Chapter

Role of Metals in Pediatric Oral Health

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Abstract

Prefabricated stainless steel crowns (SSCs) are the regular dental prosthesis cemented to primary molars in children. Previously used SSC, which contained up to 72% nickel, is associated with nickel sensitivity. Hence, the new generation of SSC that contains only 9–12% nickel was developed. Stainless steel orthodontic materials and stainless steel crowns (SSC) are the two major devices in pediatric patients that contain heavy metals. Measurable amounts of nickel and chromium in the saliva and serum are released from this prosthesis without reaching toxic levels. Allergic reaction in a form of gingivitis was reported after 3 months in 20% of the females and 10% of the males, and it disappeared a month after appliance removal. Several studies reported that there is more leaching of metals in acidic pH. Many different types of alloys are now available in the market to be used for dental restorations and fixed prostheses, and the rates of metal leaching from these alloys are not known. The common criterion for all these fixed prosthodontic materials is their permanent existence in the oral cavity for a prolonged time without the ability to be removed by the patient. Let us know these elements in detail in this chapter.

Keywords: base metal alloys, prefabricated stainless steel alloys, allergy, crowns

1. Introduction

Earlier, the precious metals such as silver and gold were commonly used for dental restoration. However, since 20th century, use of noble metals for dental prosthesis has reduced due to their high cost and unavailability; alternative metal alloys of nickel, chromium, cobalt, molybdenum, manganese, iron, copper, and zinc are used more. Numerous researchers have developed new alloys that not only are less expensive than gold but also have properties that are more suitable for specific applications [1–6].

The heavy metals used for dental prosthesis have a greater specific gravity that is five times more than water. Mainly, these heavy metals are found on the earth's outer layer in all ecosystems at varying concentration and occupy groups IIA to VIA in the periodic table [7].

The fabricated prosthesis is made of alloys containing Ni, Co, Cr, and Mo in different percentages. Biodegradation of these alloys occurs due to the different properties of oral environment such as the enzymatic, thermal, and microbiological

[8]. Elements like Ni, Co, and Cr are known to be cytogenic, mutagenic, and allergenic [9]. The most common causes of metal-induced allergic contact dermatitis are Ni and Cr [10].

In oral atmosphere, metal crowns, PFM crowns, post and core, prefabricated crowns, orthodontic brackets, and implants are continuously exposed to different conditions such as temperature, mechanical fatigue, acidic pH, and susceptibility of alloy to corrosion [11]. It is well-known from the literature that leaching of heavy metals from dental restorations occurs in saliva.

Different types of dental casting alloys are now available in the market, which mainly consist of Ni, Cr, Co, and Mo and are being used for several years in dental restorations. Leaching of these heavy metals from dental casting alloys in saliva is well documented in literature, which are absorbed across the GIT, leading to increase blood levels and then may affect the vital organs such as liver, kidney, and lung. Leaching of heavy metals from dental casting alloys is affected by various factors such as pH, duration of prosthesis used, protein-rich solution, masticatory load, wear, and diet. Acidic pH, prolonged use of prosthesis, protein-rich solution, and heavy masticatory load are directly proportional to the release of heavy metals from dental casting alloy (DCA).

2. Use of metals in pediatric oral health

Stainless steel orthodontic materials, space maintainers, and stainless steel crowns (SSC) are the major devices used in pediatric patients that contain heavy metals. In pedodontics, the prefabricated stainless steel crowns have been preferred for deciduous dentition and used temporarily for 3–4 years over the prepared tooth since ages on a deciduous tooth till the tooth is extracted or exfoliated. These are available in assorted packs of different dimensions.

Prefabricated stainless steel crowns (SSCs) are the regular dental prosthesis cemented to primary molars in children. Previously used SSC that contained up to 72% nickel is associated with nickel sensitivity [12]. Hence, the new generation of SSC that contains only 9–12% nickel was developed [13]. All these alloys have to tolerate pH from food and plaque, tooth brushing condition, and the heavy masticatory load. Wear is a key factor that can accelerate corrosive processes in vivo. It is expected that the effect of element release will have to be understood for selecting different kinds of alloys for the purpose of dental restorations. Measurable amounts of nickel and chromium in the saliva and serum were seen to be released from these prosthesis without reaching toxic levels [14]. The release from these appliances showed an increase over the first week after placement and then decreased over time [15]. Allergic reaction in the form of gingivitis was seen after 3 months in 20% of the females and 10% of the males, and it disappeared a month after appliance removal [16].

3. Alloy composition and properties

Dental alloys are described by their composition that is usually expressed as weight percentage and atomic percentage and by their phase structure (microstructure), which can be either single-phase alloys or multiple-phase alloys. Single-phase alloys have a similar composition throughout their structure, but multiple-phase alloys are

not homogenous throughout their structure. The elemental release depends on the interactions between the phase structure and the biologic environment [17]. The elemental release may be caused by a change in surface composition of the alloys. The nickel–chromium alloy, which is a multiphase alloy, is prone to higher corrosion rates, due to the galvanic effects between the microscopic areas of different compositions [18]. It has been shown that there was an alteration in cellular function due to ions released from Ni-Cr alloys [19].

The alloy reactivity is governed by thermodynamic principles and electrochemical reaction kinetics, where the alloy will either remain stable in its elemental form or oxidize into its ionic form (corrosion) Nickel–chromium alloys are not thermodynamically stable, and their corrosion resistance depends on the formation of the thin oxide layer [20].

