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Chromium Poisoning with Analytical Aspects and Management

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Abstract

Chromium is a hard grey metal. It is unstable in the presence of oxygen and produces a layer of oxide which makes it resistant to corrosion. It is a natural element, and also formed during human activities. Chromium is an essential trace element for men and works as cofactor for insulin. It takes part in metabolism of carbohydrate, lipid and protein. In industry, it is widely used in chrome plating due to its corrosion resistance property. Source of toxic exposure of chromium is occupational as well as non-occupational. Pathway of exposure is mainly through skin, inhalation, ingestion and drinking water. It produces various reactive intermediates and free radicals in the body which cause the toxicity. Its toxic effects involve all the body systems as well as local exposed region. Chromium also has genotoxicity and carcinogenicity. Management of the toxicity is mainly symptomatic. Various studies have been performed on animals to find out role of ascorbic acid, N-acetyl cysteine and other new compounds in the management of chromium toxicity.

Keywords: Chrome plating; Corrosion resistance; Essential trace element; Genotoxicity; Chrome ulcer; Carcinogenicity.

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Introduction

This review was done to accumulate the facts known about the toxicity of chromium and its management till date. Literature was searched on Google, Google Scholar, PubMed/Medline, Hinari, ScienceDirect, ResearchGate and Institutional Library portal using keyword 'Chromium Poisoning'.

Chromium[1-4]**:** It is a hard, grey, odourless metal having metallic luster and atomic weight of 52. It is unstable in the presence of oxygen and produces a thin layer of oxide which is impermeable to oxygen, so, it doesn't tarnish in air. Chromium (Cr) exists in six valence state, 0, II, III, IV, V and VI. Among these, trivalent chromium is the most stable form, insoluble in water and most commonly found chromium-form in the environment. Hexavalent chromium is the second most stable form and many of its compounds are water soluble. It is also one of the most toxic and mutagenic heavy metals in biological systems, and mainly produced by human activities. Most of the chromium compounds are solids at room temperature, though chromyl chloride is a fuming liquid.

Chromium is an essential trace element. Its dietary source includes bread, cereals, spices, fresh vegetables, meats and fish. Daily intake of chromium is not categorically defined. As per WHO, daily intake of chromium(III) should be approximately 33µg/day. As per National Academy of Sciences, adequate intake of chromium for young men is 35µg/day and for young women is 25µg/day. [10] As per COMA, an adequate intake of trivalent chromium is 25µg/day and 0.1-1µg/kg/day for children and adolescents. It works as a cofactor for insulin by facilitating binding of insulin to the receptors at cell surface. In this way, it is mainly involved in carbohydrate, lipid and protein metabolism. Deficiency

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of chromium is associated with impaired glucose tolerance, weight loss, neuropathy, elevated plasma fatty acids, abnormality in nitrogen metabolism and depressed respiratory quotient. Various studies have been done on the beneficial effect of chromium on serum glucose, lipids and insulin resistance. It is also attributed to be associated with increased lean body mass and deceased body fat, and have been used to enhanced weight loss.

Sources [5,6]**:** Chromium is a natural element and usually exists in compound forms with other chemicals, most of them are brightly coloured (Chromium, Greek: Chroma=colour). Chromite is the only ore containing a significant amount of chromium (about 55%). It is naturally present in all water sources and, in meat, fish, fruit and vegetables.

Chromium is also produced during human activities and there are many ways for chromium compounds to enter into the environment, such as sewage waste from textile printing works or electroplaters, chromium containing paints and, dust particles on roads and pavements from burning of coal and oil-based fuels. However, chromium contamination of surface water is limited and doesn't affect groundwater as it strongly attaches to the soil. Similarly, water contaminated with chromium doesn't build up in fish but accumulates in gills.

Most common chromium products are sodium chromate and dichromate. It is widely used in chrome plating, in metal ceramics and in stainless steel as it is very resistant to corrosion. Chromium compounds are used in electroplating, paints and inks as green pigments, wood preservatives, leather tanning, textiles as green dye, and in refractories for making fire bricks. Chromium oxide is used to manufacture magnetic tape. It is also used to 'get high' by adolescents.

