
# IFA INTERNATIONAL SYMPOSIUM ON MICRONUTRIENTS

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# MICRONUTRIENTS AND HUMAN HEALTH

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## INTRODUCTION

Micronutrients copper (Cu), chromium (Cr), fluorine (F), iodine (I), iron (Fe), molybdenum (Mo), selenium (Se), and zinc (Zn) are essential for human. As each essential element has a specific role in the metabolism of man as co-factors in several enzyme reactions or as necessary constituents of important structural proteins that cannot be partly or wholly replaced by any other element, its deficiency leads to impairment of biological functions from optimal to sub optimal level and result in deficiency disorders of that specific micronutrient in human.

The importance of environmental factors in the geographical distribution of diseases of human being has been well recognized. The knowledge of endemic diseases, having characteristic of geographical distribution, has increased with time and showed that environmental factors influenced several of these diseases. A classical example is the relationships between goiter and lack of iodine, caries and deficiency of F, dwarfism and lack of Zn. Deficient levels of one or more micronutrient in soils depend upon the chemical composition of parent material-the rocks and sediments from which these have formed, and in the plants grown on them, have been recorded in most of the countries and are one of the major constraints to high production and productivity in agricultural systems as well as health of humans. In developing countries land is being increasingly brought under intensive cultivation, using modern agricultural technologies, to meet the growing demand of rapidly expanding population for food, fodder, fiber, fuel and fruits. These set in processes of depletion of micronutrients from the infinite soil resource adversely affecting not only crop yields and quality of produce but also the flow of micronutrients to humans through the soil-water-plant-animal-human chain. The resulting imbalances of micronutrients in soils ultimately reflect in their deficiency diseases in human.

The population suffers and continue to suffer especially in developing countries from the deficiency of both calorie and protein and that the protein-energy-micronutrient-malnutrition syndrome prevails. One of the reasons appears to be the strategy to produce at the first instance enough food to provide a square meal to the hungry masses rather than producing protein and micronutrient rich plant food. Dietary inadequacies of I, Fe, Zn, vitamin A etc., are estimated to affect the health, mental and physical function and survival of more than two billion people world wide. The problem is much more grave among young children and women of childbearing age (United Nation, 1991, Takkar, 2003).

Soil is the major source of micronutrients that enter the food chain; it is also a sink for elements from environmental sources (Lag, 1990). Thus, in depth knowledge of the sequence of events affecting the micronutrient composition of the soil, food, feed and/or water is necessary to fully understand the soil-water-plant-animal-human interrelationships in determining the health of human beings. The extent of problems associated with micronutrients varies greatly from locality to locality and between geographical areas, depending on geological mineral, soil type, vegetation, climatic conditions, stock, farming practices-quality and quantity of manures, fertilizers and water use practices. However, human are less susceptible than animals to any deficiency of micronutrient in the plant and water they eat and drink as his food constituents are derived most of the time from diverse sources and different places in various regions of the world. Thus it has only been possible to demonstrate associations between the occurrence of certain diseases in human and the concentrations of certain micronutrients in the soil, plant and water (Prasad, 1976, Mertz, 1987, Lag, 1990, Ringstad et al. 1990, Oliver, 1997, Takkar, 2003).

Micronutrient malnutrition is now a massive and rapidly growing public health problem among nearly all poor people in many developing nations affecting about 40 per cent of the world's population (Buyckx, 1993, Ramalingaswami, 1995). During the last three decades, the rapid increase in affected people with micronutrient malnutrition coincides with the expansion of "green revolution" cropping system i.e., cereal-cereal (low nutritional quality food) than cereal-pulses/legume (high nutritional quality food) systems in developing countries. In South Asia, the spectacular increase in production of wheat (400%) and rice (200%) with introduction of their modern HYV over three decades is associated with time trends in the increase of Fe deficiency anemia among non–pregnant, premenopausal women and negatively related to time trends in Fe density (mg Fe $kcal^{-1}$of available food) of diet (United Nation ACCSN, 1992). Similar trends emerged from China, Sub Saharan Africa, South America, and Southeast Asia (United Nation ACCSN. 1992). The consequences of micronutrient deficiencies are grave as they diminish the health, livelihood and well being of the afflicted and productivity and stability of the societies in which these people live in ways that are not always obvious. Therefore global food system must be changed to insure continuously balanced nutrient supplies to all people in adequate and affordable amounts (Coombs et al.1996 and Welch et al. 1997, Welch, 2001)). This review attempts to bring in focus human health problems related to the deficiencies of essential micronutrients Cu, I, Fe, Mn, Se, Zn and F.