4. Functions of alloying elements

Cobalt: It adds strength, rigidity, and hardness to the alloy. It has a high melting point.

Chromium: The passivating result of chromium ensures corrosion resistance. The amount of chromium is directly proportional to tarnish and corrosion resistance. It reduces the melting point. Chromium with the other elements acts as a hardener. 30% chromium is thought to be the maximum for gaining mechanical properties.

Nickel: Nickel and cobalt are exchangeable. It decreases hardness, strength, fusion temperature, and modulus of elasticity. It improves ductility.

Molybdenum or tungsten: They improve the hardness. Molybdenum is chosen over tungsten as it reduces ductility and also refines grain structure.

Iron, copper: These are principally hardeners.

Beryllium: It reduces fusion temperature and refines grain structure.

Manganese and silicon: During melting, these help to avoid the oxidation of other elements. They are also hardeners.

Boron: It reduces ductility and acts as a deoxidizer and hardener.

Carbon: Small amount of carbides formed by the carbon with any of the metallic constituents improves the strength of the alloy, but excess carbide will increase the brittleness. Thus, control of carbon content in the alloy is important [21–23].

5. Elemental release

The factors that affect the elemental release from the alloy are many such as alloy composition, multiple phases, chemical character of the corrosive medium, exposure time, and temperature. There are many studies to assess the release of elements from dental casting alloys. The release of elements from dental casting alloys has been investigated by many different researchers using different materials and methods [24–33]. It is proven that at certain environmental conditions, the release of elements from the alloy is affected. Cell culture or different solutions such as normal saline, bovine serum solution, artificial saliva, tissue culture media, and diluted acids are used to evaluate the corrosion [24, 26, 29]. Leaching is tested in different mouthwashes and also in different pH solutions. An alcohol-based mouthwash resulted in the release of the highest amounts of Ni and Cr ions due to its lower pH.

5.1 Methods of testing elemental release

The elemental release can be measured by atomic absorption spectroscopy (AAS), inductively coupled plasma-atomic emission spectrometry (ICP-AES), or inductively coupled plasma mass spectrometry (ICP-MS) in different environments. AAS has been used with cell culture medium [34, 35], pH 7 phosphate buffer solution or saline, saline with 3% bovine serum albumin, and 3% serum [35]. ICP-MS was used for samples of artificial oral saliva [36]; ICP-AES was used for samples of artificial oral saliva, cell culture medium, and acidic pH [37, 38].

5.2 Effects of pH

The interest in studying elemental release is mainly due its relationship to the biocompatibility of the alloy. Elemental release has been reported for base metal alloys [39, 40] and for other types of alloys and solders [41–43], which focuses on the measurement of release during the exposure to a biologic medium or artificial saliva at different durations. The effect of a steady reduced pH on the elemental release from Ni-based alloys has been reported to increase Ni release [29, 40]. In the oral cavity, alloys may be exposed to transient pH changes either from foods or from plaque [44].

5.3 Effects of proteins

Behavior of proteins to the corrosion reactions could in 2 ways: Proteins bind to metal ions and move them far from the interface, thus aiding further dissolution, or these proteins could be engaged to the surface of the metal and obstruct the diffusion of oxygen, making it difficult to repassivate the surface.

5.4 Effects of saliva

The composition and properties of saliva may be affected by many physiological variables such as nutrition, diet, and salivary flow [45, 46]. According to Edgar and O'Mullane [47], hormones, drugs, and various diseases also influence saliva composition. Wirz et al. [48] and Grahmmer reported saliva samples of the control group without any metal restorations to contain the metals Ag, Cr, Cu, Fe, Ni, and Zn.

5.5 Effects of duration

The elemental release has been studied for different durations, and it was reported that the release may change significantly with time for some formulations over 80 h [49], and by 10 months, the release reduced lower than in the initial weeks and was constant after 100 days of exposure [28].

With the evaluation of cytotoxicity of nickel-chromium alloys after prolonged conditioning (168 h), it was found that alloy toxicity varied with the conditioning solution. The saline/BSA conditioning solution reduced the cytotoxicity of the alloys compared with unconditioned alloy cytotoxicity [50].

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6. Nickel

6.1 Properties of nickel

6.1.1 Daily requirements of nickel

A daily dose of 0.001–0.0024 mg/kg/day can be estimated using a reference body weight of 70 kg (**Figure 1**) [51].

6.1.2 Sources of nickel

Nickel is widely distributed in the environment and can be found in air, water, and soil [52, 53]. Dusts from volcanic emissions and the weathering of rocks and soils are the usual sources of atmospheric nickel. The level of Ni in ambient air is minute as 6–20 ng·m-3, but in air contaminated by anthropogenic sources, it may increase to 150 ng Ni·m-3. Ni in uncontaminated water is around 300 ng Ni·dm-3. Farm soil contains approximately 3–1000 mg Ni·kg^{-1} soil, but in the soil near metal refineries and dried sludge, the Ni concentration can reach up to 24,000–53,000 mg Ni·kg^{-1}. Ni compounds in soil at pH < 6.5 are relatively soluble, but at pH > 6.7, they are insoluble hydroxides [54–56].

6.1.3 Nickel exposure

The primary reason for Ni exposure is inhalation followed by ingestion and dermal contact. This happens in Ni and its alloy industries or during welding and electroplating. Nickel industries show up to 1 mg·m^{-3} of nickel. The advent of new technologies has reduced these exposures [57, 58]. Inhalation is the primary route of occupational exposure, and it elevates the Ni levels in blood, urine, and body tissues.

