including late-onset urticaria, angioedema, and bronchospasm accompanied by tripling of plasma histamine levels.

Many cases of nasal mucosa injury (inflamed mucosa, ulcerated septum, and perforated septum) have been reported in workers exposed to Cr (VI) in chrome-plating plants and tanneries. A 1983 study of 43 chrome-plating plants in Sweden, where workers were exposed almost exclusively to chromic (VI) acid, revealed that all workers with nasal mucosa ulceration or perforation were periodically exposed to at least 20 micrograms per cubic meter ($\mu g/m^3$) when working near the plating baths. (The current U.S. permissible exposure level in the workplace for chromates and chromic acid is 100 $\mu g/m^3$ as a ceiling.) The period of exposure for workers experiencing nasal mucosal ulceration varied from 5 months to 10 years.

Renal Effects

Studies of welders and chromium platers have found that workers with higher levels of exposure to airborne chromium (typically greater than 20 $\mu g/m^3$) show damage to renal tubules. Adverse renal effects have been

reported in humans after inhalation, ingestion, and dermal exposure to chromium. Renal effects in animals occurred only after parenteral administration of large doses.

Although glomerular injury has been noted in chromium workers, the predominant renal injury is tubular, with low doses acting specifically on the proximal convoluted tubules. Low-dose, chronic chromium exposure typically results only in transient renal effects. Elevated urinary $ß_2$-microglobulin levels (an indicator of renal tubular damage) have been found in chrome platers, and higher levels have generally been observed in younger persons exposed to higher Cr (VI) concentrations. However, in a study of tannery workers (Cr [III] exposure) whose duration of employment ranged from 1 month to 30 years, urinary $ß_2$-microglobulin levels were within normal limits, even though urinary chromium levels clearly indicated chromium exposure. A suggested urinary threshold for nephrotoxic effects is 15 µg chromium/g creatinine.

- Low-dose, chronic chromium exposures generally cause only transient renal effects.
- Acute Cr (VI) exposure can result in renal tubular necrosis.

Hepatic Effects

Acute chromium exposure can result in hepatic necrosis. In one case, external chromic acid burns over 20% of a worker's body resulted in severe liver damage and acute renal failure. Limited data indicate that chronic inhalation of chromium compounds also can cause hepatic effects. Acute hepatitis with jaundice was reported in a woman who had been employed for 5 years at a chromium-plating factory. Tests revealed large amounts of urinary chromium, and liver biopsy showed abnormalities. Three co-workers exposed to chromic acid mists from the plating baths for 1 year to 4 years also had mild to moderate liver abnormalities, as determined by liver function tests and liver biopsies.

- Cr (VI) can cause mild to moderate liver abnormalities.

Carcinogenic Effects

Epidemiologic studies of occupational cohorts exposed to chromium aerosols provide clear evidence of carcinogenicity. In one key epidemiologic study involving workers at a chromate production plant who had worked at the plant for more than 1 year from 1931 to 1949, the percentage of deaths due to lung cancer was 18.2%; the percentage expected was 1.2%. For the 322 workers first employed from 1931 to 1937, the percentage of deaths due to lung cancer was close to 60%, with a latency period of approximately 30 years. Studies of workers in the chromium pigment, chrome-plating, and ferrochromium industries also suggest a statistically significant association between worker exposure to chromium and lung cancer. Increased lung cancer mortality has been associated with occupational exposures as short as 2 or 3 years. On the basis of these and other studies, EPA and the International Agency for Research on Cancer (IARC) have classified inhaled Cr (VI) as a known human carcinogen.

- Occupational exposure to Cr (VI) has long been associated with increased lung cancer mortality.
- Latency for chromium-induced lung cancer is greater than 20 years; exposure duration can be as short as 2 years.

Because it is an essential nutrient and it exhibits low acute and chronic toxicity, and because no evidence exists to indicate that Cr (III) can cause cancer in animals or humans, Cr (III) has not been classified as a human carcinogen by the National Toxicology Program, EPA, or IARC.