## ZINC

Zinc is an essential as well as a toxic micronutrient; it's poisoning rarely occur under natural conditions. It is an essential constituent of large number of vital proteins. More than 70 enzymes, including DNA and RNA, require Zn for their proper functioning (Burch and Sullivan, 1976). Human require Zn relatively in large amount because of its crucial role in nucleic acid and protein synthesis. Its deficiency causes hypozincemia and intestinal mal-absorption.

Zinc deficiency is widespread in the soils of many countries of the world (Robson, 1993, Takkar, 1991, Takkar, et al. 1989). In India about 49 per cent soils are deficient in Zn and nearly 1.6 million ha area is receiving 5 kg Zn ha-1 Y-1. In Bangladesh, more than 2 million ha of the wet cultivable area is deficient in Zn . In China, the calcareous and neutral sandy paddy soils along the Yangtee River and throughout Northern China are deficient in Zn and Mn. In Australia widespread Zn deficiency is found in the famous Ninety-mile desert on the border of Victoria and

South Australia. Also 8 million ha of most extensive Zn and Cu deficient areas exist in the south-west of Western Australia. Nearly 0.5 million ha of irrigated rice soils in the Philippines and over 8 million ha in South East Asia suffer from Zn deficiency. In USA extensive Zn-deficiency has been recorded in an area of more than 600 km long in California. Zinc deficiency is widespread in arid calcareous soils of Iran and South West of Cape Province of South Africa. In tropical Latin America Oxisols and in Brazil and Columbia Ultisols have shown problems of Zn deficiency and more than one million ha area is receiving Zn application. Zinc deficiency occurs in crops and human on a world scale and is now regarded as second in importance only to Fe in human health (Alloway, 1995, Kickens, 1995, Takkar and Walker, 1993, Takkar, 1996, SSSA, 1965).

Zinc concentration in human depends on their diet. WHO (1996) reported that it is difficult to establish indices of Zn deficiency but considers that sub-optimal Zn supply is more widespread than had been thought? The dietary intake of 0.2-0.3 mg Zn $day^{-1}$ is regarded deficient. Pulses, whole grain and unpolished rice are good sources of Zn in the diet. Also red meat is a better source of Zn than chicken and pork.

In human diet Zn deficiency was reported as early as 1961 (Prasad et al. 1961; Prasad, 1978) and its deficiency in human has been observed in Africa and Asia. In Iran, Armenia and Egypt, males expressed its syndrome: hypogonadism, dwarfism, hepatosplenomegaly, anemia and geophagia (Prasad, 1976, Ringstad et al. 1990). The subjects had markedly low Zn concentration because of excessive intake of wheat flour bread generally rich in phytate (inositol hexa-phosphate) that adversely affect Zn absorption in the body. WHO (1996) considered that if phytate:Zn ratio exceeds 15 then absorption would be small? Also delayed wound healing and low resistance towards infection result from Zn deficiency (Pories and Strain, 966); Zn values were low, particularly in the diabetic and diabetic ulcer patients than normal surgical patients without metabolic diseases (Spears et al. 1974). Zinc deficiency also cause anorexia (failure to eat), growth retardation, skin lesions, rough and dry skin, immuno-suppression, loss of taste, infertility, premature birth and low birth weight (Hambridge et al. 1987, Ringsted et al.1990). Impaired sensory functions, loss of the sense of taste and smell, night blindness are restored with Zn therapy., Supplementation of Zn to stunted infants improved their height by 1.4 cm more than the children given the placebo In Guatemala (Riverra et al.1998). Similarly Zn therapy to infants and children from low-income families increased their growth rates in Bangladesh, Iran, Turky, Ecuador, and Chile and even in the developed countries: United States, Canada and France, suggesting that Zn deficiency is widespread globally (Welch, 2001). Zinc supplements in diet reduced diarrhea in infants (Sazawal et al. 1996). The presence of Zn, Cu, Fe and Mn in drinking water and soil correlated with dental caries in 1516 children (7 to 17 years age) in 10 rural areas in the district of Ludhiana, India (Guaba, 1983). Zinc showed an inverse relationship with dental carries.

The suggested safe recommended intake of Zn is 15-ug $day^{-1}$ (NRC, 1980). WHO (1996) recommended 45-ug Zn $day^{-1}$ as the upper limit and concentration of 150-ug $day^{-1}$ is toxic and cause impairment of health? In some countries food and milk is being fortified with Zn to correct its deficiency in human. Many doctors/nutritionists prescribe capsule and tablets containing Zn and vitamins to suspected Zn-deficient individuals.