6.1.4 Absorption of nickel

Nickel acts as a cofactor in the absorption of iron from the intestine. Also, Ni may be absorbed as the soluble nickel ion and soluble nickel compounds may be

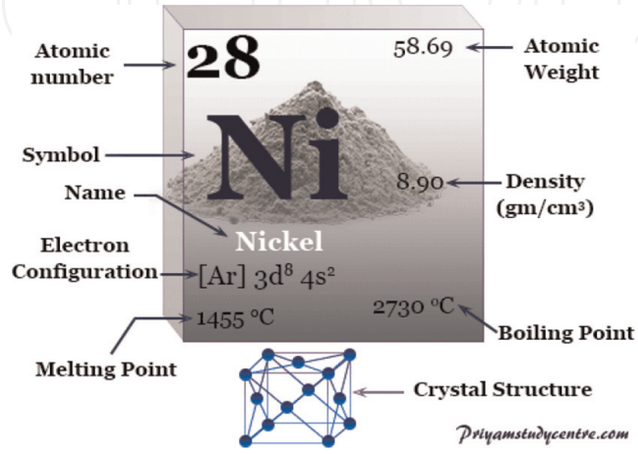

Figure 1.
Properties of nickel. Source: https://www.priyamstudycentre.com/2021/01/nickel.html.

phagocytized. The extent of absorption of Ni in the lungs depends on its chemical form and deposition site and also determined by the size, shape, density, and electrical charge [51, 59]. The mucociliary transport of the respiratory tract removes portions of Ni, which results in the material entering the GIT. Ni is inadequately absorbed from the GIT, but exposure from diet and drinking water provides most of the intake of nickel and nickel compounds [60, 61]. Dermal absorption of Ni is poor, but its compounds like nickel chloride or nickel sulfate can penetrate the skin. Pharmacokinetic studies indicate that nickel is absorbed through the lungs [62–64], GIT [65–67], and skin [68, 69]. Following absorption from the lungs and the GIT, nickel is excreted in the urine [70–72].

6.1.5 Metabolism of nickel

Nickel metabolism approximately occurs by binding to form ligands and its transport throughout the body. The chemical form of nickel may be altered in the body without being destroyed. Nickel toxicity may be associated with its interference with the physiological processes of manganese, zinc, calcium, and magnesium [61]. Altered transport and serum concentrations of nickel are associated with diseases such as myocardial infarction and acute stroke and burn injury (**Figure 2**) [59].

6.1.6 Excretion of nickel

Most of the ingested Ni is not absorbed and is eliminated mostly through feces. The Ni absorbed from the GIT is excreted in the urine and is mainly associated with low molecular weight complexes that contain amino acids. Nickel can also be eliminated through sweat and milk [73].

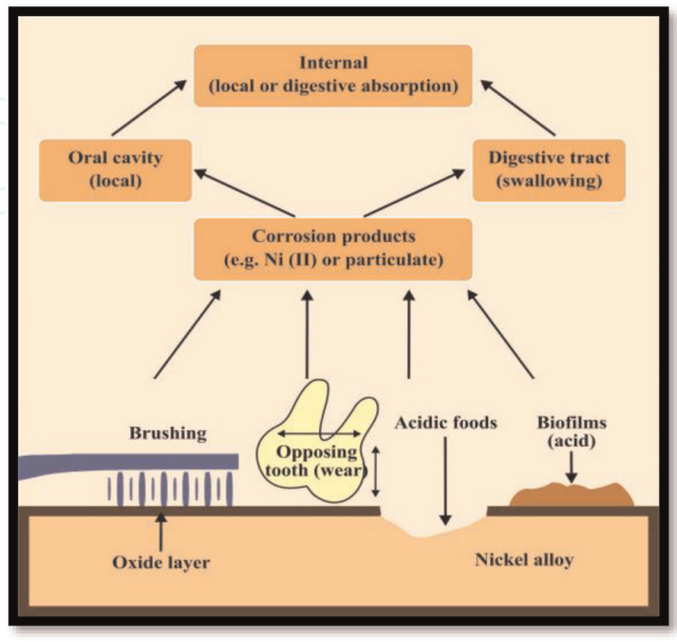

Figure 2.
Corrosion of nickel-based alloys.

6.1.7 Effect on health due to nickel

The toxic effect of Ni is related to the route through which it gets into an organism. Nickel enters the body through inhalation, ingestion, and skin absorption, but the route is determined by its chemical form like the fat soluble Ni carbonyl enters by diffusion or through calcium channels [74], while insoluble nickel particles enter the vertebrate cells by phagocytosis [75]. The main transport protein of nickel in blood is albumin, but nickel can also bind to histidine and α2-macroglobulin [57, 76] and in this form is circulated throughout the tissues. A number of nickel-binding proteins including α1-antitrypsin, α1-lipoprotein, and prealbumin were also described [77]. Nickel is found in high concentrations in bone, brain, respiratory organ, liver excretory organ, and endocrine glands. It is also marked in hair, breast milk, nails, and saliva. It is also proved that Ni was capable of transplacental transfer in rodents. Ni gets excreted through sweat, urine, feces, and bile. It does not get accumulated in the body [78]. The effects of Ni contact manifest as respiratory tract cancers, contact dermatitis, fibrosis of lung, and kidney and cardiovascular diseases [58, 79–81]. Long-term exposure to pollutants of low concentrations leads to chronic effects, and short-term exposure to high concentrations of pollutants leads to acute health effects such as abdominal discomfort, nausea, vomiting, diarrhea, headache, visual disturbance, and cough.

