Metals and Health: A Clinical Toxicological Perspective on Tungsten and Review of the Literature

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Tungsten and tungsten compounds are considered toxicologically relatively safe. Concern regarding the potential health and environmental effects of depleted uranium and lead in military applications has lead many countries to explore the possibility of applying toxicologically safer metals. Heavy metal tungsten alloy-based munitions have been therefore introduced as a replacement in munitions and as kinetic energy penetrators. Although the toxicological profiles of all these metals are well known, their internalization as embedded shrapnel may be considered a new route for long-term exposure. Studies in experimental animals and cell culture indicate that pellets based on heavy metal tungsten alloy possess carcinogenic potential previously unseen for depleted uranium and/or lead. Other metals in the tungsten alloy such as nickel or cobalt may contribute to such a risk. Accordingly, the long-term tungsten-related health risk is reason for concern. This article reviews toxicological and clinical literature and provides new perspectives on tungsten and tungsten-based alloys.

History

The history of tungsten goes back to the 18th century.[1,2] In 1758, the Swedish chemist Axel Fredrik Cronstedt discovered an unusually heavy mineral. He named this "tung-sten" which is Swedish for "heavy stone." Cronstedt was convinced that this mineral contained a new, and at that time undiscovered, element. In 1781 another Swedish investigator, Carl Wilhelm Scheele, succeeded in isolating tungsten trioxide.

Physical and Chemical Characteristics

Tungsten (chemical symbol W, atomic number 74, atomic weight 183.85) is a greyish-white lustrous metal which is solid at room temperature.[1,2] Tungsten is found in group VIb of the periodic system under chromium and molybdenum. Tungsten has the highest melting point (3,410°C) and lowest vapor pressure of all metals and has the highest tensile strength at temperatures over 1,650°C. It is resistant to corrosion and is attacked only slightly by most mineral acids. Tungsten, being one of the highest melting point materials, exhibits excellent high temperature properties, especially hardness. It is a heavy metal and has the lowest coefficient of expansion of all metals (4.5×10^{-6} cm/°C).

Occurrence

Tungsten is a naturally occurring element in rocks and minerals combined with other chemicals but never as a pure metal.[1-3] Tungsten occurs naturally in the form of chemical compounds with other elements. Although more than 20 tungsten-bearing compounds have been discovered, only 2 of them have industrial importance, i.e., wolframite ((Fe, Mn) WO_4, 76.5%) and scheelite ($CaWO_4$, 80.5%).

The world's greatest tungsten reserves are estimated at 3.3 million tons and will last until approximately 2097 at current usage rates.[2] The largest reserves are located in China, followed by Canada and the former Soviet Union.

Mining and Processing

Tungsten is usually mined underground although open cast mines do exist but are rare.[1,2] Most tungsten concentrates are chemically processed to form ammonium paratungstate, the main intermediate in tungsten processing. Wolframite concentrates can be smelted directly with charcoal or coke in an electric arc furnace to form ferrotungsten which is used as an alloying material in steel production.

Uses

The most widespread application of tungsten is as the wire in lamp bulbs. In general, tungsten is used in four physicochemical forms.[1,2,4] (1) Tungsten carbide is used in metallurgy combined with cobalt as a binder to form cemented carbides which are hard substances and are used to manufacture cutting and perforating tools. (2) Metallic tungsten and (3) tungsten alloys dominate the market in applications for which a high-density material (19.3 g/cm^3) is required, such as kinetic energy penetrators, counterweights, and flywheels. Other applications include radiation shields and x-ray targets. In wire form, tungsten is used extensively for lighting, electronic devices, and thermocouples. (4) Industrial tungsten chemicals (oxides) are used for organic dyes, pigment phosphors, catalysts, cathode-ray tubes, and x-ray screens.

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TABLE I

COMPOSITION OF THE MOST COMMON HEAVY METAL TUNGSTEN ALLOYS

Tungsten plus nickel plus copper
Tungsten plus nickel plus iron
Tungsten plus nickel plus iron plus cobalt
For special applications
Tungsten plus nickel plus cobalt
Tungsten plus molybdenum plus nickel plus iron
Tungsten content ≥90 weight percent
Density ≥17 g/cm^3

Tungsten Alloys and Military Uses

Concern regarding the long-term health and environmental effects of lead and depleted uranium has forced the military to apply toxicologically safer metals with comparable materials potential. Therefore, in military applications, heavy metal tungsten alloys (HMTA) have recently gained interest as a replacement for these elements.[2,4] These are a category of tungsten-based materials that typically contain 90 to 98 weight percent with some mix of nickel, iron, copper, and or/cobalt, their features being high-density and high-elastic stiffness (Table I). The first HMTA developed was a tungsten-nickel-copper alloy. However, the majority of the current uses for HMTAs are best satisfied with a tungsten-nickel-iron compound. The addition of cobalt is a common approach for slight enhancement of strength and ductility. The HMTAs are used in high-performance, lead-free, shot-balancing weights for ailerons in commercial aircraft, helicopter rotors, and for guided missiles, kinetic energy penetrators for defeating heavy armor, and fragmentation warheads. A number of potentially military useful alloy systems are still in development.