Although epidemiologic evidence strongly points to Cr (VI) as the agent in carcinogenesis, solubility and other characteristics of chromium compounds might be important in determining cancer risk. Data from animal studies have not resolved the issues of identities and potencies of various chromium-containing compounds as respiratory carcinogens. No chromium compound has been unequivocally shown to cause a significant increase in the number of neoplasms in experimental animals after exposure by natural routes (inhalation, ingestion, or dermal absorption), unless the animals were exposed until death. (Standard protocols for animal experiments involve termination after 24 months.) However, intratracheal instillation, intrabronchial implantation, or injection of various chromium-containing compounds have produced tumors in some cases at the site of application.

No cancers, other than lung cancer, are associated with occupational chromium exposure. All pathologic cell types have occurred in chromium-induced lung cancers; however, small-cell and poorly differentiated cancers predominate. Findings of some epidemiologic studies and animal experiments suggest that chromium is also associated with nonrespiratory cancers, but the evidence is insufficient to consider the nonrespiratory cancers to be of a causal nature.

Reproductive and Developmental Effects

- Data indicate that chromium has effects on reproductive organs and is teratogenic in animals.
- Potential reproductive effects of chromium in humans have not been adequately investigated.

Cr (III) is an essential element that is transported to the developing fetus. Less than 0.5% of Cr (III) was found to cross the placenta in mice when the chromium was administered as an inorganic salt, but concentrations of 20% to 25% were found in litters when chromium was administered in a biologically active form (brewer's yeast). Adverse developmental effects in animals include cleft palate, hydrocephalus, delayed ossification, edema, and incomplete neural tube closure. Data implicating chromium in adverse human reproductive or developmental effects are unavailable.

Challenge

(4) Could chromium toxicity account for the symptoms experienced by the patient described in the case study? Explain.

(5) Is the patient at increased risk of chromium-induced lung cancer?

Clinical Evaluation

History and Physical Examination

Often, no clear diagnostic clues exist in chromium-poisoned patients. A thorough history is therefore critical in evaluating a potentially exposed person. The patient's recent activities are important when health effects other than cancer are the major concern. Occupation, location of residence and workplace in relation to industrial facilities or hazardous waste sites, and source of drinking water supply should be investigated. In patients with known chronic chromium exposure, the physical examination should include evaluation of the respiratory system (if inhalation is involved), kidneys, liver, and skin.

- If chromium exposure is suspected, the respiratory system, kidneys, liver, and skin should be evaluated.

Signs and Symptoms

Acute Exposure

Severe exposures to chromium compounds are usually accidental or suicidal, and are rarely occupational or environmental. Short-term, high-level exposure to Cr (VI) produces irritation at the site of contact, including ulcers of the skin, irritation of the nasal mucosa, perforation of the nasal septum, irritation of the gastrointestinal tract, impairment of olfactory sense, and discoloration (yellowing) of teeth and tongue.

About 1 gram (g) of potassium dichromate (VI) is considered a lethal dose. Persons who ingested 5 g or more experienced gastrointestinal bleeding, massive fluid loss, and death within 12 hours after ingestion. When the ingested dose was 2 g or less, renal tubular necrosis or diffuse hepatic necrosis resulted, with acute renal failure before death in some cases. Typically, the kidney and liver effects develop 1 day to 4 days after ingestion of a sublethal dose. Other symptoms of acute Cr (VI) ingestion include vertigo, thirst, abdominal pain, and vomiting. Oliguria, anuria, shock, convulsions, coma, and death can ensue. Gastrointestinal hemorrhage and coagulopathy can also occur. Acute chromium poisonings are often fatal regardless of the therapy used.

- Ingestion of a lethal dose of chromate can result in cardiovascular collapse due to severe hypovolemia.
- Sublethal doses of chromate can lead to renal and hepatic necrosis 1 day to 4 days after ingestion.

Dermal contact with Cr (VI) compounds can result in severe systemic toxicity. In one case involving intact skin, antiscabies ointment containing Cr (VI) resulted in necrosis of skin at application sites, nausea, vomiting, shock, coma, and death. Two other cases involved broken skin: severe nephritis and death followed cauterization of an open wound with Cr (VI) oxide, and an occupational fatality was described after an accident in which a worker was burned on the arms and trunk with hot potassium dichromate.