6.2 Chromium

6.2.1 Properties of chromium

6.2.1.1 Daily requirements of chromium

The National Academy of Sciences has established a safe and adequate daily intake for Cr(III) in adults of 50–200 micrograms per day (**Figure 3**) [82].

6.2.2 Sources of chromium

Cr(III) and Cr(VI) are released to the environment from human activities. Coal and oil combustion contributes an estimated 1723 metric tons of chromium per year in atmospheric emissions; however, only 0.2% of this chromium is Cr(VI). In air, Cr(III) does not undergo any reaction, while Cr(VI) reacts with dust particles or other pollutants to form Cr(III). Large amounts of chromium are released in surface waters due to leather tanning, electroplating, and textile industries. The natural source of Cr entry into bodies of water is by leaching from topsoil and rocks. Improperly disposed solid wastes from chromate-processing amenities can be sources of contamination for groundwater, where the chromium dwelling time might be several years. Wind erosion of the soil also makes settled particles airborne, which increases the opportunity for inhalation of chromium. Cr compounds leached by rainwater also migrate through cracks in soil, blacktop roadways, and masonry walls, forming high-content Cr crystals on their surfaces [82].

6.2.3 Exposure of chromium

Inhalation, ingestion, and dermal absorption are the means for Cr to enter the human body. Inhalation and dermal contact are the major causes for occupational

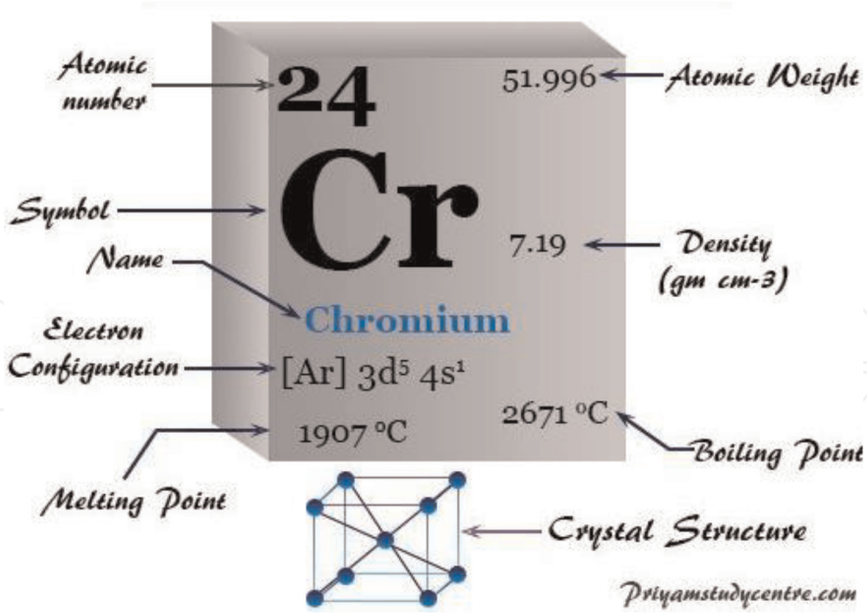

Figure 3.
Properties of chromium. Source: https://www.priyamstudycentre.com/2020/12/chromium.html.

exposure, while ingestion is the main source of exposure through food and water for the general population [54]. Studies have shown increased urinary concentrations of chromium after exposure to Cr(III) by inhalation, indicating respiratory absorption [83–85].

In ingestion of Cr(VI) compounds, they are better absorbed through the intestinal mucosa than the Cr(III) compounds. However, due to the actions of acids in the stomach and other components within the GIT, most of an ingested Cr(VI) dosage is converted to Cr(III) [86]. There is evidence from occupational studies that absorption of Cr(VI) compounds can occur through intact skin [87].

6.2.4 Absorption of chromium

The rate of Cr absorption from the GIT is moderately low and depends on factors like valence state where Cr[VI] is more easily absorbed than Cr[III], the chemical form where organic chromium is more easily absorbed than inorganic chromium, the water solubility of the compound, and gastrointestinal transit time. Absorption of Cr(VI) occurs rapidly through erythrocytes and is reduced to Cr(III) inside the red blood cells. On the contrary, Cr(III) binds directly to transferrin, an iron-transporting protein in the plasma, without crossing red blood cell membranes [82, 85, 88].

6.2.5 Metabolism of chromium

Glutathione reduces Cr(VI) in the RBC into Cr(III), which gets trapped in the RBC as the membrane is not permeable. Ultimately, the diffusion of Cr(VI), the reduction to Cr(III), and the complexing to nucleic acids and proteins within the cell will cause the concentration equilibrium to change [82]. Extracellular reduction of Cr(VI) to Cr

(III) reduces the toxicity. The difference between the extracellular Cr(VI) and intracellular Cr(III) dictates the amount of toxic effects [86].

In spite of the source, Cr(III) is present in the body in plasma or tissues. Lungs, spleen, bone marrow, kidney, liver, and lymph nodes take up the greatest amount of Cr(III) as a protein complex.

6.2.6 Excretion of chromium

Absorbed chromium is excreted primarily as urine. Within 8 hours of ingestion, the kidney excretes about 60% of absorbed Cr(VI) in the form of Cr(III), and around 10% is eliminated by biliary excretion. Also, small amounts of Cr are excreted through sweat, nails, milk, and hair (**Figure 4**) [82, 89].