Environmental Exposure

Tungsten is naturally occurring in the environment and plays an important role in the microbiology of the soil.[5] Despite its widespread use, the potential environmental effects of tungsten released in the environment are unknown and no data are as yet available to make an environmental risk assessment. The environment is exposed to both particulate and soluble forms of tungsten and, to a growing extent, to tungsten alloy components, as are present in some munitions formulations.[6] Effects appear to be related to soil acidification occurring during tungsten dissolution. Tungsten powder mixed with soils at rates higher than 1% on a mass basis trigger changes in soil microbial communities resulting in the death of a substantial portion of the bacterial component and an increase in the fungal biomass. It also induces the death of red worms and plants. Dissolved tungsten species significantly decrease microbial yields. Soluble tungsten concentrations as low as 10^{-5} mg/L cause a decrease in biomass production by 8% and are possibly related to production of stress proteins. Plants and worms take up tungsten ions from soil in significant amounts while an enrichment of tungsten in the plant rhizosphere is observed. This may indicate that tungsten compounds could even enter the food chain.

Human Exposure and Biokinetics

Since tungsten is a naturally occurring element, exposure to very low levels of tungsten occurs by breathing air, eating food, or drinking water that contains tungsten.[7] In general, exposure to tungsten from air, drinking water, and food is expected to be very low. Air normally contains less than 10 ng of tungsten/m^3. Urban air generally contains more tungsten than rural air. The reference levels for tungsten in food and drinking water are not reliably available, one reason being that their values are below the detection limits of most analytical equipment.[7]

Occupational exposure to higher than background levels of tungsten may occur if persons use tungsten metal or are engaged in the processing of these metals. Occupational exposure to tungsten carbide occurs during the machining of tungsten carbide tools in the manufacturing process. Occupational exposure focuses on the inhalatory exposure route and the dermal route.[7]

Tungsten can enter the blood through ingestion, inhalation, or injection and is predominantly and rapidly excreted in urine with only a very small proportion being incorporated into the kidneys, liver, spleen, and skeleton. Under conditions of chronic uptake, it is projected that levels in soft tissue will take up to 3 years to reach a plateau but that the level in bone will continue to increase throughout life.[8]

Human Health Effects

Tungsten plays an essential role in the biology of microbial organisms[5]; usually it is present as an active site in specific microbial enzymes.[9,10] As yet, no essential role for tungsten is recognized in the biology of humans.

Tungsten has been the subject of numerous in vivo experimental and in vitro studies in view of determining its metabolic and toxicity profile.[11] However, tungsten and its compounds are not considered very toxic for humans. Most existing human toxicology information comes from chronic occupational exposure.

Chronic Tungsten Poisoning

Chronic intoxications related to the use of different forms of tungsten have been described in the literature. They usually concerned metallurgy workers after long-term respiratory or cutaneous contact with tungsten carbide particles.[12] In most of these studies, the question remains open as to what extent tungsten is really implicated compared to other metals such as cobalt.[12]

Lung

Tungsten may play a role in cases of pulmonary fibrosis related to hard metal lung disease.[12,13] This is a giant cell interstitial pneumonitis which is contracted from inhaling the dust formed during the processing of hard metal, a material composed of tungsten carbide and cobalt. However, the majority of the toxicity reports may be attributable to the effects of cobalt on respiratory tissues in susceptible individuals and not to tungsten.

Skin

A dermatitis is often observed in hard metal workers but may also be largely due to the effects of cobalt. Tungsten carbide appears to modify the toxicity of cobalt and cobalt alone does not have the same toxic effects.[12,14]

Nervous System

Neuropsychological impairment, particularly with regard to memory function, is also reported in hard metal workers.[12,15]

Arterial Embolization Coils

It has recently been reported that tungsten embolization coils used in vascular radiology may corrode or even dissolve.[12,16,17] This has consequences for their ability to maintain arterial occlusion and for possible toxic effects due to the distribution of the material into the bodies of patients. However, follow-up studies and in vitro analysis predict very little risk of toxicity.[17,18] Mobilization of tungsten from the site of implantation to other distant sites has been suggested and in patients with these types of coils significantly elevated blood tungsten levels have been detected. The long-term significance or possible toxicological effects of this elevation are uncertain.[16,17]

Acute Tungsten Poisoning

Acute tungsten intoxication is an extremely rare phenomenon.[12] Much of the information on human toxicity derives from a case report of an acute toxic reaction to tungsten dissolved in alcoholic drinks, following a tradition of French army artillery recruits to drink wine or beer which has rinsed a recently fired gun barrel.[12,19,20] The introduction of tungsten into the manufacturing alloy of the barrel to harden the steel was the cause of this novel poisoning event. Toxicological analysis confirmed significantly elevated levels of tungsten in blood, urine, hair, and nails. The symptoms of this acute intoxication were: nausea within 15 minutes of ingestion, sudden onset of seizures, rapid onset of clouded consciousness leading to coma and encephalopathy, moderate renal failure progressing to acute tubular necrosis with anuria within 24 hours, and hypocalcemia. A gradual symptomatic recovery followed in weeks with complete recovery of clinical and chemical parameters after 5 months.