## COPPER

Copper play important role in the metabolisms of plant, animals and human. Copper content of soils and number of soil conditions and factors, besides species and cultivars, affect its concentration in the edible parts of plants.

Being an essential micronutrient for man, it is a constituent of specific cuperoenzymes: cytoplasmic sueroxides dismutase, cytochrome c oxidase, dopamine-B-monoxygenase and tyrosinase. It is involved in lipid metabolism, bones development, and maturation of connective tissue. Signs of Its deficiency are amemia (hypocupremic), neutropenia and leucopoenia (lack of white blood cell), skeletal defects, degradation of nervous system (Prasad, 1976), defective melanin synthesis which manifests as depigmentation or hypopigmentation (lack of color) of hair and skin, keratinization of hair, steely hair, disorders of connective tissue, cardiovascular disorders, osteoporosis, arthritis, infertility and diarrhea (Fishbein, 1987, Davis and Mertz, 1987). Copper depletion in man leads to elevated levels of serum cholesterol and reversed upon its supplementation. In variance to this, smokers with greater cardiovascular risks factors have high serum Cu concentrations, an anomaly to the above finding. Copper deficiency also results from large intake of Zn and Fe as a result of their antagonistic interaction with Cu. NRC (1980) recommend safe and adequate dietary intakes of 2-3 mg Cu $day^{-1}$ for adults. While Fishbein (1987) suggested that an intake of 2 mg Cu $day^{-1}$ is adequate for healthy adults, 80-ug $day^{-1}$for infants and 40-ug $day^{-1}$for children. Though apparent signs of Cu deficiency have not been observed, the WHO (1996) consider that does not mean that people get enough Cu particularly in many developing countries where its content is insufficient in their diet.

## IODINE

Iodine is essential as well as toxic element. It is a principal component of thyroid hormones thyroxine (T4) and tri-idothyronine (T3), which are essential for normal growth-physical and mental development in man. Iodine deficiency disorder (IDD) term includes all effects of iodine deficiency it has on growth and development including brain development (Hetzel, 1989). The deficiency cause severe retardation of groth and maturation of almost all organ systems, including bones and body weight.

Iodine deficiency is the most common preventable cause of mental deficiency in the world today. About 1.5 billion people are at risk of IDD in the developing countries. Out of this, 655 million suffer from goiter-a swelling of the thyroid gland in the neck. Elimination of I deficiency would prevent the brain damage that has caused irreversible mental handicap to at least 43 million people in the world today (WHO, 1996). Out of 15-20mg I in healthy adult 9-16 mg is concentrated in the thyroid that weighs around 15-25 g only. To maintain an adequate supply of thyroxine, thyroid has to trap around 60 ug of I/day. In humans IDD arise when its level drop below the recommended dietary intake levels of 150-ug capita-1 day-1(NRC,1980) or 1 mg or less in the thyroid gland.. The risk arises from the effect of dietary I deficiency on the early development of the brain (Hetzel, 1997). Goiter is the most common form of IDD. Endemic goiter has been reported from all over Asia. Its deficiency causes cretinism in children born of parents residing in goiter endemic areas (Aswathanarayana, 1990).

The most severely affected areas are those of Himalayas in India and Nepal, the Alps in Europe, the Andes in South America, the mountains of China and several other countries. It also occurs in the flooded river valleys such as ganges in India. IDD in India has been recorded in geographical areas of over of 2400 km along the Himalayas and the Satpura and Vindyachal ranges (Ray et al. 1959). About 9 million Indians are said to be suffering from either goiter or sub clinical thyroid function, which impairs their health and mental capabilities. In African continent 21 countries have severe IDD and 15 mild to moderate IDD. In Africa, where the soil, water and food grown are low in iodine, about 8 million people are inflicted with severe IDD. Deficiency of I is associated with soil type or parent bedrock, In France, Germany, Ireland and Norway soils near the sea contained 8.5 to 16.8 mg I kg-1, while it was 1.7 to 3.7 mg I kg-1 in inland (Fuge, 1987, 1996; Lag, 1972, Takkar and Randhawa, 1990, Takkar, 2003).