Environmental effect of chromium[5,7]**:** Chromium comes into the environment through natural process as well as through human activities. Chromium compounds are mostly present as fine dust particles in air. It remains in the air for fewer than 10 days. Rain and snow helps to remove it from air. Water contamination is limited to surface water and it will not affect ground water as it is strongly attached to soil and remains in the silt layer. Chromium naturally occurs in rivers, but high level of dissolved chromium can cause damage to aquatic animals and plants. Its toxicity depends upon the valency of chromium, trivalent or hexavalent. Toxicity of chromium is reduced when it is bound to particulate matters in the river. Hard water reduces toxicity of chromium. Chromium is often admixed with industrial effluents which are used for irrigation purposes. During the process, uptake of excess amount can reduced growth potential of the plants. It also inhibits various metabolic process, osmoregulation and respiration in fish. In this way, chromium causes imbalance of ecosystem. Water contaminated with chromium will not accumulate in the fish when consumed but accumulates in the gills causing various negative effects. The state and federal drinking water standard has set a total amount of less than 100 ppb of chromium. Likewise, for air, chromium level is recommended at 0.2μg/m^3.

Exposure of chromium [8,9]**:** Sources, to which people are exposed, can be divided into two groups: occupational and non-occupational. Occupational exposures occur during chromate production, welding, chrome pigment manufacture, chrome plating and spray painting. The exposure is mainly through inhalational or dermal contact.Non-occupational exposure occurs through food, air and water. People are exposed to chromium by inhalation, or by ingesting food and drinking water containing chromium, or through dermal contact with certain products containing chromium, or through cigarette smoke. Chromium poisoning may occur due to metal-on-metal hip plants.

Human intake of chromium: a. Inhalation: Inhalation exposure occurs mainly during occupational activities while working on chromium compounds and breathing in the dust, fumes or mist. [8]

b. Ingestion[3]**:** Chromium(III) is the most commonly found compound due to presence of reducing agents in the food. All food contains some amount of chromium, in the range of 20-590μg/kg. Drinking water found to contain 0.4-8μg/L of chromium in US. Chromium intake from typical North American diets may be in the range of 50-200μg/day. Alcoholic beverages also contain chromium compounds.Upper limit of chromium intake is not well defined. It is approximately 0.15mg/kg/day or 70-80μg/day. Upper limit for chromium in drinking water is 100ppb. As per WHO, maximum concentration of chromium(VI) in water is 0.05 mg/L. The LD50 for chromium(VI) is between 50-150 mg/kg. Average oral lethal dose of chromium(VI) is 1-3 gm. The US National research Council specified an estimated safe and adequate daily intake of 0.05-0.2 mg/day for adults and 0.01-0.04 mg/day for infants (0-1/2 years).

c. Dermal: Dermal exposure occurs during

occupational activity when skin comes into contact with various solution or solids of chromium, or during usage of consumer products containing chromium, such as wood treated with copper dichromate and leather tanned with chromic sulphate. [10]

Mechanism of toxicity[11,12]**:** Chromium(VI) enters the cell through carboxylate, sulphate and phosphate carrier system. It causes toxicity through reduction in which glutathione and cysteine are the most important co-factors. Chromium (VI) sequentially reduces to Chromium (III) within cells, using hydrogen peroxide (H_2O_2), glutathione reductase, glutathione and ascorbic acid. During the process it produces reactive intermediates and hydroxide free radicals. Oxidative stress, caused by free radicals, has been proposed as a major pathway of chromium induced toxicity. They could attack proteins and membrane lipids, and disrupts cellular integrity and functions. The intermediates, produced during the process of reduction, bind to macromolecules, including DNA leading to genotoxicity. The initial binding with macromolecules occurs in pentavalent form. Free radicals also play a role in this. Carcinogenicity of chromium(VI) is a function of the rate of cell turnover in the target tissue.

Metabolism of chromium[3,4,13,14]**:** Absorption of chromium depends upon the valency and solubility of chromium. Chromium(VI) compounds are absorbed more, approximately 2-8%, as compared to chromium(III) compounds, about 0.5-1%. Most of the chromium(VI) compounds are reduced to chromium(III) in the stomach itself prior to absorption. Rest of the chromium(VI), which is absorbed unchanged, reduces to chromium(V), chromium(IV), then to stable chromium(III), using endogenous reducing agents. In blood, chromium(VI) is taken up. Chromium(III) doesn't cross RBC membrane. 95% of chromium(III) is bound to large molecular mass protein transferrin, only a small portion associates with low molecular mass oligopeptides. Within blood cells chromium(VI) reduces to chromium(III), which binds to hemoglobin. Some individuals have a lesser ability to reduce highly toxic chromium(VI) to chromium(III) and more likely to be affected by chromium exposure. This ability of reducing chromium(VI) to chromium(III) might be related to the level of ascorbic acid in plasma. The reduction of chromium(VI) to chromium(III) inside of cells, near to the target tissues, is the mechanism for the toxicity of chromium, whereas, reduction of chromium(VI) outside of cells, away from the target tissues, is the major mechanism of detoxification.