- In occupational settings, the most commonly reported effects of chronic chromium exposure are contact dermatitis and irritation and ulceration of the nasal mucosa.
- Less common are reports of hepatic and renal damage and pulmonary effects.
- Lung cancer is a potential long-term effect of chronic Cr (VI) exposure.

Chronic Exposure

Repeated skin contact with chromium dusts can lead to incapacitating eczematous dermatitis with edema. Chromate dusts can also produce irritation of the conjunctiva and mucous membranes, nasal ulcers and perforations, keratitis, gingivitis, and periodontitis. When a solution of chromate contacts the skin, it can produce penetrating lesions known as chrome holes or chrome ulcers, particularly in areas where a break in the epidermis is already present. These ulcers are usually painless, but might persist for months. Acute hepatitis with jaundice has also been observed in workers chronically exposed to Cr (VI). Lung cancer is the most serious long-term effect.

Low-level environmental exposures have not resulted in adverse effects in human populations. Long-term studies in which animals have been exposed to low levels of chromium in food or water have produced no harmful effects.

Laboratory Tests

A general medical workup for a patient with suspected chronic chromium exposure might include the following:

Screening Tests

- Complete blood count
- Blood panel
- Liver function tests (AST or SGOT, ALT or SGPT, and bilirubin)
- Blood urea nitrogen (BUN) and creatinine
- Urinalysis

Specialized Tests

- Blood and urine chromium levels
- $ß_2$ microglobulin.

If chromium inhalation has occurred, a chest radiograph, pulmonary function testing, and a nasal smear for eosinophils should be included.

Direct Biologic Indicators

When obtaining biologic specimens for chromium analysis, care must be taken to avoid sample contamination and chromium loss during collection, transportation, and storage. For example, use of stainless steel utensils to collect tissue samples might raise tissue chromium levels, as will stainless steel grinding and homogenizing equipment. Some plastic containers contain significant amounts of leachable chromium; therefore, specially prepared acid-washed containers should be obtained from the laboratory. Considerable care also must be taken in the analysis to minimize chromium volatilization during sample ashing.

Another difficulty in the available techniques is the inability to distinguish between Cr (III) and Cr (VI). This is particularly important in environmental samples because Cr (VI) has been associated with serious health hazards, whereas Cr (III) is of far less concern.

Blood or serum chromium levels. Blood distribution of chromium appears to be divided evenly between plasma and erythrocytes. In the absence of known exposure, whole blood chromium concentrations are in the range of 2.0 µg/100 mL to 3.0 µg/100 mL; lower levels occur in rural areas, and higher levels occur in large urban centers. Values above background levels are considered potentially toxic, but levels have not been correlated with specific physiologic effects. Chromium rapidly clears from the blood, and measurements relate only to recent exposure.

- Chromium can be measured in blood and urine; hair or nail analysis has no clinical value.

Urinary chromium levels. Wide individual variation in metabolism and rapid depletion of body burden limit the value of urinary chromium monitoring. Urinary chromium excretion reflects absorption over the previous 1 or 2 days only. If sufficient time has elapsed for urinary clearance, a negative biomonitoring result can occur even with injurious past exposure. Assuming no source of excessive exposure, urinary chromium values are typically less than 10 µg for a 24-hour period.

- Urinary chromium excretion is a useful index of exposure in occupational settings.

In occupational settings, a urinary chromium concentration of 40 µg/L to 50 µg/L immediately after a work shift reflects exposure to air levels of 50 µg/m^3 of soluble Cr (VI) compounds, a concentration associated with nasal perforations in some studies. The American Conference of Governmental Industrial Hygienists has set a workplace biologic exposure index for total urinary chromium as follows: no more than 10 µg chromium per gram creatinine increase during a work shift, and a urinary value of less than 30 µg chromium per gram creatinine at the end of the work week.

Hair or nail analysis is of little use in evaluating an individual patient because it is impossible to distinguish chromium bound within the hair during protein synthesis from chromium deposited on the hair from dust, water, or other external sources. Populations with no known chromium exposure reportedly have hair levels ranging from 50 parts per million (ppm) to 100 ppm chromium.