6.2.7 Effects on health due to chromium

Chromium compounds are respiratory tract irritants and can cause pulmonary sensitization. Chronic inhalation of Cr(VI) compounds increases the risk of lung, nasal, and sinus cancer [90]. Contact with Cr(VI) compounds can cause severe dermatitis and usually painless skin ulcers [91, 92]. Cr(VI) is recognized as a human carcinogen. Reversible renal tubular damage can occur after low-dose, chronic Cr(VI) exposure [93]. Cr(VI) compounds can cause mild to severe liver abnormalities. Some Cr(VI) compounds, such as potassium dichromate and chromium trioxide, are caustic and irritating to the gastrointestinal mucosal tissue.

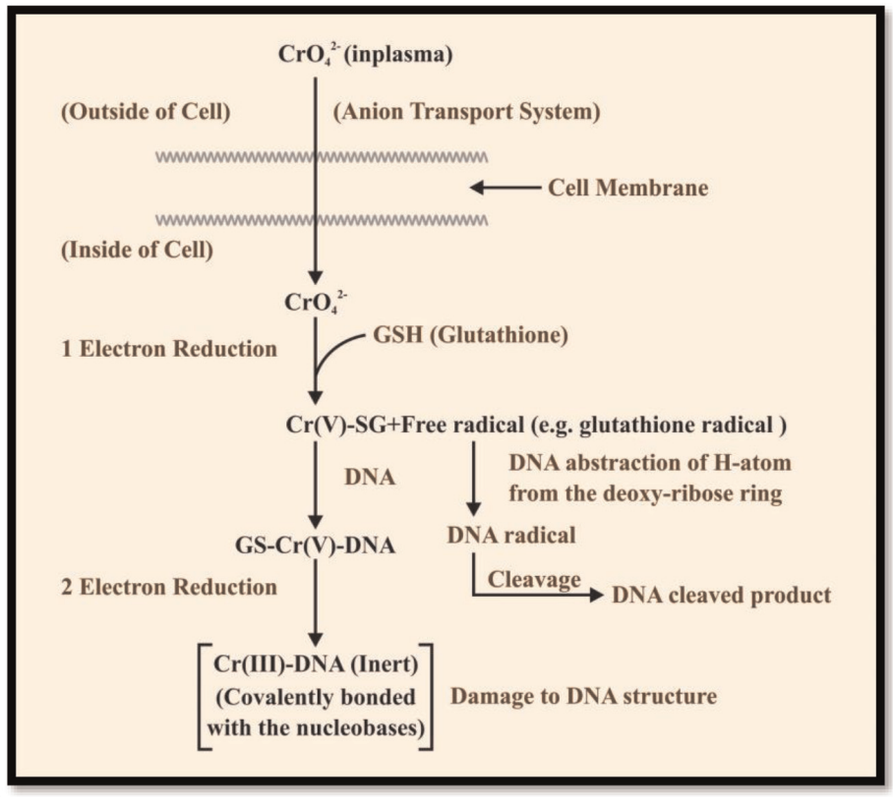

Figure 4.
Schematic representation of uptake reduction model.

6.3 Cobalt

6.3.1 Properties of cobalt

6.3.1.1 Daily requirements of cobalt

As a component of cyanocobalmin (vitamin B12), cobalt is essential in the body; the Recommended Dietary Allowance of vitamin B12 is 2.4 μg/day, which contains 0.1 μg of cobalt (**Figure 5**) [94].

6.3.2 Sources of cobalt

Cobalt is naturally available in water, soil, rock, plants, and air. Also, it may settle on land from forest fires, seawater spray, volcanic eruptions, and windblown dust. It can again get into surface water due to leaching and overflow by rainwater wash. High concentrations of cobalt are seen in phosphate rocks, soil near ore deposits, and soils contaminated by traffic, industrial pollution. Coal-fired power plants and incinerators, vehicular exhaust, mining and processing of cobalt-containing ores, and the production and use of cobalt alloys and chemicals also release small amounts of cobalt [94].

6.3.3 Exposure to cobalt

Cobalt is widely dispersed in the environment in low concentrations. One can be exposed to small amounts of cobalt by breathing air, drinking water, and eating food containing it. Food is the largest source of cobalt intake; about 11 micrograms of cobalt is consumed in a day [95].