***Iodine cycle***

Sea (50ug/L) → Atmosphere (400,000 tonnes/year) → normal rain (1.8-8.5 ug/L), snow → mountains and soils → high rainfall, snow, glaciations, floods, → Leaching & erosion → underground water/ sub-soil, lakes, rivers → sea

The rate of return of I is slow and small in quantity and repeated cycles of I in nature leads to its deficiency in soils and the plants grown on such soils contain as low as 10 ug I/kg compared to 1.0 mg I/kg in adequate soils. Human population largely depended on the food produced in these areas suffer from IDD. This is the reason for the occurrence of wide spread IDD in the population of mountainous or sub-mountainous as well as flood-plains and sandy leached soil tracts of the world such as in India, Bangladesh, Nepal, Myanmar etc. Iodine level in the drinking water indicates its content in soil. Its level in the drinking water from severely deficient areas of Nepal is 2.0 ug/L and of India 0.1-1.2ug/L as compared to 9.0 ug/L in mildly I deficient Delhi. Supplementation of I in the diet such as use of iodized table salt, or providing food from the I-adequate areas is the sole solution to eliminate IDD in the I-deficient areas. Iodized salts now used in most of the affected countries as a therapist remedial measure. The effects of iodine deficiency control are dramatic and are shown for China as an example in Table 1. This demonstrate that the impact of correction of IDD are remarkable in bringing communities to life in iodine deficient environment.

**Table 1. Effects of iodine deficiency control* in Jixian village**

| Heilongiang province, China | Before 1978 | After 1986 |
|---|---|---|
| Goiter Prevalence | 80% | 4.5% |
| Cretinism Prevalence | 11% | None |
| School ranking** | 14th | 3rd |
| School failure rate | >50% | 2% |
| Valu of farm production (yuan) | 19,000 | 1,80,000 |
| Per capita income (Yuan) | 43 | 550 |

* Through iodized salt program
**Of 14 schools in the district

In many countries the level of thyroid hormones are checked soon after birth and the deficient levels, if any, is made up through thyroxine therapy.

## FLUORINE

Fluorine has been considered as an essential trace element because of its prophylactic effects in human's caries. The F content in soil varies widely from place to place mainly because of differences in parent material (MacDowell, 1992). In Newzeland, Papu New Guinea (Barmes etal 1997) and USA (Ludwig and Bibby, 1969) close relation of dental caries with particular soil types has been recorded; but several other environmental factors are also involved. Human get most of their F from water that in turn comes from the soil as well as the underlying rocks. The F concentration in water generally range between 0.1 F $L^{-1}$ to moe than 20 mg F $L^{-1}$.In Asia and Africa the F concentration in water is at the higher range while in Europe and USA at the lower end of the range.
The relationship between F in drinking water and a reduced incidence of dental caries is one of the best establish links between geochemistry and diseases. An inverse relationship exists between dental caries and F concentration of water. Drinking water that contains less than 0.5 mg F $L^{-1}$ provides no grantee against dental caries (Edmunds and Smedley, 1996) but the ones that contain more than 0.8-1.0 mg F $L^{-1}$ does (WHO, 1996). Its content in water assumes special significance because of the margin of safety between the deficiency and the toxicity condition, resulting from low and excessive intake, respectively is very narrow. Intake of 0.2 to 2.0 mg F $day^{-1}$ (WHO, 1996) and 1.5 to 4.5 mg $day^{-1}$ for adults (NRC, 1980) from water and food are recommended.

A concentration of 1 mg F L1 is essential for the prevention of dental caries in human. Concentrations of F greater than this are likely to manifest toxicity symptoms; mottling of teeth occurs when concentration in water exceeds 4.5 mg L-1 (WHO, 1996). Drinking water that contains recommended F concentration should be supplied to humans in the afflicted areas so that neither its deficiency nor excess affect human health. Also humans should be provided diet that contains optimum concentrations of F. Toothpaste containing F are recommended as a remedial measures to check dental caries.

## SELENIUM

Selenium in small amounts is an essential element for human health but in high amount it becomes toxic. It is not an essential element for plant growth, but its concentration in food crops and water is important to human health. The range of Se content in soils vary very widely from trace to more than 8000 mg $kg^{-1}$. Also Se concentration in plants varies considerably and provides a good indication of its availability in soil (Neal, 1995; WHO, 1996). By and large all the Se in human diet comes from the food having strong influence of the Se levels of the geographical region.

Selenium deficiency has been detected in many parts of the world. The biological action of Se is similar to that of vitamin E. Both substances are antioxidants in their own way and at its specific sites that protect the cells of the body against oxidative damage. Deficiency disorders often arise as a result a combined deficiency of these two nutrients; the most important disease that result from their deficiencies is "Nutrient Muscular Dystrophy" (NMD) termed as "White Muscle Disease". It manifests as degenerative changes in skeletal musculature and also in the musculature of the heart.