The presence of chromium and chromium complexes in biologic complexes can be determined using chromatographic and colorimetric techniques; patch testing and lymphocyte proliferation testing have been used to determine chromium sensitivity.

Challenge

(6) Analysis of the tap water in the patient's home reveals a greenish tinge and a chromium concentration of 746 µg/L. Your diagnosis is chromium toxicity. Are there any other tests the patient should undergo?

(7) The patient described in the case study insists on obtaining a hair analysis. The chromium content of the hair sample is 1,038 ppm. How will you interpret this result?

Treatment and Management

Acute Exposure

- No proven antidote is available for chromium poisoning.
- Acute poisonings are often fatal regardless of therapy.

Treatment in cases of acute, high-level chromium exposure is usually supportive and symptomatic. Supportive measures may include ventilatory support, cardiovascular support, and renal and hepatic function monitoring. When renal function is compromised, urine alkalinization and maintenance of adequate urine flow are important. Progression to anuria is associated with poor prognosis.

If the eyes and skin are directly exposed, flush with copious amounts of water. Topical ascorbic acid has been successfully used to prevent chromium dermatitis and dermal burns caused by dichromate. The ulcers heal in several weeks without specific treatment. Ethylenediaminetetraacetic acid (EDTA) ointment 10% might facilitate removal of chromate scabs.

Gastric lavage with magnesium hydroxide or another antacid might be useful in cases of chromium ingestion. Fluid and electrolyte balance is critical. The efficacy of activated charcoal has not been proven. Hemodialysis, exchange transfusions, or chelating agents such as dimercaprol or EDTA have not been shown to be effective in the treatment of human poisoning. Orally administered ascorbic acid was found to be protective in experimental animals and was reported beneficial in at least one patient after chromium ingestion; however, no clinical trials have been conducted to confirm the efficacy of this treatment. Induction of vomiting is contraindicated.

Chronic Exposure

- Treatment consists of removal of the patient from further chromium exposure, reliance on the body's naturally rapid clearance of the metal, and symptomatic management.

In most patients with chronic, low-dose exposure, no specific treatment is needed. The mainstay of management is removing the patient from further exposure and relying on the urinary and fecal clearance of the body burden. Although normal urinary excretion is quite rapid, forced diuresis has been used. Except in the lungs, only small amounts of chromium are retained several weeks after exposure has ceased. Dermatitis and liver and renal injury will not progress after removal from exposure, and, in most cases, the patient will recover. Weeping dermatitis can be treated with 1% aluminum

acetate wet dressings, and chrome ulcers can be treated with topical ascorbic acid.

If the exposure has been lengthy (i.e., 2 years to 3 years), the increased risk of lung cancer should be discussed with the patient. Although no reliable tests are currently available to screen patients for lung cancer, the physician can intervene with advice and education in smoking cessation, exposure to other known pulmonary carcinogens, and general preventive health education. Annual chest radiographs might be advisable in carefully selected cases.

Challenge

(8) What is the recommended treatment for the patient described in the case study?

Standards and Regulations

Table 1 summarizes the U.S. standards and regulations for chromium salts.

Workplace

Air

The Occupational Safety and Health Administration (OSHA) mandated a permissible exposure limit (PEL) ceiling of 100 µg CrO_3/m^3 for chromic acid and chromates. For Cr (II) and Cr (III) salts, the PEL is an 8-hour time-weighted average (TWA) of 500 µg Cr/m^3. For chromium metal and for insoluble salts, the TWA is 1,000 µg Cr/m^3.

- OSHA mandates a ceiling concentration of 100 µg CrO_3/m^3 for chromic acid and chromates.

The National Institute for Occupational Safety and Health (NIOSH) has recommended a 10-hour TWA exposure limit of for all Cr (VI) compounds of 1 µg Cr (VI)/m^3. For chromium metal and Cr (II) and Cr (III) compounds, the recommended exposure limit is 500 µg Cr (VI)/m^3 as a 10-hour TWA.

On the basis of current evidence, NIOSH considers all Cr (VI) compounds potentially carcinogenic.