Distribution of chromium(VI) compounds is greater than chromium(III) compounds. It is widely distributed in the body, with liver, kidney, spleen and bone having higher concentrations. Total amount of chromium in human body is between 0.4-6 mg. Chromium is found to cross placental barrier and transmits to fetal tissue. Chromium concentration is higher in the tissue of newborn babies which decreases with age upto the age of 10 years. Then, its level increases in the lungs and decreases in other tissues.

Elimination of the chromium from the body is biphasic, a rapid phase with clearance from blood and a slow phase with clearance from the tissues. Primary route of excretion is urine, about 50%, in the form of chromium(III) and fecal excretion is only 5%. A small amount is eliminated in hair, sweat and bile. Many factors influence urinary excretion of chromium, such as, stress and carbohydrate rich diet increases its excretion. As such, half-life of chromium is 22 days for chromium(VI) and 92 days for chromium(III) on intravenous administration.

Interaction of chromium with other compound within the human body is complex. It interacts with iron by affecting its binding to transferrin, and impairs iron metabolism and storage. Ascorbic acid reduces highly toxic chromium(VI) to chromium(III). Vitamin E protects while vitamin B2 found to enhance the cytotoxicity and DNA strands break up by enhancing the formation of hydroxyl radicals. N-Acetyl Cysteine is found to be effective in increasing the urinary excretion of chromium.

Onset and duration of action[6]**:** Respiratory airways edema was seen within hour of inhalation but may be delayed upto 72 hours. After ingestion gastrointestinal symptoms appear immediately. Renal failure can develop 12-24 hours of exposure and, thrombocytopenia and anemia after 3 to 7 days, if the person survives initial insult.

Fatal dose and fatal period: The average oral lethal dose of chromium (VI) in human is 1-3 gm and can cause death within 12 hours. Lethal dose of dichromate is estimated to be 0.5 to 5 gm.

Local effect of chromium: Acute poisoning is mainly through the oral route while chronic poisoning is through the inhalational or dermal route.

a. Acute effect [4,13]**:** Respiratory tract is the primary target organ. Inhalation of chromium can irritate nose and throat causing sneezing and coughing. Exposure to chromium fumes causes 'metal fume fever'; however, the

symptoms may be delayed for several hours. Eye contact irritates them and can cause eye damage.

b. Chronic effect [4,13]**: i. Nasal effect** [1,7]: It is commonly seen in occupational exposure. Chronic inhalation of chromium can cause atrophy of nasal mucous membrane, followed by ulceration and perforation in the septum of nose, and sometimes, bleeding and discharge. It may be due to deposition of chromium(VI) containing particles.

ii. Dermal effect [1,15]: Chromium is one of the most common skin sensitizers and often causes sensitizing effect among general population. Dermal absorption of hexavalent chromium is rapid and peak level is reached within 5 hours of exposure. A study has recommended occupational exposure of a maximum level of 5 ppm. Chronic low level exposure can lead to allergic contact dermatitis with exposure between 4-25 ppm of chromium(VI) and 500 ppm of chromium(III). [2] It is long lasting and more severe with repeated skin contact. Changes in occupation did not improve the skin condition. When comes in contact with non-intact skin, a Chromium(VI) level above 20-25 ppm causes painless erosive skin ulcers with delayed healing, also known as 'chrome ulcers'. However, it also can lead to skin allergy, itching and rash. Prolong exposure can lead to burn, blisters and ulcers, mainly seen among workers in electroplating, tanning and chrome producing plants where they are exposed to strong chromate solution. Severe systemic acute chromium poisoning can occur after dermal exposure and significant morbidity and mortality has been seen with chromium burn involving >10% of body surface area (TBSA).