Laboratory Diagnosis

To confirm whether the symptoms of acute poisoning, as outlined above, in industrial workers or soldiers may be attributed to tungsten, their tungsten levels in blood and urine may be investigated.[12] Inductively coupled plasma (ICP) with optical emission or mass spectrometry may be the methods of choice to determine the concentration of tungsten in body fluids/tissues.[7,16,17,19,20]

In cases of acute poisoning, initial blood levels of 5 mg/L have been detected.[19,20] In the patients with degraded embolization coils in situ, average blood levels of 8.4 (4.7–15.1) μg/L have been detected.[16] Average blood levels in controls who had undergone aortic aneurysm grafting without coil embolization were 0.44 μg/L.[16] It may be inferred from these poisoning cases that normal blood levels should be found below 0.5 μg/L and that lethal levels will move above 5 mg/L.

In the case of chronic occupational exposure, the analysis of tungsten in urine is preferred. An elevated tungsten level in urine confirms exposure but is much less correlated to health effect. Tungsten occurs in human urine at low concentrations. Between 2001 and 2002, the geometric mean concentration (95% confidence limits) of tungsten in urine for a U.S. population aged 6 years and older was 0.078 μg/g creatinine.[21] Representative occupational levels though are significantly elevated from the levels found in controls and can reach 94.4 μg/g creatinine.[22] Levels in these biological media may be used in conjunction with biokinetic models to estimate previous exposure levels.[8]

Clinical Management

From the above-mentioned case history, it was reported that treatment of acute poisoning cases is mainly supportive.[12,19,20] Charcoal may be given if not contraindicated. In addition, oxygen should be given for respiratory symptoms and benzodiazepines for seizures. Hemodialysis was used in this case for renal failure, but with limited effect on tungsten clearance. It appears that patients who survive an acute tungsten poisoning episode have a good chance of short- and long-term recovery if they receive appropriate supportive therapy and hemodialysis.

Treatment of chronic poisoning, e.g., hard metal disease, is also symptomatic and does not concentrate on tungsten or cobalt levels. Treatment focuses on cessation of exposure and administration of corticosteroids. In some cases, desensitization procedures are suggested.

Tumorigenic Potential and Shrapnel Pellets

There is not enough information yet to determine whether inhalation, oral, or dermal exposure to tungsten or tungsten compounds can cause cancer in humans.[7] However, experimental animal and in vitro studies do not exclude the possibility. This question becomes more relevant in view of the long-term tungsten exposure from internalized HMTA-based shrapnel embedded in tissue. The health risk of this very new and specific type of exposure should not be underestimated and is reason for concern.

Implanted pellets of tungsten alloy in rat experiments resulted in tumor development.[23] In this study, the intramuscularly embedded tungsten alloy pellets (91.1% tungsten, 6% nickel, 2.9% cobalt) not only resulted in aggressive localized tumors (high-grade pleomorphic rhabdomyosarcomas) that rapidly metastasized to the lungs, but also caused significant hemopoietic changes well before the carcinogenic effect was observed. Earlier experiments studying exposure of in vitro cell cultures to tungsten alloys already indicated triggering of tumorigenesis.[24–26] Immortalized human osteoblast-like cells were shown to be transformed to the neoplastic phenotype in the presence of metal powder mixtures following the composition of tungsten alloys. The expression of a number of stress genes was significantly activated in the presence of such a powder mixture using a human hepatoma cell line.

A crucial issue in these experimental observations is the role of the additional metals used in the tungsten alloy. The actual role for tungsten may not be considered in isolation; nickel, copper, iron, cobalt, or molybdenum may contribute to or modify the development of tungsten toxicity (Table I). Nickel and cobalt compounds by themselves are known to be associated with cancer development.[27,28] Therefore, it may be implied from these experimental results on tungsten alloys that their cancer risk is associated and comparable with the risk known for other biologically reactive and insoluble carcinogenic heavy metal compounds (e.g., nickel oxide). Although the health risks of tungsten compounds for humans may be appreciated as limited, in the 2005 summary review of the Agency for Toxic Substances and Disease Registry,[7] this may be misleading.

The increasing military use of tungsten and its alloys demands more attention to these problems. It is recommended that metal fragments surgically removed from wartime casualties be analyzed for their gross composition of the metals as part of diagnostic service. The aforementioned techniques of ICP-optical emission and ICP-mass spectrometry may provide outcome in such an analysis. These data may not only affect immediate medical treatment, such as further surgery, but will also provide and secure important information for long-term follow-up of these patients. Further research in this area is essential.

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