Environment

Air

EPA regulates chromium emissions under the Clean Air Act of 1990. EPA uses technology-based standards for categories of industries, rather than numerical emission standards, to reduce chromium levels in ambient air. These maximum achievable control technology (MACT) standards are based on emissions levels already achieved by the best-performing similar facilities.

- The current maximum contaminant level for chromium in drinking water is 100 µg/L.

Drinking Water

EPA has an enforceable maximum contaminant level of total chromium in drinking water of 100 µg/L (100 ppb) for public water systems.

Table 1. Standards and Regulations for Chromium

Agency	Focus	Level	Comments
American Conference of Governmental Industrial Hygienists	Air: workplace	10 µg/m^3 as Cr	Advisory; TWA* to avoid carcinogenic risk from insoluble Cr (VI) compounds
		50 µg/m^3 as Cr	TWA for water-soluble Cr (VI) compounds
		500 µg/m^3 as Cr	TWA for chromium metal and Cr(III) compounds
National Institute for Occupational Safety and Health	Air: workplace	1 µg/m^3 as Cr	Advisory; TWA (10-hour) for chromic acid and all Cr (VI) salts
		500 µg/m^3 as Cr	Advisory; TWA (10-hour) for chromium metal and Cr (II) and Cr (III) salts
Occupational Safety and Health Administration	Air: workplace	100 µg/m^3 as CrO_3	Regulation; PEL† for chromic acid and chromates (ceiling)
		500 µg/m^3 as Cr	PEL for Cr (II) and Cr (III) salts (8-hour TWA)
		1,000 µg/m^3 as Cr	PEL for chromium metal and insoluble salts (8-hour TWA)
U.S. Environmental Protection Agency	Air: environment	Not applicable	Chromium is listed as a hazardous pollutant
	Drinking water	100 µg/L	Regulation; current MCL‡ for total chromium

*TWA (time-weighted average): TWA concentration for a normal workday and a 40-hour workweek to which nearly all workers may be repeatedly exposed.
†PEL (permissible exposure limit): highest level of chromium in air to which a worker may be exposed, averaged over an 8-hour workday.
‡MCL (maximum contaminant level) enforceable level for drinking water.

Suggested Reading

General

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Powers WJ, Gad SC, Siino KM, Pechman JC. 1986. Effects of therapeutic agents on chromium-induced acute nephrotoxicity. In: Serrone DM, editor. Chromium symposium 1986: an update. Pittsburgh (PA): Industrial Health Foundation, Inc. p. 79–86.

Related Documents

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National Institute for Occupational Safety and Health. 1999. NIOSH pocket guide to chemical hazards. Cincinnati (OH): National Institute for Occupational Safety and Health. Available from URL: www.cdc.gov/niosh/npg/pgdstart.html.

US Environmental Protection Agency. 1984. Health assessment document for chromium. Research Triangle Park (NC): Environmental Protection Agency, Environmental and Criteria Assessment Office. EPA report no. 600/8-83-014F.

US Environmental Protection Agency. 1984. Health effects assessment for hexavalent chromium. Cincinnati (OH): Environmental Protection Agency, Environmental and Criteria Assessment Office. EPA report no. 540/1-86-019.

US Environmental Protection Agency. 1984. Health effects assessment for trivalent chromium. Cincinnati (OH): Environmental Protection Agency, Environmental and Criteria Assessment Office. EPA report no. 540/1-86-035.

US Environmental Protection Agency, Office of Ground Water and Drinking Water. 2000. Current drinking water standards. Washington (DC): Environmental Protection Agency. Available from URL: www.epa.gov/safewater/mcl.html.

Answers to Pretest and Challenge Questions

Pretest

(a) A problem list for this patient would include upper and lower respiratory irritation, multiple skin lesions and edema of the hands, loss of appetite and weight loss, liver and renal dysfunction, and cigarette smoking.

(b) Information suggesting an environmental etiology includes the following: onset of the patient's symptoms coincides with activity outside the usual routine; in addition, the patient mentions that he first noticed the sores on his hands and forearms while digging up the sewage system to make repairs. Another clue to a possible environmental cause is temporary relief of symptoms when the patient leaves his usual habitat, such as when he visited Chicago. Proximity of the patient's home to an industrial facility (i.e., the electroplating plant) is also an important clue.

