What is Chromium?

Chromium (chemical symbol, Cr) is a naturally-occurring, grayish, metallic element, typically found in soil, rocks, and most species of plants and animals. The three main forms of chromium are Cr(0) (metallic chromium), Cr(III) (trivalent chromium), and Cr(VI) (hexavalent chromium). The predominant form of chromium in most soils and rocks is various forms of Cr(III). Under the right environmental conditions, some Cr(III) in soils or water may be oxidized to Cr(VI). Cr(0) or metallic chromium does not generally occur naturally in the environment.

Chromium(III) is an essential nutrient that helps the body use sugar, protein, and fat. In 1989, the National Academy of Sciences established an “estimated safe and adequate daily dietary intake” of Cr (III) for adults and adolescents of 50 to 200 μg per day. On average, adults take in an estimated 76 μg (range 25 to 224 μg) of Cr (III) per day in food. Therefore, some people’s diets may not provide enough Cr(III), particularly if the diets are high in simple sugars. Without sufficient Cr(III) in the diet, the body can lose the ability to properly use sugars, proteins, and fat resulting in weight loss, decreased growth, improper function of the nervous system, or a diabetic-like condition. Many “multivitamins with minerals” formulations and some individual dietary supplements contain 50-200 μg of Cr (III).

Routes of Exposure

Like many chemicals (dietary or otherwise), Cr can enter the body through ingestion, inhalation, or dermal absorption. Occupational exposure to Cr generally occurs through the inhalation of chromium-containing particulates, chromic acid mists, metal fumes, or through skin contact with various chromium compounds or solutions. Since most plants, animals, and soils contain a certain amount of chromium, ingestion of food, water, and small amounts of dust or soil are the most common ways that people are exposed to Cr. Most of the chromium present in food is of the trivalent form; an essential dietary nutrient.

Who Is At Risk from Chromium Exposure?

Workers in industries producing and using chromium have the greatest risk of exposure to Cr. Chromium is one of the most widely used industrial metals. Several million workers worldwide are estimated to be exposed to chromium compounds in a variety of industries such as chrome plating, pigment production, stainless steel welding, leather tanning, and Portland cement production. The American Conference of Governmental Industrial Hygienists (ACGIH) has adopted a Threshold Limit Value (TLV) of 50 μg/m³ for occupational exposures to soluble Cr(VI) compounds.

The general population may be exposed to Cr through inhalation if they live near power generation facilities, facilities handling fly ash or cement dust, manufacturing facilities that use or produce chromium products, or in areas with high vehicular traffic. The Agency for Toxic Substances and Disease Registry (ATSDR) has established an inhalation Minimum Risk Level (MRL) of 0.005 μg/m³ for both intermediate and chronic duration exposures to Cr(VI) oxide and chromic acid mists in ambient air. The ATSDR has also established an intermediate inhalation MRL of 0.3 μg/m³ for other hexavalent chromium compounds in air.

People also may be exposed to Cr in their drinking water when public or private wells are screened in aquifers with ground water either contaminated with chromium or with naturally occurring chromium. The ATSDR has established an intermediate MRL of 0.005 mg/kg/day and a chronic MRL of 0.001 mg/kg/day for hexavalent chromium compounds by the oral exposure route. These doses translate to drinking water Environmental Media Evaluation Guides (EMEGs) for adults of 200 μg/L and 40 μg/L for intermediate and chronic duration exposures, respectively.
Everyone receives a certain amount of chromium in the food they eat, and some people receive additional chromium through dietary supplements or vitamins with minerals. Absorbed chromium can be transferred to the fetus through the placenta and to infants via breast milk. Since tobacco contains chromium, people who use tobacco products will be exposed to higher levels of chromium.

What Happens to Chromium After it Enters the Body?

The majority of ingested Cr(VI) is quickly reduced to Cr(III) in the stomach by gastric acids. Depending on nutritional status, less than 10% (and usually less than 3%) of the total ingested dose (the Cr(III) and some of the original Cr(VI)) is absorbed into the blood, primarily though the small intestines. The rest passes out in the feces. In this process, however, the gastric and intestinal mucosa may sustain some degree of erosive damage, depending on the concentration and total ingested dose. Inhaled Cr(VI) may be absorbed from the lungs into the bloodstream to a greater or lesser degree depending on the solubility of the specific chromium compound. Trivalent salts generally are absorbed poorly through intact skin, but once the dermal barrier is broken, absorption may occur. Hexavalent salts, however, are relatively well absorbed through intact skin.