Systemic effect on body [1,3]**:** It is commonly seen after intentional exposure. Acute inhalation of chromic acid mist may result in pulmonary edema. Acute involvement of gastrointestinal system causes massive inflammation and necrosis from mouth to jejunum leading to abdominal pain, vomiting, diarrhea and hematemesis. This may cause death by circulatory collapse. Manifestation of hepatic and renal necrosis appears 12 to 20 hours later.

Chronic effect of chromium(VI) causes GI bleeding from ulcerations of the intestinal mucosa, renal failure beginning with tubal necrosis, intravascular hemolysis, liver involvement with diffuse necrosis and loss of architecture, shock, coma and sometimes death. [3]

Effect on respiratory system [3,6]: Uptake of chromium in the airways depends on the size of particles. Average retention of chromium compounds after inhalation is about 3-400ng, which may vary depending upon other relevant factors such as tobacco smoking. Its accumulation in the lungs increases with age. Approximately 5% is absorbed within few hours and occurs more rapidly for water soluble chromium(VI). Likewise, water soluble chromium(III) compounds aerosols of respirable size are more readily absorbed, but uptake of insoluble chromium(III) oxide particles is slow and may retain in the lung for years. Prolonged exposure can lead to bronchitis, rhinitis, sinusitis, formation of nasal mucosal polyp. Occupational asthma occurs to the people who are exposed to chromic acid fumes with shortness of breath, wheezing and tightness of chest. This may be a delayed bronchospastic reaction accompanied by an anaphylactoid reaction including urticaria, skin swelling and release of histamine. Some studies have found pneumoconiosis in chromite workers after exposure to chromite ore dust, but not confirmed by others.

Lung cancer is the most serious effect. Chromium produces its carcinogenic effect mainly on bronchial tree. Risk of lung cancer is exacerbated in people who smokes or excessively exposed to passive smoke, as these smoke might itself cause squamous metaplasia in the respiratory mucosa.

Effect on cardiovascular system: Chromium can cause cardiovascular arrest with hypoxic changes in the myocardium. It can also cause hypotension, ventricular arrhythmia and respiratory distress.

Effect on gastro-intestinal (GI) system[7,16]**:** Chromium compounds are corrosive to the GI mucosa. With ingestion of chromate dust, GI mucosa is directly exposed. It can lead to hypertrophic gastritis, ulcer formation and GI hemorrhage. Absorption of chromium through GI tract is low, less than 5%. Rate of chromium uptake from GI tract depends upon a number of factors such as, valency, chemical form, water solubility and GI transit time. Chromium(VI) is more readily absorbed than chromium(III) and organic chromium is more readily absorbed than inorganic. About 10% of chromium(VI) is absorbed from the gut but only less than 1% of chromium(III) is absorbed. GI secretions reduce Chromium(VI) to chromium(III) in the stomach, so the oral toxicity is low. This reduction is greatly enhanced by low pH and after meals.

Effect on liver: Chromium(VI) can cause derangement of liver cells, necrosis, lymphocytic and macrophage infiltration, and an increase in Kupffer cells. However,

exposure to chromium(III) has not been found to cause any liver effects.

Effect on renal system[3,7,17]**:** Necrosis of kidney occurs at high dose of chromium (10-20 mg/kg). Predominant renal injury is tubular with low dose acting on proximal convoluted tubules. A feature of chromium nephropathy is injury to brush border membrane. Severe poisoning can lead to acute tubular necrosis and acute renal failure, contributed by intravascular hemolysis. Chromium induced renal injury may be reversible as suggested by study on biomarkers.

Hematological effect[17]**:** It can cause decrease hemoglobin level, increase total leucocyte count and increased reticulocytes count, all indicative of intravascular hemolysis.

Reproductive & developmental effects[1,18]**:** Potassium dichromate may be toxic to the reproductive organs and developing fetus. It significantly decreases sperm counts and motility, cause abnormality in sperm, decrease number of follicles and increases follicle stimulating hormones. Chromium enters into the young through placenta and mother's milk. Studies among animals have found fetal anomalies associated with chromium exposure, however, in human, no such association has been found. Cucurmin has a protective role on chromium(VI) induced damage.