(c) You might identify possible causes for the dermal lesions by consulting with a dermatologist. The cause of the persistent respiratory symptoms (2 to 3 months) that do not respond to OTC decongestants in a person with no history of allergies should be pursued; the patient should be queried about whether the onset of symptoms coincided with the move to his home, whether odors have emanated from the plant, and so forth. More information regarding the patient's observations and activities while digging up the sewage system may also be helpful.

(d) See answer to Challenge question 8.

Challenge

(1) If effluent from the plant has reached the groundwater, community residents who drink well water might be at risk. Airborne plant emissions might have also reached nearby residents. Plant workers who prepare the plating baths and work near them might be receiving significant exposure.

(2) The most important pathways for possible chromium exposure in this case are dermal contact during the unearthing of the sewage system; inhalation of emissions from the plant or soil particles if the pond dries up; and ingestion, if the drinking water has been contaminated by effluents from the plant.

Minor inhalation sources of chromium might include road and cement dust, erosion products of brake linings and emissions from automotive catalytic converters, and tobacco smoke. Cigarettes contain 0.24 mg/kg to 14.6 mg/kg

chromium, although it is not known how much of this is inhaled. Foodstuffs (ingestion) generally contain extremely low chromium levels.

(3) Cr (VI) is a powerful oxidizing agent. In the plasma and cells, it is readily reduced to Cr (III), which is excreted in the urine.

(4) Yes. Persistent dermal ulcers, respiratory tract irritation, and pulmonary sensitization are all possible effects of chromium exposure.

(5) Although it cannot be ruled out, it is unlikely that the dermal and inhalation chromium exposure of this patient will cause lung cancer. Workers who had significant inhalation exposure to chromium for 2 years or longer have developed lung cancer. Because this patient's inhalation exposure is at ambient air levels and probably of 2 years duration at most, any increase in his relative risk would not be great. The patient should be advised to stop smoking cigarettes because smoking may act synergistically to increase risk and is itself a significant risk factor for lung cancer. The data are insufficient to estimate the risk from ingestion of the contaminated drinking water.

(6) If exposure was recent, chromium levels in blood or urine may be used to confirm exposure. Renal function should be tested (urinalysis, blood urea nitrogen, creatinine, and $ß_2$-microglobulin) to determine if renal tubular damage has occurred.

(7) No useful interpretations can be drawn from the hair analysis. A result of 1,038 ppm is beyond the range for unexposed persons (50 ppm to 1,000 ppm); however, the sample could have been environmentally contaminated with chromium from the water during bathing, or by chromium in ambient air polluted by the plant emissions. No standard methods exist for obtaining a hair sample or for washing and preparing the sample for analysis, and these techniques can greatly influence results. Finally, no research exists to prove a correlation between chromium content of hair and exposure levels or physiologic effects; therefore, the result has no clinical significance.

(8) If the sources of chromium exposure can be eliminated for this patient, no further treatment would be required, except for the skin lesions. Topical ascorbic acid has been useful in the treatment of chrome ulcers, and 1% aluminum acetate wet dressings can be used to treat the dermatitis.

This patient's case might be a sentinel for community exposure. You should contact the local health department, OSHA, and EPA to report your patient's adverse effects and discuss your suspicions of the chromium source. Chromium levels in and around the plant should be measured. If a hazard exists, workers should be provided proper protective gear, trained, and medically monitored. Because EPA does not have an emission standard, it might be difficult to abate the atmospheric source of chromium. Decontamination of the pond might require regulatory action and litigation. Residents who use well water should be encouraged to use an alternative water source for drinking and cooking.

Sources of Information

More information on the adverse effects of chromium and the treatment and management of chromium-exposed persons can be obtained from ATSDR, your state and local health departments, and university medical centers. *Case Studies in Environmental Medicine: Chromium Toxicity* is one of a series. For other publications in this series, please use the order form on page 31. For clinical inquiries, contact ATSDR, Division of Toxicology and Environmental Medicine at 770-488-3490.