Low Se areas exist from the northeastern to the southwestern part of China (Yang, 1987). The soils of the eastern coast of North America contain low Se level. Also several countries in Africa have low Se areas: Zambia, Zimbabwe, and Zaire. New Zeeland and the Scandinavian countries, especially Finland where the fertilizers have been enriched with Se, belong to areas with naturally low Se concentration in rocks, soil and plants (Aaseth and Ringstad, 1991). Also Se deficiency has been reported in Canada, Australia, and other parts of the world where soils and food or diet are Se deficient.

Selenium is a component of one of the antioxidant defense systems, the glutathione peroxidase enzyme of the body and is being used to monitor the Se status of the body (WHO, 1996). A daily Se intake below 20-ug caused **Keshan** disease- development of a cardiac disease, identified in 1935 in human in Keshan County, Heilongjiang Province and that of **Kashin-Beck**, endemic osteoarthrosis, the first Se disorder discovered in 1849 (Xu and Jiang, 1986, Yang, 1987, Levander, 1987, WHO, 1996) in the mountains and hills of central China. Selenium deficiency alone was the main cause. This disease also reported to occur in northern Korea and eastern Siberia. It is an endemic osteoarthropathy caused by a disturbance in the ossification of the ends of bones "endochondral ossification" and result in chronic arthritis and deformity of the affected joints "enlarged joint disease" in teenagers and children as well as muscular weakness. While Keshan disease stretches in a band of counties from northeast to southwest China and mainly occurs in rural population depending solely on food and water derived locally from leached mountain soils.

The Keshan disease is a cardiomyopathy and characterized by multifocal necrosis and fibrous replacement of the heart muscle cells. The disease occurs in young women and children. Selenium deficiency appears to impair the antioxidant defense system of the body allowing injuries to the heart muscle (Xia et al. 1989). Also the disease is associated with vitamin E deficiency (Yang et al. 1984; WHO, 1996). Both vitamin E and Se act synergistically to reduce damage from oxidative reaction. Selenium supplements in diet have reduced the Kheshan disease (Keshan Disease Research Group, 1979). Incidentally, endemic goiter and fluorosis also occurred in the Keshan disease areas and may also be the contributing factors to promote the disease. Whether or not multiple micronutrient deficiency of I, F and Se in a geographical region have any role in the recorded deficiency disorder attributed to the individual micronutrient needs to be examined. Peak incidence of Se disorder occurred in winter in the north-east China and in summer in the south-west as a result of seasonal variation in Se concentration. It is also suggested that the disease might have caused by a virus that thrives among the Se deficient population (Levander, 1987). Whether the recent outbreak of diseases in humans resulting from animal virus: SARS and Chicken Flue in China have any relation with Se deficiency status of the population or not need to be examined?
In Scandinavia Se deficiency occur in soils derived from glacial till containing 0.1 to 2.0 mg Se $kg^{-1}$ soil. In Norway both Se and I deficiency has similar pattern of distribution (Lag, 1986). In Finland Se deficient soils contained 0.2 to 0.3 mg Se $kg^{-1}$ and is weakly available (Kiovistoinen, 1986). In view of the exceptionally low Se levels in the agricultural products (Kiovistoinen, 1986; Varo et al.1994), despite no records of its association with specific Se deficiency disorder, the Finish Ministry of Agriculture started fortifying fertilizers with Se in 1983 (Wang et al. 1991). Though it has increased the Se of cereals from 10-ug $kg^{-1}$ in 1983 to 300-ug $kg^{-1}$ in 1989, it is not certain whether or not it has reduced the incidence of heart and cancer diseases (Varo et al. 1994). Similarly in Serbia, low concentration of Se in soils, wheat and human was recorded without any evidence of specific Se-disorder (Matesic et al. 1981; Maksimovic et al. 1992). WHO (1995)

recommended an intake of 50 to 200-ug Se $day^{-1}$; the average requirement for 65 kg male and 55 kg female is 26 and 11-ug $day^{-1}$, respectively.

Nevertheless geographic areas with low Se levels in soils, food, diet or in serum samples generally have higher cancer rates than areas with higher Se levels; reflecting an inverse relationship between dietary Se and incidence of certain forms of cancer and heart diseases in human. In many countries, particularly in Finland, application of Se either as Se containing fertilizers or its top-dressing to pasture/fodder crops is made. As this practice may lead to excess Se intake and may do more harm than good, a very careful monitoring of the Se-fertilization of crops and its levels in food and diet has to be made to keep it within safe limits (Takkar, 2003). However, capsule and tablets containing Se and vitamins are available in the market and medical practitioners prescribe these to heart and cancer patients suspected to suffer from its deficiency.