Genotoxicity & mutagenicity effect[18]**:** Chromium(VI) compounds are found to have carcinogenic property and classified as Group 1 known human carcinogen. International Agency for Research on Cancer (IARC) has classified inhaled chromium(VI) as known human carcinogen. Carcinogenicity is due to production of chromium(V) from chromium(VI) which lodges in the tissue leading to cancerous growth. Chromium(III) also binds directly to the DNA strand. It can produce stable DNA-chromium complex, DNA strands break, DNA-DNA cross link and DNA-protein cross links. Site predilection of mutagenicity of chromium compound is determined by its size. Because of the large size, it is not adopted by a tissue. It only lodges in some of the fine capillaries in the kidney, lungs or intestines. Chromium(V) is also found to be a factor for senility in parts of Russia.

Other effects: Chromium(VI) compounds exposure can cause erosion and, yellowish discoloration of teeth and tongue. It can also lead to gingivitis and periodontitis. Papilloma of oral cavity and larynx has also been reported. Concentrated chromium solution can cause conjunctivitis, severe corneal injury with ocular contact and vision impairment. It can cause loss of hearing.

Normal/reference value[19]**:** Level of chromium in blood and serum of healthy population is 0.12-0.34 μg/L and 0.035-0.040 μg/L, respectively. Basal serum concentration in adults is 0.13±0.02 μg/L. However, serum concentration is not regarded as good indicator of chromium status as it only represents recent exposure. Concentration of chromium in urine doesn't exceed 5 μg/g creatinine or 10μg/L/day. It reflects absorption for previous 1-2 days.

Biomarkers[7]**:** 24-hour chromium excretion in urine is a good indicator of daily intake of chromium. However, sequential urine sampling was more accurate than 24-hour and spot urine collection. Low level intermittent exposure may not be detected with urinary monitoring. Chromium stores do not equilibrate with blood chromium, so plasma or serum concentration may not be an indication of chromium status.

Level of β2-microglobulin and N-acetyl-β-glucosaminidase was found significantly higher in recent exposed workers. These work as early indicators of renal dysfunction. In a study, level of IL-6 was found significantly decreased in monocytes in chromium exposed.

Hair or nail analysis is of little use. Normal level of chromium is ranging from 50-100 ppm.

Other investigations: Some necessary test to be considered: complete blood count, liver function tests, blood urea nitrogen and creatinine, and urine analysis. If there is history of inhalational exposure, a chest radiograph and pulmonary function test should be included.

Care must be taken during collection, transportation and storage for chromium analysis. Specially prepared acid washed containers should be used instead of plastic or stainless steel containers. Stainless steel container can raise chromium level as well as some chromium containing plastic containers.

Chemical test of chromium poisoning[20]

Qualitative analysis: a. Diphenyl carbazide Tests: One drop of acidified solution of extract is placed on a spot plate.Two drops of 0.1M Peroxydisulphate solution and 1 drop of 0.1M silver nitrate solution are added and allowed to stand for 2 min.Then 1 drop of Diphenyl carbazide is added to it.A violet or red color is formed which confirms the presence of chromium.

Chromotropic acid Tests: One drop of extract is placed in a semi-micro test tube. One drop of Chromotropic acid solution and 1 drop of dilute nitric acid are added. A red coloration is observed which confirms the presence of chromium.

Sodium hydroxide Tests: 4ml of chromium solution is

placed in a 10ml test tube. Add 2ml of sodium hydroxide solution in above solution. A blue/light green precipitate is observed but on adding more sodium hydroxide solution the precipitate dissolved into a green solution which confirms the presence of chromium.

Sodium carbonate Tests: 4ml of chromium solution is placed in a 10ml test tube. Add 2ml of sodium Carbonate solution in above solution. A light greyish blue precipitate was observed which confirms the presence of chromium.

Potassium ferro(II)cyanide Tests: 4ml of chromium solution is placed in a 10ml test tube. Add 2ml of Potassium ferro(II)cyanide solution in above solution. No reaction or precipitation but on heating a deep dark green solution formed which confirms the presence of chromium.

Quantitative analysis: UV-Visible Spectrophotometer: Chromium quantitatively can be determined by using UV-Visible spectrophotometer using Diphenylcarbazide as chromogenic reagent.

Conditions for UV-VIS spectrophotometer are:

Mode: Absorption; Range: 650-400nm; Slit Width: 0.2nm; Band Width: 1.5nm; Scanning Speed: 400nm/min

Management/treatment of chromium poisoning First aid [1,4]: If eyes are involved, immediately flush with large amount of water and seek medical attention. If skin is exposed, immediately remove contaminated clothes and wash the skin with water and soap. If exposure is through inhalation, remove the person from the exposure and starts rescue breathing. Seek medical attention.

