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Invited review

# Trace element research-historical and future aspects☆

Monica Nordberg[a,*], Gunnar F. Nordberg[b]

[a] Institute of Environmental Medicine, Karolinska Institutet, SE- 171 77 Stockholm, Sweden
[b] Department of Public Health and Clinical Medicine, University of Umea, SE-901 87 Umea, Sweden

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ABSTRACT

During the last 30 years the International Society for Trace Element Research and the Nordic Trace Element Society has been active . During this period the importance of these elements for human diseases has been increasingly recognized, including their contribution to the global burden of disease. New analytical methods allow biomonitoring data to be related to health outcome. Future research using modern chemical methods will focus more on elemental speciation and on measuring lower concentrations leading to further identifying adverse effects and critical organs. Extensive knowledge about essentiality and toxicity of trace elements in humans has emerged during the last two decades and at present the difficulties in defining a range of acceptable oral intakes for essential elements has largely been overcome. Biological monitoring of trace element concentrations in various media such as blood or urine is of great importance and an overview is given. As an example, a more detailed description of biological monitoring of cadmium is given, explaining biokinetics including the role of metallothionein in modifying kinetics and toxicity. Finally future challenges related to risk assessment of newly developed metallic nanomaterials and metal containing medical devices are discussed.



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## 1. Historical development of the international society for trace elements research in humans (ISTERH) and the nordic trace element society (NTES)

Ever since its inauguration the International Society for Trace Elements Research in Humans (ISTERH) has organized conferences as seen in Table 1. The conferences have been held in various parts of the world. A more detailed account of the ISTERH conferences has been given by Prasad et al. [1]. During the years ISTERH and the Nordic Trace Element Society (NTES) have interacted. Conferences organized by NTES are listed in Table 2.

ISTERH and NTES started their activities in the Mid 1980s and now we all attend the 11th and/12th conference. Sometimes the conferences have been in collaboration with National Societies related to trace elements.

The ISTERH society follows the stated mission and goal set since the inauguration (Table 3). A strength and likely explanation of success is that many disciplines e.g., nutrition, toxicology, chemistry,

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* Corresponding author.
*E-mail address:* gunnar.nordberg@envmed.umu.se (G.F. Nordberg).

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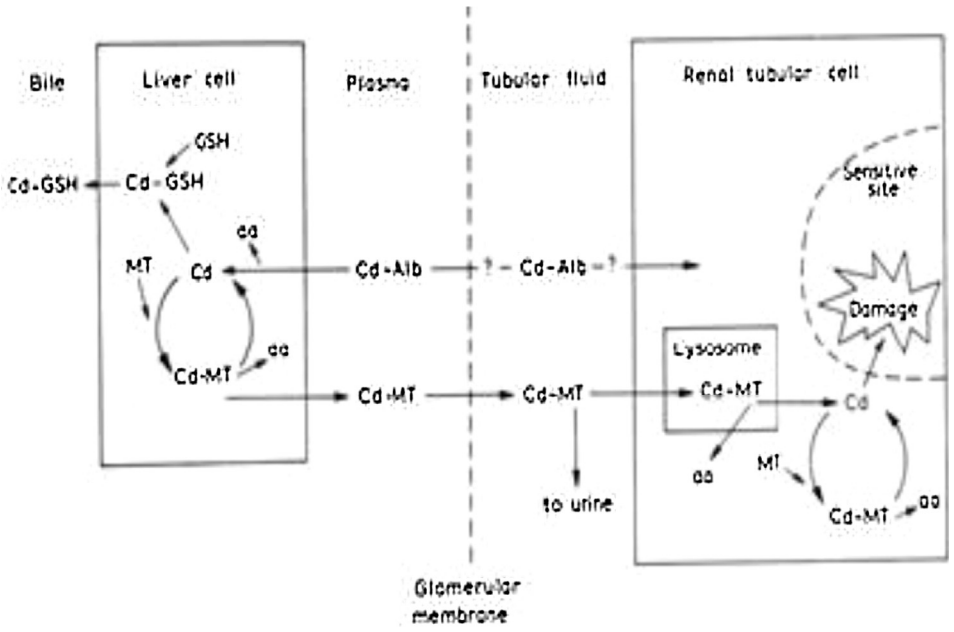