## CHROMIUM

The concentration of Cr in soil range between trace and 100 mg $kg^{-1}$ and in plants between 0.23 and 1.0 mg $kg^{-1}$. Leafy vegetables contain more Cr than cereals (Alloway, 1995).
It is an essential element required for insulin action, though relationship between the two has not been defined, that influence lipid, carbohydrate and protein metabolism.

Freud et al. (1979) clearly showed essentiality of Cr for human by demonstrating the reversal of the developed impairment of glucose tolerance or hyperglycaemia or glucose utilization in patients with Cr supplementation. It is considered to be a part of cofactor (glucose tolerance factor, GTF) that facilitates the insulin-regulated transport of glucose into the cell (Krause-Jarres, 987). Lack of Cr leads to cardiovascular problem as it may disturb normal cholesterol and sugar metabolism (Anderson, 1981, Virtamo and Huttunen, 1988). Regions that have large Cr content in soil and water (Punsar and Karvonen, 1979) have low death rates from heart diseases, yet direct relationships have not been established. NRC (1980) recommends an intake of 0.05–0.2 mg Cr $day^{-1}$ for adults and WHO (1996) 24.5- 37 ug Cr $day^{-1}$ for elderly people. The tolerable limit of Cr is quite high and could be above 250 ug Cr $day^{-1}$. However supplementation of Cr should not exceeds this amount until more information is available. By and large trivalent Cr has low toxic effect while hexavalent is highly toxic.

## IRON

Iron is essential to all higher forms of life. Both in developing and developed countries Fe deficiency is generally recognized as the most common single nutritional deficiency in spite of that it is being one of the most abundant minerals on earth. The main cause for this is low bioavailability of dietary Fe together with the Fe content being related to the energy content of the diet. In the body 2-6 g Fe is bound to protein as haem and non-haem compounds. It is divided into two functional compartments: functional Fe (“essential”: 70 %) and storage Fe (“non-essential”: 30 %). The functional Fe comprises of: circulating haemoglobin (85%), tissues as myoglobin (5%) and various haem (cytochromes, peroxidase, catalase, etc.) and non-haem enzymes (succinate, dehydrogenase, xanthenes oxidase, aconitase, etc.) and transport Fe bound to transferrin in plasma (0.1 %) and lactoferrin in milk secretions. Iron functions as red-ox component in the respiratory chain enzymes as oxygen carrier in haemoglobin, and as oxygen stores in myglobin. One molecule of hemoglobin is able to carry 4 molecules of oxygen into the

tissues and on return it takes up $CO_2$ from the tissues to the lungs. Iron transport oxygen through reversible combination to hemoglobin-$Fe^{2+}$ and myoglobin-$Fe^{2+}$. It also participates in biochemical red-ox reactions involving $Fe^{2+}/Fe^{3+}$-interchanges, e.g., in cytochrom oxidase in the mitochondria. Cytochrom oxidase, is an electon pair transferring enzyme system that contains both Fe and Cu, uses red-ox reactions to convert oxygen to water. It also plays essential role in the synthesis of DNA, peroxide breakdown, etc. The storage Fe exist as the non-haem compounds ferritin and haemosiderin, largely in liver, spleen, and bone marrow, and is considered to have no physiological function other than being a reserve Fe (Bothwell et al. 1979 and Fairbank and Beutler, 1988, Takkar and Randhawa, 1990, Takkar, 2003).

The causes for the deficiency are: low Fe content in the diet and/or low Fe bioavailability, blood loss from the body: large menstrual losses, occult gastrointestinal blood loss, frequent nose bleeding etc., defective absorption mechanism, and parasites: hook worms. The clinical syndromes in Fe deficient individuals are: usually nervous, easily fatigued, listleness, lower weight gain, reduced appetite, palpitation on mild exercise, sore tongue, angular stomatitis. The values for Fe deficiency status are: <10 g/100ml Hb, <100-200-ug/dl or 17.9-35.8 umol/l serum Fe and <13-15% reduced transferring saturation (McDowell, 1976).

Iron deficiency in human largely result from its low dietary intake especially by poor individuals in developing countries depending mainly on cereal diets having low Fe content as well as in its bioavailability. Iron malnutrition is now a global problem of immense proportions as over 2 billion people mostly poor women, infants and children in the world are now Fe, I, and/or vitamin A deficient (Mason and Garcia, 1993). Iron deficiency anemia is often associated with malaria and hookworm infections. Ramalingaswami, 1995) suggested that prevention of trace element deficiencies can contribute to the control of infectious diseases. Iron deficiency is associated with poor attention span, inadequate fine motor skills and reduced memory retention in children. In Chile, Fe deficient infants have learning disabilities later in school even if the Fe deficiency condition is corrected early on (McGuire, 1993).