Hospital management[1]**: a. Acute Chromium Poisoning:** Acute chromium(VI) poisoning is often fatal regardless of the therapy. Supportive measures are mostly considered. Extracorporeal removal measures are not helpful.

Chronic Chromium Poisoning[21]**:** With low dose chronic exposure no specific treatment is needed. Remove the patient from the exposure and chromium will be cleared through urine and faeces. Dermatitis, liver and renal injury will not progress and most of the patient will recover except only slight amount of chromium remains in the lung.

No proven antidote is available for chromium and mainstay of treatment is supportive and symptomatic. Emesis is contraindicated as chromium compounds have corrosive effect. Gastric lavage with magnesium hydroxide may be used in case of ingestion but role of activated charcoal is not proven. Dilution of the ingested agent may be attempted using water or demulcent like milk within minutes of exposure. Maintenance of adequate urine flow is important; progression to anuria is associated with worse prognosis. Systemic toxicity of chromium through cutaneous absorption from burns can be prevented by early excision.

Exchange transfusion was also found useful in reducing blood chromium level but there is no concluding evidence is available. Hemodialysis or charcoal hemoperfusion don't enhance chromium removal substantially but hemodialysis may be necessary for correction of renal failure itself. Chelation with EDTA doesn't found to be beneficial clinically but 10% ointment may facilitate removal of chromate scab.

Animal studies have shown that ascorbic acid enhance the conversion of hexavalent chromium to less toxic trivalent chromium. N-acetyl cysteine and DMPS significantly increase chromium excretion. Study on animals showed ascorbic acid to be useful in chromium poisoning if used within one hour of exposure. Topical 10% ascorbic acid is found useful in guinea pigs, in reducing the healing time of chrome ulcers. [14,22] It can also be used orally or through nasogastric route, if chromium is still in the stomach. It reduces chromium(VI) to chromium(III) which is less toxic to gastric and intestinal mucosa. It also has a protective effect against lethal dermal dose of chromium and chrome ulcers formation. It also protects against nephrotoxicity.

In a study, it has been found that aqueous and methanolic extracts of *Lawsoniainermis* (Henna) have high antioxidant potential which inhibits chromium(VI) induced oxidative stress and thereby prevents cell death. [2] Another study suggested that chromium induced testicular toxicity can be prevented by simultaneous administration of Moringaoleifera (Drumstick) leaf extract. [12] In another study, efficacy of quercetin-5'-sulfonic acid sodium salt (NaQSA) was tested in treatment of acute poisoning, where it was found useful as it converts highly toxic chromium(VI) to low toxic chromium(III). Another study on rats showed that combination of desferasirox+deferiprone effectively increases the elimination of chromium and the symptoms are greatly reduced. [23]

Reducing agents ascorbic acid, cysteine and glutathione were found to provide concentration dependent protection. Ascorbic acid at 500 μM completely inhibited cellular toxicity of chromium(VI).

Glutathione may form complexes with chromium(VI) leading to formation of chromium(III). 4-acetamido-4'-isothiocyanato-2,2-stibenedisolphonic acid (SITS) and 4,4'-diisothiocyanato-2,2'-stilbenedisulphonic acid (DIDS) may inhibit the cellular uptake by altering the non-specific membrane anion carrier. [24]

In a study done on rats, Ethylenediamine N,N'-diacetic acid (EDDA) found to remove significant amount of chromium from the heart and liver. Ethylenediamine N,N'-di(O-hydroxyphenyl) acetic acid (EDDHA) removes chromium from brain, heart and kidney. N-(2-hydroxyethyl) ethylenediaminetriacetic acid (HEDTA) removes chromium from liver and kidney. Triethylenetetramine N,N,N',N',N",N"-hexaacetic acid (TTHA) removed significant amount of chromium from the liver. However, these have not been studied on human.

Conclusion/precautions

As the main source of exposure to chromium is occupational, work place precaution is foremost. Wash or shower whenever skin comes into contact with a hazardous material. Do not eat, drink or smoke within the chemical area, hands should be washed carefully before eating, smoking, drinking or applying cosmetics. Always use personal protective equipment while working on hazardous material. Sometimes, it is necessary to wear special clothing and 10% ascorbic acid solution or cream. Ascorbic acid ointment is also recommended to protect the nasal mucosa membrane.

Conflict of Interest

None Declared

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