Notes

Case Studies in Environmental Medicine:

Chromium Toxicity

Course Goal: To increase the primary care provider's knowledge of hazardous substances in the environment and to aid in the evaluation of potentially exposed patients.

Objectives

- Discuss the major exposure route for chromium.
- State two reasons why chromium is a health hazard.
- Describe three factors contributing to chromium toxicity.
- Describe two potential environmental and occupational sources of exposure to chromium.
- Identify evaluation and treatment protocols for persons exposed to chromium.
- List sources of information on chromium.

Tell Us About Yourself

Please carefully read the questions. Provide answers on the answer sheet (page 31). Your credit will be awarded based on the type of credit you select.

1. **What type of continuing education credit do you wish to receive?**
   ****Nurses should request CNE, not CEU. See note on page 30.**
   A. CME (for physicians)
   B. CME (for non-physicians)
   C. CNE (continuing nursing education)
   D. CEU (continuing education units)
   E. [Not used]
   F. [Not used]
   G. [Not used]
   H. None of the above

2. **Are you a...**
   A. Nurse
   B. Pharmacist
   C. Physician
   D. Veterinarian
   E. None of the above

3. **What is your highest level of education?**
   A. High school or equivalent
   B. Associate, 2-year degree
   C. Bachelor's degree
   D. Master's degree
   E. Doctorate
   F. Other

4. Each year, approximately how many patients with chromium exposure do you see?

A. None
B. 1–5
C. 6–10
D. 11–15
E. More than 15

5. Which of the following best describes your current occupation?

A. Environmental Health Professional
B. Epidemiologist
C. Health Educator
D. Laboratorian
E. Physician Assistant
F. Industrial Hygienist
G. Sanitarian
H. Toxicologist
I. Other patient care provider
J. Student
K. None of the above

6. Which of the following best describes your current work setting?

A. Academic (public and private)
B. Private health care organization
C. Public health organization
D. Environmental health organization
E. Non-profit organization
F. Other work setting

7. Which of the following best describes the organization in which you work?

A. Federal government
B. State government
C. County government
D. Local government
E. Nongovernmental agency
F. Other type of organization

Tell Us About the Course

8. How did you obtain this course?

A. Downloaded or printed from Web site
B. Shared materials with colleague(s)
C. By mail from ATSDR
D. Not applicable

9. How did you first learn about this course?

A. State publication (or other state-sponsored communication)
B. *MMWR*
C. ATSDR Internet site or homepage
D. PHTN source (PHTN Web site, e-mail announcement)
E. Colleague
F. Other

10. What was the most important factor in your decision to obtain this course?

A. Content
B. Continuing education credit
C. Supervisor recommended
D. Previous participation in ATSDR training
E. Previous participation in CDC and PHTN training
F. Ability to take the course at my convenience
G. Other

11. How much time did you spend completing the course, and the evaluation and posttest?

A. 1 to 1.5 hours
B. More than 1.5 hours but less than 2 hours
C. 2 to 2.5 hours
D. More than 2.5 hours but less than 3 hours
E. 3 hours or more

12. Please rate your level of knowledge before completing this course.

A. Great deal of knowledge about the content
B. Fair amount of knowledge about the content
C. Limited knowledge about the content
D. No prior knowledge about the content
E. No opinion

13. Please estimate your knowledge gain after completing this course.

A. Gained a great deal of knowledge about the content
B. Gained a fair amount of knowledge about the content
C. Gained a limited amount of knowledge about the content
D. Did not gain any knowledge about the content
E. No opinion

Please use the scale below to rate your level of agreement with the following statements (questions 14–25) about this course.

A. Agree
B. No opinion
C. Disagree
D. Not applicable

14. The objectives are relevant to the goal.

15. The tables and figures are an effective learning resource.

16. The content in this course was appropriate for my training needs.

17. Participation in this course enhanced my professional effectiveness.

18. I will recommend this course to my colleagues.

19. Overall, this course enhanced my ability to understand the content.

20. I am confident I can discuss the major exposure for chromium.

21. I am confident I can describe two potential environmental and occupational sources of exposure to chromium.

22. I am confident I can state two reasons why chromium is a health hazard.

23. I am confident I can describe three factors contributing to chromium toxicity.

24. I am confident I can identify evaluation and treatment protocols for persons exposed to chromium.

25. I am confident I can list sources of information on chromium.

Posttest

If you wish to receive continuing education credit for this program, you must complete this posttest. Each question below contains five suggested answers, of which one or more is correct. Choose all correct answers for each question.