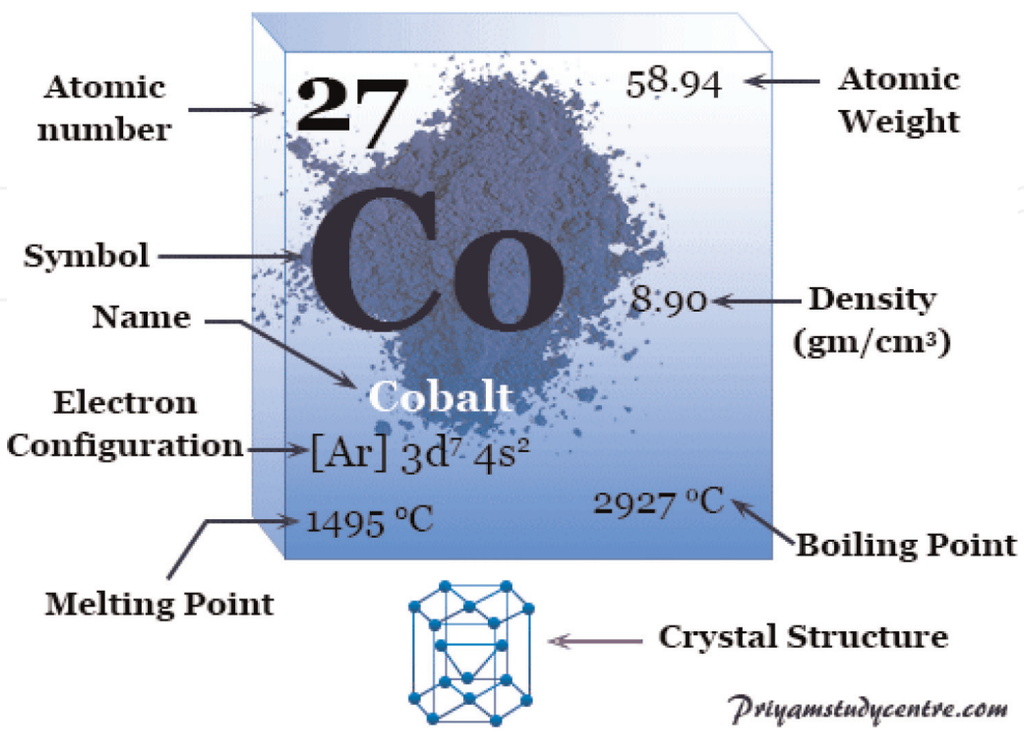

Figure 5.
Properties of cobalt. Source: https://www.priyamstudycentre.com/2021/01/cobalt.html.

6.3.4 Absorption of cobalt

Cobalt compounds deposit in the lungs after inhalation exposure based on their aerosol characteristics. Cobalt particles that are physiologically insoluble are removed by phagocytosis and/or mucociliary transport [96]. Soluble forms of cobalt enter the bloodstream through the alveolar or bronchial walls. Nutritional status also is an important factor in cobalt absorption due to oral exposure, with both overnight fasting and iron deficiency resulting in increased cobalt absorption [97, 98]. It is also found that Co and Fe share a common absorptive pathway in the intestines, though cobalt absorption takes place without ferritin.

6.3.5 Metabolism of cobalt

Cobalt is essential in the body because it is a component of cyanocobalamin (Vit B12) [99], which is also involved in hematopoiesis; deficiency of this leads to pernicious anemia (**Figure 6**) [100].

6.3.6 Excretion of cobalt

Presently, there are no available data on the excretion of soluble cobalt particles in humans. Following an exposure to insoluble cobalt compounds (cobalt metal, cobalt oxides), elimination from the body appears to follow three-phase kinetics (**Table 1**).

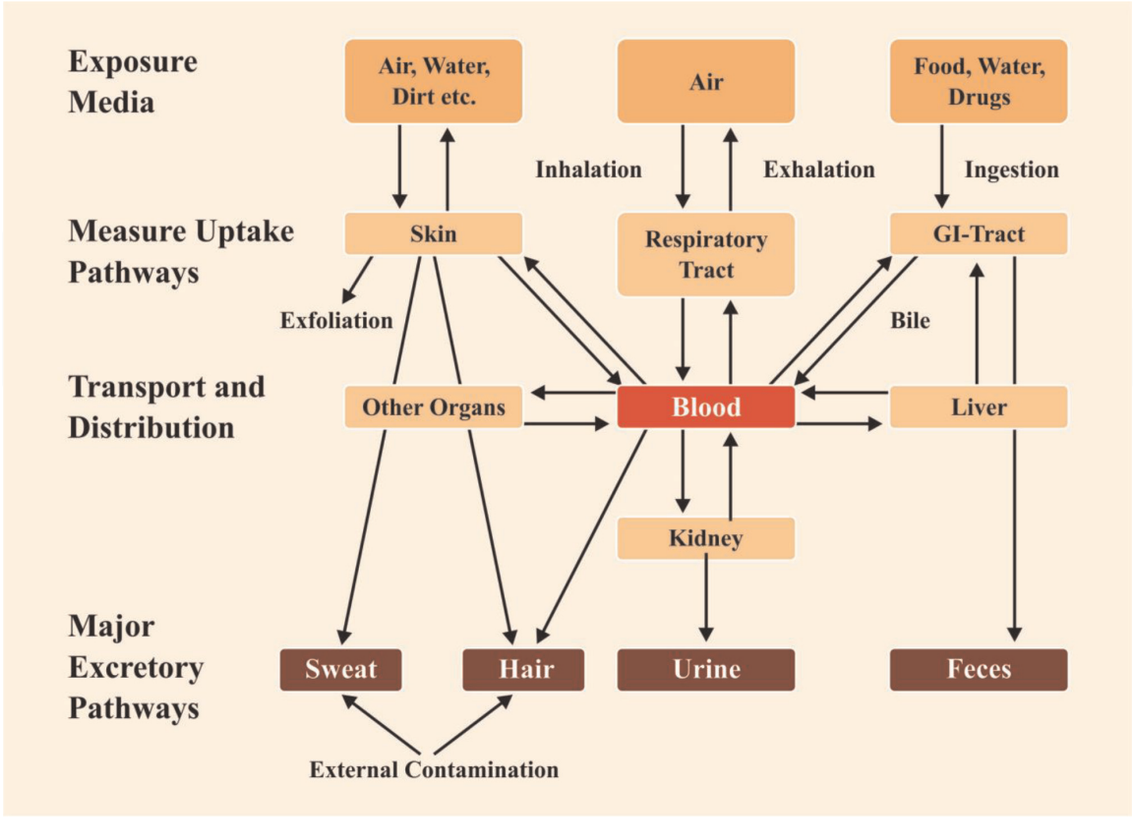

Figure 6.
Metabolism after exposure to heavy metals.