To combat Fe and other micronutrient deficiency in human, milk is being fortified with Fe, Zn, and Cu before it is marketed in some developed countries. This practice needs to be adopted especially in the developing countries to correct trace element deficiencies. In India fortified wheat floor with irn and vitamin is marketed by the Hindustan Liver Limited.

## MOLYBDENUM

Generally Mo deficiency occurs in sandy soils, podzolic soils and serpentine soils that contain low total Mo content. As well as on soils having low pH, high Fe content, and high anion exchange capacity (Davies, 1956). It is a constituent of xanthine dehydrogenase/oxidase, aldehyde oxidase andsulfite oxidaseenzymes enzymes of human. Their reaction with oxygen produces a series of highly reactive oxygen-rich free radicals believed to be responsible for some features of tissue damage induced by physical injury and wide variety of toxins, including excess Mo. However, its deficiency disorder in human has not definitely been identified and there are conflicting reports of its involvement of human diseases. While both Se and Mo are considered to be involved in Keshan disease as soils and plant food of the area contain little Mo and Se in China (Wang et al. 1991), but in another Kehan endemic area Mo levels were very high in soils, rice, wheat as well as in human tissues and hair (Yang, 1978).

## SUMMARY AND CONCLUSIONS

Deficiency of essential micronutrients: Cu, Cr, I, F, Fe, Zn, Se, Mo in human and their resultant health problems are highlighted. Micronutrient deficiency emanates as a result of their meager flow to human through the soil-water-plant-animal-human chain in a geographical area and/ or low content in diet and their bioavailability, especially in the developing countries. Their malnutrition is now a massive and rapidly growing public health problem affecting about 40 per cent of the world's population. The problem of I, Fe, Zn and vitamin A is much more grave among young children and women of childbearing age. Micronutrient deficiency in soils, water, plants and the resultant deficiency diseases/disorders in humans are reported and pointed out anomalies emanating from one or more micronutrient deficiencies or excess. The essential roles of these micronutrients and syndromes of their deficiency are described. Remedial measures for combating their deficiency are suggested. Supplementation of micronutrient projects in the endemic areas of micronutrient deficiency needs to be further encouraged. The quantitative data regarding the extent and magnitude of micronutrient deficiency, both apparent and hidden, as well as cause and effects of their disorders in human are far from adequate and needs to be assessed through case studies in multidisciplinary modes, involving all concerned disciplines. To achieve this liberal funds and facilities need to be provided besides education and training to the worker and the public in general through electronic media etc to help achieve this colossal task. This in the long run would help in successfully mitigating human suffering from micronutrient deficiency disorders as well as in maintaining sustainable human health and societies.

## REFERENCES


Aaseth, J. and Ringstad, J. (1991). In: Human and animal health in relation to circulation processes of selenium and cadmium (Ed. J. lag).The Norwegian Academy of Science and Letters. Oslo. Pp. 29-46.

Alloway, B.J. (1995). In: Heavy Metals in Soils. 2nd edn (Ed. B.J. Alloway). Blackie Academic and Professional. Glasgow. Pp. 38-55. Anderson, R.A.(1981). Sci. Total Envn. 17, 13-29.

Arora, S.P. Parvinder, P.K., Khirwar, S.S., Chopra, R.C. and Ludri, R.S. (1975). Indian J. Dairy Sci. 28, 249-.

Aswathanarayna, U. (1990). In: Geomedicine (Ed.J. Lag). CRC, Boca Raton. Pp. 235-244.

Bothwell T. H, Charlton, R W, Cook, J.D, Finch, C. A. (1979). Iron Metabolism in Man Oxford Blackwell Scientific Publications.

Castro RU (1977). IRRI Research Paper Series 9, 1-18.

Davies, B.E. (1956). Soil Sci., 81. 209- 221.

Davis, O.k. and Mertz W. (1987). Copper. In:. Trace Elements in human and Animal Nutrition(Ed. W.Mertz). Vol. 1. 5th ed. Academic Press, London. Pp. 301-306.

Edmunds, W.M. and Smedley, P. (1996). In: Environmental Geochemistry and Health. (Eds. I.P. Appleton, R, Fuge & G.J.H. McCall). Geological Society, London. 113, 91-105.

Fairbank, V.E, Beutler, E. (1988). Iron. In: Modern Nutrition in Health and disease. (ed. M. E. Shils, and V.R. Young). Philadelphia: Lee & Febinger.).