26. Which of the following statements(s) is (are) true?

(A) Chromium is excreted in urine and bile as Cr (III).
(B) Cr (III) is generally more toxic than Cr (IV).
(C) Cr (III) is absorbed more quickly than Cr (VI).
(D) Cr (VI) is carcinogenic when inhaled.
(E) Chromium is stored in bones and teeth.

27. Biologically active chromium is in the

(A) 0 valence state
(B) +1 valence state
(C) +2 valence state
(D) +3 valence state
(E) +6 valence state.

28. Significant chromium uptake occurs in the

(A) adrenal gland
(B) lung
(C) kidneys
(D) muscle
(E) liver.

29. Dermal signs of chromium exposure can include

(A) angioneurotic edema
(B) penetrating, painless, and persistent ulcers
(C) scleroderma-like lesions
(D) dermatitis with eczema and edema
(E) erythema nodosum.

30. Treatment recommendations for patients with chronic chromium poisoning can include

(A) prolonged chelation therapy with dimercaprol
(B) cessation of further exposure
(C) a half-face canister respirator in areas with high airborne concentrations
(D) surveillance for lung cancer
(E) topical ascorbic acid treatment for chrome ulcers.

31. Which of the following statement(s) is (are) true?

(A) Chromium deficiency might result in glucose intolerance.
(B) Cr (VI) compounds are irritating and corrosive.
(C) Cr (III) readily passes through cell membranes.
(D) Chrome holes are most often found on the legs and back.
(E) Chromium compounds might be skin and pulmonary sensitizers.

32. Effects of chronic chromium exposure can include

(A) pancreatitis
(B) nasal mucosal irritation
(C) central nervous system depression
(D) chromium-induced asthma
(E) lung cancer.

33. Because Cr (VI) is a powerful oxidizing agent, it

(A) causes gastrointestinal hemorrhage when ingested
(B) causes skin necrosis on dermal contact
(C) is transported readily in air and water
(D) causes dysrhythmias
(E) is eliminated in the urine.

Note to Nurses

CDC is accredited by the American Nurses Credentialing Center's (ANCC) Commission on Accreditation. ANCC credit is accepted by most State Boards of Nursing.

California nurses should write in "ANCC - Self-Study" for this course when applying for relicensure. A provider number is **not** needed.

Iowa nurses must be granted special approval from the Iowa Board of Nursing. Call 515-281-4823 or e-mail marmago@bon.state.ia.us to obtain the necessary application.

Case Studies in Environmental Medicine:

Chromium Toxicity

Answer Sheet, Course Number SS3048

Instructions for submitting hard-copy answer sheet: Circle your answers. To receive your certificate, you must answer **all** questions. Mail or fax your completed answer sheet to

Fax: 770-488-4178, ATTN: Continuing Education Coordinator

Mail: Agency for Toxic Substances and Disease Registry
ATTN: Continuing Education Coordinator
Division of Toxicology and Environmental Medicine
1600 Clifton Road, NE (MS F-32)
Atlanta, GA 30333

Remember, you can access the case studies online at www.atsdr.cdc.gov/HEC/CSEM/ and complete the evaluation questionnaire and posttest online at www2.cdc.gov/atsdrce/.

Online access allows you to receive your certificate as soon as you complete the posttest.

Be sure to fill in your name and address on the back of this form.

1. A B C D E F G H
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5. A B C D E F G H I J K
6. A B C D E F
7. A B C D E F
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28. A B C D E
29. A B C D E
30. A B C D E
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33. A B C D E

Name: E-mail (not required):

Address:

Zip code:

○ Check here to be placed on the list to pilot test new case studies

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Access the case studies online at www.atsdr.cdc.gov/HEC/CSEM/ and complete the evaluation questionnaire and posttest online at www2.cdc.gov/atsdrce/.

Online access allows you to receive your certificate as soon as you complete the posttest.

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