Most of the Cr(VI) that makes it into the bloodstream is reduced to Cr(V), Cr(IV), and then to Cr(III) by ascorbate, glutathione, and a number of other substances over a period of a few hours. The circulating chromium distributes to nearly all body tissues, with the highest concentrations being found in the kidneys and liver. Excretion of absorbed chromium occurs primarily through the urine. In humans, the kidneys excrete about 60% of the absorbed Cr(VI) dose in the form of Cr(III) within 8 hours of ingestion. Approximately 10% of the absorbed dose is excreted by the gallbladder into bile which is then eliminated in the feces; smaller amounts are excreted in hair, nails, milk, and sweat. Clearance from plasma is generally rapid (within a few hours), whereas elimination from tissues is slower (with a half-life of 5-7 days).

Adverse Effects of Chromium Exposure

Major factors governing the toxicity of chromium compounds are oxidation state and solubility. Cr(VI) compounds, which are powerful oxidizing agents, tend to be irritating and corrosive and are 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 [Cr(V) and Cr(IV)].

Acute Exposures

Acute, life-threatening poisonings in the general environment are rare. Severe no occupational exposures to Cr(VI) compounds are more likely to result from accidental ingestions by children or intentional ingestions (suicide attempts) by adolescents or adults.

Occupational poisonings are more likely to result from dermal contact (splashes to the eyes or skin or partial body immersions) or inhalation exposure to excessive Cr(VI) dusts or acid mists.

Acute Cr(VI) ingestion poisonings are often fatal regardless of the therapy used. Lethal quantities of potassium dichromate have ranged from as little as 7.5 mg in a 14-year-old boy and 29 mg in a 17-year-old male up to 25 g in a 35-year-old female.

Ingestion of potentially lethal quantities of Cr(VI) compounds in acute poisoning cases may cause: caustic burns in the mouth and pharynx, intense gastrointestinal irritation, corrosion, and/or ulceration, epigastric pain, nausea, bloody vomitus, diarrhea, irregular respiration or labored breathing, inhibition of blood coagulation, hemorrhagic diathesis, intravascular hemolysis, circulatory collapse, toxic nephritis, renal failure, severe liver damage, acute multisystem organ failure, coma, and death.

Depending on the body surface area exposed, the Cr(VI) concentration, and the dose absorbed through the skin, acute dermal exposure to Cr(VI) compounds such as chromic acid or potassium chromate solutions may cause blisters and burns on exposed skin, necrosis and sloughing of the skin, and signs and symptoms of systemic toxicity.
**Clinical Assessment**

Often, no clear diagnostic clues exist in chromium-exposed patients; thus, a thorough history is critical. Information on recent activities, occupation, proximity of residence and workplace to industrial facilities or hazardous waste sites, and source of drinking water all are important. An evaluation of patients with known chromium exposure should include an evaluation of the upper and lower respiratory tract, kidneys, liver, and skin.

**Chronic Exposures**

Chronic exposures to Cr(VI) may occur through ingestion, inhalation, or dermal contact. The liver and kidneys are the main target organs for chronic Cr(VI) toxicity.

**Ingestion:** Chronic oral exposure to high levels of Cr(VI) in drinking water (approximately 20,000 μg/L) has been associated with oral ulcers, indigestion, abdominal pains, vomiting, diarrhea, diffuse epithelial hyperplasia of the duodenum, leukocytosis, and immature neutrophils in the blood smear.

**Inhalation:** Characteristic signs and symptoms of patients with chronic inhalation exposure to Cr(VI) compounds, particulates, and acid mists include irritation and ulceration of the nasal mucosa; perforation of the nasal septum; keratosis of the lips, gingiva, and palate; inflammation of oral structures; periodontitis; tonsillitis; pharyngitis; sinusitis; respiratory irritation; bronchitis; asthma; and lung cancer.

**Dermal:** The most commonly reported effects of chronic dermal exposure to Cr(VI) solids, liquids, surface residues, or airborne Cr(VI) dusts or acid mists are penetrating ulcers of the skin (chrome holes), scars from healed skin ulcers, skin blisters and burns, ocular burns, conjunctivitis, allergic contact dermatitis in sensitized individuals, generalized skin irritation, and rashes.

**Laboratory Tests**

With excessive exposure, there may be evidence of renal and hepatic damage. Proteinuria and hematuria often precede anuria and uremia. The following laboratory tests should be considered in patients with moderate to severe Cr(VI) exposures and significant symptomatology:

- Complete blood count (CBC)
- Aspartate aminotransferase (AST) or serum glutamic-oxaloacetic transaminase (SGOT)
- Alanine transaminase (ALT) or serum glutamic-pyruvic transaminase (SPGT)
- Bilirubin
- Lactic dehydrogenase (LDH)
- Red blood cell (RBC) and urine chromium levels (for acute exposure within the past 48 hours)
- Serum blood urea nitrogen (BUN) and creatinine, and complete urinalysis

For occupational settings, the American Conference of Governmental Industrial Hygienists (ACGIH) recommends measuring the increase in total urine chromium during a work shift, with an upper limit of 10 μg per g of creatinine and the total urinary chromium at the end of the last shift of the work week, with an upper limit of 30 μg per g creatinine.