**Fig. 1.** Simplified flow scheme of cadmium in the mammalian body demonstrating the role of binding forms in blood plasma and synthesis and degradation of metallothionein (MT).
From Nordberg et al. [3].

epidemiology, medicine, environmental medicine and professions are attracted to participate. This interdisciplinary interaction contributes to important understanding of the combined knowledge of trace elements/metals. Trace elements are established as causative agents of a number of diseases. During the years when ISTERH and NTES have been active there has been a tremendous development in general molecular biology. Research on trace elements will go on and be increasingly recognized as important for improved therapeutic and preventive action for human health. Of particular interest are interactions between trace elements and essentiality versus toxicity. Other important issues are biological monitoring and risk assessment of toxic metals.

## 2. Metals and disease

Diseases related to deficiency of essential trace elements are well known. Examples are iron deficiency anemia, goiter related to iodine deficiency, skin, neurological, immunologic and hormonal changes in zinc deficiency. Such deficiency states are relatively common and contribute to the global burden of disease (see later). Wilson disease and Menkes disease are rare genetically determined diseases related to disturbed copper metabolism [2]. Hereditary hemochromatosis is a disease caused by mutations in genes important for regulation of iron uptake in the intestine leading to iron overload. It occurs in 1:300 people in Northern European populations [2]. Outbreaks of disease have historically been related to excessive exposure to certain toxic metals and their compounds. For example, Minamata disease, a neurological and developmental disease caused by methylmercury, and itai–itai disease, a bone and kidney disease related to cadmium, were identified as health problems in Japan [2]. Epidemiological studies from China with non-occupational cadmium-exposed humans have confirmed that osteoporosis and bone fractures are caused by long term cadmium exposure. Population studies in China also contributed to new information about the link between cadmium and various forms of cancer [3]. A significant part of the human population in several countries is now exposed to excessive amounts of inorganic arsenic following major changes in the sources of drinking water in the affected regions e.g., Bangladesh. A large number of cases of diseases such as skin lesions, skin cancer and lung, bladder hepatic and renal cancer and adverse effects on foetuses and infants have been described in the exposed populations. In China, the indoor use of arsenic containing coal has given rise to excessive exposure to inorganic arsenic and related adverse health effects from arsenic which is adsorbed on foodstuffs kept indoors [2]. Low concentrations of aluminum (Al) are maintained in humans by efficient Al excretion through the kidneys. In persons with kidney disease who are on dialysis treatment, increased aluminum concentrations occurred when there were elevated concentrations of aluminum in the water used for dialysis and when aluminum

**Table 1**
International Society for Trace Elements Research in Humans (ISTERH) Conferences.

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| 1986 1st Palm Springs, Ca, USA |
| 1989 2nd Tokyo, Japan |
| 1992 3rd ISTERH/4th NTES Stockholm, Sweden |
| 1995 4th, Taormina, Italy |
| 1998 5th Lyon, France |
| 2002 6th ISTERH Quebec, Canada, (2001) |
| 2004 7th Bangkok,Thailand |
| 2007 8th Crete, Greece jointly 9th Nordic Trace Element Society (NTES) and the Vth Hellenic Trace Element Society (HTES) |
| 2011 9th Belek, Turkey,NTES |
| 2013 10th, Tokyo Japan, jointly Japanese Society for Biomedical Research on Trace Elements |
| 2013 11th NTES/ISTERH,Loen Norway |
| 2015 11th, ISTERH, 12th NTES Dubrovnik, Croatia and the Croatian Society of Biochemistry and Molecular Biology (CSBMB) |

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