Kinetics	Clearance
First phase [101, 102]	Mucociliary clearance of particles deposited in the tracheobronchial region. *Half-time* on the order of **2–44 hours**
Second phase [103, 104]	Macrophag mediated clearance from the lung. *Half-time* on the order of **10–78 days**
Third phase [103–106]	long-term clearance from the lungs. *Half-time* on the order of years

Table 1.
List of different phases of kinetics in cobalt excretion.

6.3.7 Effect on health due to cobalt

Cobalt has both beneficial and harmful effects on human health. Cobalt is beneficial for humans because it is a part of vitamin B1. 0.16–1.0 mg cobalt/kg of body weight has been used as a treatment for anemia, including in pregnant women, as it causes production of RBCs. Exposure to 0.005 mg cobalt/m3 causes effects on the lungs, including asthma, pneumonia, and wheezing [106]. People exposed to 0.007 mg cobalt/m3 at work have also developed allergies to cobalt that have resulted in asthma and skin rashes [107].

6.4 Molybdenum

6.4.1 Properties of molybdenum

6.4.1.1 Daily requirement of molybdenum

Molybdenum is an essential nutrient; the nutritional requirement for adults is 45 μg/day (0.64 μg/kg/day) (**Figure 7**) [108, 109].

6.4.2 Sources of molybdenum

Molybdenum is found in higher concentrations in air, water, and soil. Molybdenum concentrations in ambient air have been reported to range from below detection limits to 0.03 mg/m^3 [110].

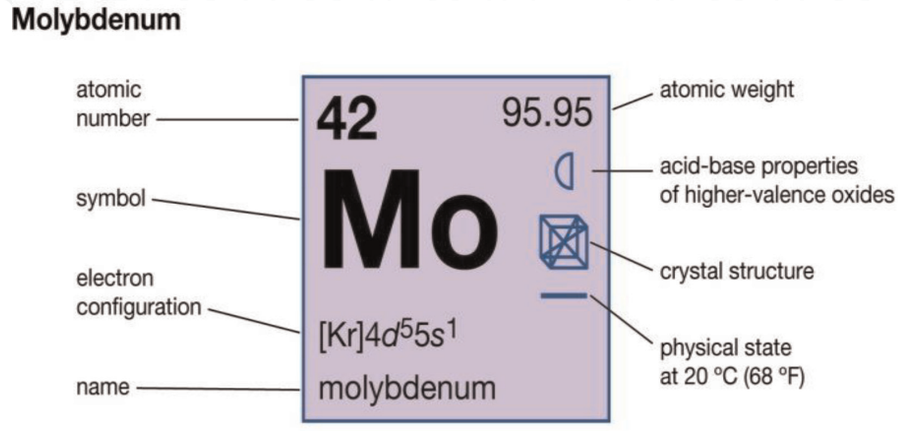

Figure 7.
Properties of molybdenum. Source: https://www.priyamstudycentre.com/2021/01/molybdenum.html, https://www.google.com/url?sa=i&url=https%3A%2F%2Fwww.britannica.com%2Fscience%2Fmolybdenum&psig=AOvVaw36J2pmNBtTjQzFFax0VK7I&ust=1675683204305000&source=images&cd=vfe&ved=2ahUKEwjc37rCpP78AhVyC7cAHSoEAikQr4kDegUIARDeAQ

6.4.3 Exposure to molybdenum

The general population's exposure to molybdenum is almost entirely through food. Rich sources of molybdenum are found in beans, cereal grains, leafy vegetables, legumes, liver, and milk [111]. Molybdenum contamination of drinking water is seen due to influence of industrial effluents (**Figure 8**).

6.4.4 Absorption of molybdenum

Inhaled molybdenum particles are distributed via (1) bronchial and tracheal mucociliary transport to the gastrointestinal tract; (2) transport to thoracic lymph nodes; or (3) absorption into blood and/or lymph and transfer to other tissues. Particles are cleared from the pulmonary region primarily by absorption, lymph drainage, macrophage phagocytosis and migration, and upward mucociliary flow. Dissolved molybdenum is absorbed into the blood. The rate of absorption depends on solubility. Ingested molybdenum that is absorbed depends on numerous factors, including molybdenum dose level, fasting, diet, and nutritional status [112, 113].

6.4.5 Metabolism of molybdenum

Molybdenum exists in several valence states and may undergo oxidation and reduction. The primary form of molybdenum that interacts with enzyme systems is MoVI, as the molybdate anion (MoVIO22-) [114]. After molybdate is taken into a cell, it is incorporated into a molybdopterin to form molybdenum cofactor (Moco). Moco is a sulfur-molybdate complex that forms the prosthetic group in molybdenum-dependent enzymes [115, 116]. Moco is extremely sensitive to oxidation, and it binds

