

Heavy Metal Toxicity

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In general, irritable health concern related to heavy metal (accumulation) might be mainly divided into 2 types, i.e. heavy metal poisoning caused by excessive extrinsic exposure and genetic disorders such as Wilson disease (as reviewed by Osredkar et al. in this issue). As for the former type, unlike the latter one, it can be said that the health damage spread with the development of the civilization.

Of the known elements, nearly 80% are either metals or metalloids. Many metals, in trace amounts, are generally vital to normal physiological processes; for examples, iron in oxygen transport, manganese and selenium in antioxidant system and zinc in metabolism. With these essential metals toxicity occurs when concentrations are either too low or too high. For some metals, on the other hand, there are no physiological concentrations detected; as such, these metals (even) only have the potential to cause toxicity like arsenic, mercury, lead and thallium [1]. Acute and chronic arsenic toxicity, as well as arsine gas toxicity involves adverse impacts on the nervous, cardiovascular, respiratory, gastrointestinal, hepatic, renal, hematopoietic, immunological, and dermatologic systems. Mercury exposure, including exposure to short chain alkyl mercury, elemental mercury, and acute inorganic salt, historically induced catastrophic health concerns such as serious neurologic disorders found in Minamata area in Japan [2,3]. It is generally accepted that food crops grown on cadmium containing soils or soils naturally rich in this metal are the major source of exposure to humans other than exposure from smoking of cigarettes [4]. Lead, cadmium, and manganese have found a variety of uses in industry, craft, and agriculture owing to their physical and chemical properties. Poisoning induced by high concentration of these metals adversely influence on kidney, hematopoietic cells, nervous system, and bones. It also appears that the consequences of exposure to lead in adults are less severe than the types of exposure associated with hyperactivity in neonates. Experimental study has shown that these metals produce behavioral changes by altering the metabolism of brain neurotransmitters, especially catecholamines. It has also been hypothesized that these metals exert their toxic effect by damaging biological defense, which exist in the body to serve as protective mechanisms against exogenous toxins. The problem of metal toxicity becomes even more complex owing to simultaneous or successive exposure of the general population to different physical, chemical, biological, and psychological factors in the environment [4]. To date, large numbers of people in particular in Asia still troubled by metal pollution [5], suggesting that special issues focusing on the matter lead to problem submission to the world.

Based on above mentioned historical and modern overview in terms of heavy metal poisoning, the special issue of the journal entitled "Heavy metal toxicity" was recently released in a one volume compendium of almost every imaginable aspect of toxicity elicited by exposure to heavy metals. This definition casts an all-encompassing net, resulting in the inclusion of topics ranging from eradication system of heavy metals from environment to the immunotoxicity. This special issue is comprehensive having 6 chapters. The text is organized in a very straightforward manner, with general introductory material being set forth in the first few chapters, followed by poisoning, remediation, immuno- and metabolic- toxicity. Almost all manuscripts generally consist of abstract/overview, introduction, role of heavy metals in the

chapters, conclusive remarks, and future perspectives, in relatively easily understood terms, which are helped by clear line drawing.

Reading impressions

This special issue is well organized, with an overview of the introductory subject matters relating to biological significance of several heavy metals and their toxicity in the initial few chapters. The materials are then described to influence several immune response and metabolism and several related cascades related to these phenomenon. Finally, the toxicological implications of heavy metals are considered, as well as its ethical and regulatory aspects and future perspectives. At first, Osredkar et al. and Koyano et al. focus on biology regarding zinc and copper, followed by health impacts by excess volume of these metals and genetic disease such as Wilson disease. Next, Hong Zhang et al. show possible role of biological remediation of excess copper and lead from environment using fungi. Thomas and colleagues illustrate a risk of careless use of bismuth, widely used in medical scenes. Theron et al. refer to immunotoxicity of relatively hazardous types of heavy metals such as cadmium, mercury, lead, vanadium, platinum, and palladium in terms of innate immunity. Finally, Shokooh Saljooghi et al. indicate effects of mercury in iron metabolism by using in vivo experiments.

On the other hand, due to the extremely broad nature of the field of heavy metal toxicity, it would have been exceedingly difficult to include the extensive number of citations necessary to fully reference every aspect of the text. Thus, almost all the authors selected seminal references to illustrate their intension and direction. Overall, this approach makes sense and is applied properly throughout the text. Nonetheless, there may be many times when new subjects were introduced with limited background information and an appropriate references, were not available for further investigation.

Conclusive Remark

I want to add two points to the special issue. One point is description about therapeutic potential of some of these heavy metals. Arsenic was used to treat chronic myelogenous leukemia in the 18th and 19th centuries (but was discarded as a treatment in the early 20th) [6]. Today, the metal is being expected to cure acute promyelocytic leukemia combined with retinoic acid, molecurally targeting some orphan receptors such as retinoic acid receptors and retinoid X receptors [6,7]. Magnesium oxide and zinc oxide are used against constipation and skin inflammation. As well, metalloproteins may be considered for therapeutic strategy against several human disorders. Metallothionein, a cysteine-rich, low molecular weight ($M_r \approx 6000$) protein with a high

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affinity for heavy metals such as cadmium, zinc, copper, and mercury and is induced by these metals and many other factors including glucocorticoids and cytokines, is reportedly and experimentally shown to play a role in cytoprotection and exacerbation against inflammatory pathophysiology [8]. Therefore, it is likely that these metals and related metalloproteins can be therapeutic option to some diseases, which depend on their kind, dosage, and/or applicable diseases; thus, future researches handling these materials are expected in medical scene. In summary, I hope this textbook would lead development of environmental science and provide significant insights in toxicology, immunology, metabolism, environmental, occupational, and public health, preventive medicine, therapeutics.

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