**Occupational Sources of Chromium:**

- Anti-algae agents, antifreeze
- Portland cement
- Chrome alloy production
- Chrome electroplating
- Copier servicing
- Glassmaking
- Leather tanning
- Paints, pigments
- Photoengraving
- Porcelain and ceramics manufacturing
- Production of high-fidelity magnetic audio tapes
- Tattooing
- Textile manufacturing
- Welding of alloys or steel
- Wood preservatives
Managing Patients Exposed to Chromium

Regardless of how the exposure occurred, the initial approach should include a thorough assessment of their clinical status accompanied by immediate support of basic cardiopulmonary functions as necessary. There are no specific antidotes for Cr(VI) poisoning, but ascorbic acid, administered orally or nasogastrically, may reduce Cr(VI) to the less toxic Cr(III).

Dilution of ingested Cr with water or milk may help reduce damage to the gastric mucosa if provided within minutes after the agent is ingested. Gastric lavage can reduce the ingested dose if the agent is still in the stomach.

Low chromium levels in RBCs along with high chromium concentrations in urine is a good indicator that extracellular reduction of Cr(VI) to Cr(III) will be sufficient for detoxification. Patients with elevated RBC chromium levels should be monitored closely for evidence of gastrointestinal bleeding, hemolysis, methemoglobinemia, coagulopathy, seizures, or pulmonary dysfunction. Fluid balance must be maintained carefully.

Hemodialysis may be necessary in severe poisonings or if renal failure ensues. Activated charcoal is not anticipated to be beneficial in the treatment of chromate poisoning. Chelation with ethylenediaminetetraacetic acid (EDTA) or British anti-Lewisite (BAL) also does not seem to be of clinical benefit.

Following inhalation exposures to Cr(VI) compounds, patients should be monitored for respiratory distress or cyanosis and treated with oxygen and bronchodilators as necessary. Patients with inhalation exposures to concentrated chromic acid mists (or other highly soluble hexavalent chromium compounds) should be carefully observed for signs of pulmonary edema up to 72 hours after exposure.

Relatively asymptomatic patients with acute-duration, low-level chromium exposures should be removed from any further exposure and observed for respiratory signs or symptoms. Patients should contact their physician if they develop urinary, respiratory, or gastrointestinal problems or have other sudden health changes.

Key points:

- Cr(VI) compounds are more readily absorbed from the lungs, gut, and skin than Cr(III) compounds.
- After absorption, Cr(VI) is ultimately reduced to Cr(III) and excreted, primarily in the urine.
- The difference in bioavailability and bioactivity between Cr(III) and Cr(VI) might account for the differences in toxicity.
- Cr(III) is an essential dietary nutrient whereas Cr(VI) poses a significant health risks.
- Some Cr(VI) compounds, such as potassium dichromate and chromium trioxide, are caustic and irritating to the skin, eyes, and gastrointestinal mucosa.
- Oral exposure to high doses of Cr(VI) compounds may result in caustic burns to the gastrointestinal tract, hematological toxicity, mild to severe kidney and liver damage, and cardiovascular collapse.
- Some studies have found equivocal evidence of reversible renal tubular damage after low-dose, chronic Cr(VI) exposure.
- When inhaled, Cr(VI) compounds are respiratory tract irritants that can cause pulmonary sensitization and erosion or even perforation of the nasal septum.
- Cr(VI) compounds are readily absorbed from the lungs and can cause systemic toxic effects similar to orally absorbed doses.
- Cr(VI) is recognized as a human carcinogen through the inhalation route, and occupational exposure to Cr(VI) in a number of industries has been associated with increased risk of respiratory tract, nasal, and sinus cancers.
- Latency for Cr(VI)-induced lung cancer can be greater than 20 years.
- Cr(VI) compounds and solutions are readily absorbed through intact skin and direct contact can cause severe dermatitis and skin blisters, burns, and ulcers as well as systemic toxicity.
- Potential reproductive effects of Cr(VI) in humans have not been adequately investigated, but data indicate that Cr(VI) compounds are teratogenic in some animal species.
- Cr(VI) compounds induced DNA damage, gene mutation, sister chromatid exchange, and chromosomal aberrations in a number of targets, including animal cells in vivo and animal and human cells in vitro.
For more information about chromium exposure:

The Agency for Toxic Substances and Disease Registry (ATSDR) has several physician resources for chromium. Resources include:

The Public Health Statement for general information

An environmental medicine case study about chromium
http://www.atsdr.cdc.gov/csem/chromium/

How to take an environmental exposure history
http://www2a.cdc.gov/TCEOnline/registration/detailpage.asp?res_id=1766

For more information contact:

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