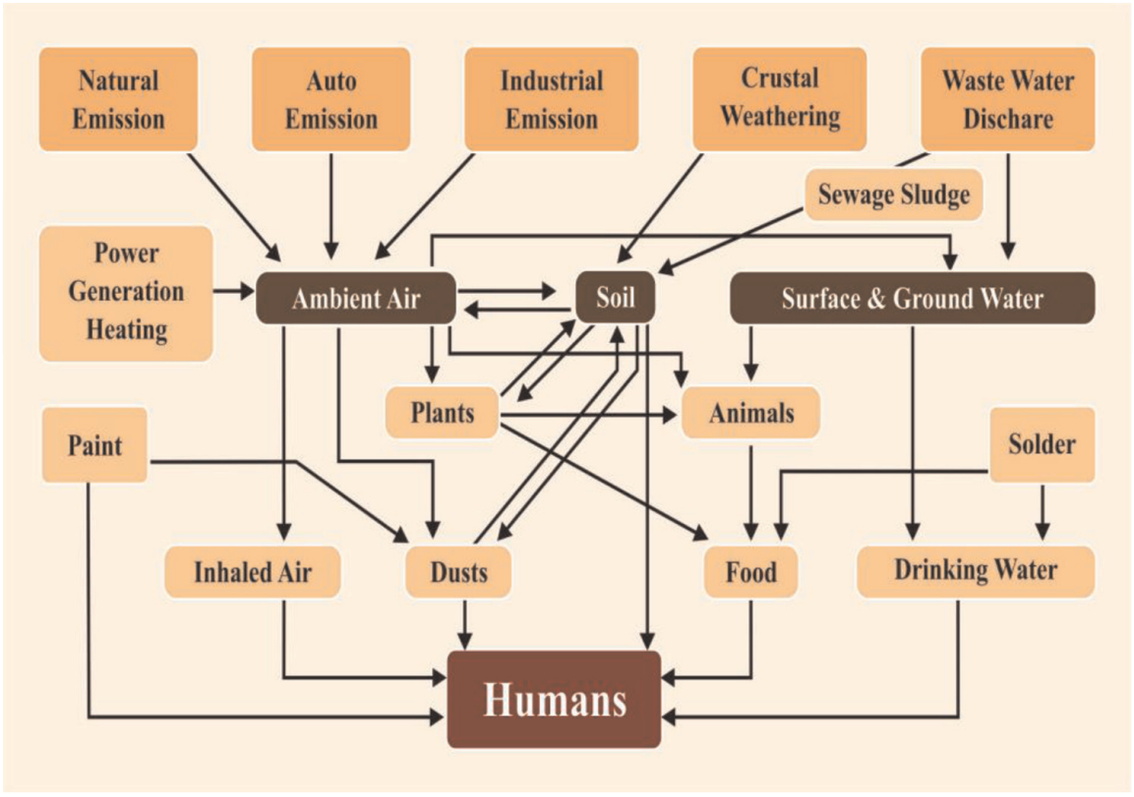

Figure 8.
Pathways of human exposure to heavy metals [ATSDR 2005].

to a Moco-binding protein in the cell (Mendel and Kruse 2012) where it is stored to meet the cell's demand for molybdenum enzymes. Molybdate forms complexes with copper and binds to plasma proteins as a copper-molybdenum-sulfur (Cu-Mo-S) complex [117, 118].

6.4.6 Excretion of molybdenum

Absorbed molybdenum is excreted as urine and feces in humans. Urine is the dominant excretion route, accounting for the excretion of approximately 75–90% of the absorbed dose [119, 120].

6.4.7 Effects on health due to molybdenum

Tetrathiomolybdate forms a tripartite complex with copper and protein and prevents copper absorption through the gastrointestinal tract [121]; thus, tetrathiomolybdate is used in the treatment of Wilson's disease. Significant increases in serum and urine copper levels were observed in men exposed to 0.022 mg molybdenum/kg/day for 10 days, as compared to exposure to 0.00771 mg molybdenum/kg/day for 10 days [122]. However, there was no difference in fecal excretion of copper, suggesting that copper absorption was not affected. In contrast, another study [123] showed no significant changes in serum copper levels when exposed to molybdenum levels of 22–1490 μg/day (0.0003–0.02 mg/kg/day) for 24 days (**Table 2**).

Sr. No.	References	Study hypothesis	Research finding
1	Ros C. Randall et al. [13]	To carry out an extensive literature review of the use and efficiency of preformed metal crowns for primary and permanent molar teeth.	PMCs are superior to amalgam restorations for multi-surface cavities in primary molar teeth.
2	Bhaskar V et al. [124]	To evaluate *in vitro* biodegradation of space maintainers made of two different company bands (Dantaurum, Unitek) using atomic adsorption spectrophotometer.	Ni ranging from 4.95 to 7.78 ppm and chromium from 1.70 to 4.54 ppm were released through an artificial salivary medium. Release of Ni and Cr reached a peak level on the 7th day, then decreased with time.
3	David Keinan et al. [125]	To analyze the absorption of metal ions released from stainless-steel crowns by root surface of primary molars.	Stainless-steel crowns release nickel, chromium, and iron in the oral environment, and the ions are absorbed by the primary molar roots.
4	Hiroe Kodaira et al. [126]	To assess alterations in levels of iron, chromium, and nickel released from preformed crowns and compare these levels with standard values.	Accumulation of trace elements released from preformed crowns used in restoration of primary teeth (3 M stainless-steel primary molar crowns) does not affect the body.
5	Kulkarni P et al. [127]	To measure the Ni ion release from conventionally preformed stainless-steel crowns (SSCs), and to determine the maximum no of appliances that can be given to an individual without reaching toxic levels.	The release of nickel and chromium was very much below when compared with the average dietary intake of nickel (200–300 ppm/day), which was not capable of causing any toxic effects.

Sr. No.	References	Study hypothesis	Research finding
6	Leila Basir et al. [128]	To evaluate the effect of pH, time, oral temperature, and SSCs' trimming on the nickel releasing.	The concentration of released nickel decreased with trimming of margins and increased when temperature increased. Time and pH had no significant effect on released nickel.

Table 2.
List of previous literature related to different pre-fabricated crowns.

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