Fishbein, I. (1987). Toxicological and Environmental Chemistry. 14, 73-99.

Freud, J., Atamian, S. and Fisher, J.E. (1979). Chromium deficiency during total parentral nutrition. JAMA. 241: 496.

Fuge, R. (1987). In: Trace Substances in Environmental Health (Ed D.D. Hemphill). Pp. 74-87. University of Missouri, Colombia.

Fuge, R. (1996). In: Environmental Geochemistry and Health. (Eds. I. P. Appleton, R, Fuge & G.J.H. McCall). Special Publication No. 113. Geological Society, London. Pp 201-211.

Guaba, K. (1983). Master's Thesis. Post Grad. Inst. Med. Ed. Res., Chandigarh.

Hetzel, B.S. (1989) The story of iodine deficiency an international challenge in nutrition. Oxford/Delhi. Oxford Univ. Press.

Hetzel, B.S. (1997). S.O.S for a Billion-The nature and magnitude of iodine deficiency disorder. In. S.O.S for a Billion- The Conquest of iodine deficiency disorder , B.S. Hetzel and C.S. Pandav eds. Oxford Univ. Press. Calcutta.

Hambridge **,** K.M., Casey, C.E., and Krebs, N.F. (1987). Zinc. In: Trace Elements in Human and Animal Nutrition.(Ed W. Mertz). Academic Press. Florida. Pp. 1-137.

Keshan Disease Research Group. (1979). Chinese Medical Journal. 92, 471-476.

Kiekens, L. (1995). Zinc. In: Heavy Metals in Soils. (Ed B.J. Alloway). Blackie Academic and Professional. Glass glow. pp.284-305.

Kiovistoinen, P. (1986). In: Proceedings of the first international Symposium on Geochemistry and Health. (Ed. I. Thornton). Science Reviews limited. Northwood, UK.

Krause-Jarres, J.D. 1987. Clinical indicators for trace element analysis. Trace element Electrolytes Health Dis., 1: 5).

Lag, J. (1972). Soil Science and Geomedicine. Acta Agric, Scand. 22, 150-152.

Lag, J. (1986). In: Proc.First Int. Symp. on Geochemistry and Health. (ed. I. Thornton). Science Reviews limited. Northwood, UK. Pp. 107-112.

Lag, J. (1990). In: Geomedicine(Ed. J Lag ). CRC, Boca Raton. Pp. 1-24.

Levender, O.A. (1987). Selenium In: Trace Elements in Human and Animal Nutrition. (Ed W. Mertz). Academic Press. Orlando, Florida. Pp. 209-279.

Maksimovi, Z, Iovic, V., Djujie, I., and Rsumovic, M. (1992).Environmental Geochem.and Health. 14, 107-111.

McDowell, L. R. (1976). In: Beef Cattle Production in Developing Countries (Ed.A. J. Smith). Univ. Edinburgh Press, Edinburgh, Scotland. Pp. 216.

McDowell, L.R. (1992). Minerals in Animal and Human Nutrition. Academic Press. San Diego, California.

McGuire, J. (1993). Addressing micronutrient malnutrition. SCN News. 9. 1-10.

Mason, J.B. and Garcia, M. (1993). SCN News. 9, 11-16.

Matesic, D., Kos, K., and Strasek, A. (1981). Veterinarskiarhiv. 51. 79-82.

Mertz, W. (1987). Trace elements in human and animal nutrition. Vol II. (Ed.W. Mertz). Academic Press, London. Pp.369.

National Research Council (1980). Recommendeddietary allowances.7th ed. National Academy of Science, Washington, D.C.

Neal, R.L. (1995). Selenium. In: Heavy Metals in Soils. (Ed B.J. Alloway) Blackie Academic and Professional. Glass glow. Pp. 260-283.

Oliver, M.A. (1997). European J. Soil Sci. 48, 573-592.

Peerebhoom-Stegeman, J.H.J.C.(1987).Toxicological Environ.Chem.15,273-292.

Pories, W.J. and Strain, W.H. (1966). In: Zinc Metabolism C.S.R.S. (Ed. A.S. Prasad). Charles C. Thomas. Springfield, Illinois. Pp. 378-394.

Prasad, A.S. (1976). Trace elements in human health and disease. Vol. I. Zinc and copper, Academic, New York. 562 p.

Prasad, A.S. (1978). Trace Elements in Human Metabolism. (Ed. A.S. Prasad). John Wiley & Sons. Chichester.

Prasad, A.S., Halsted, J.A. and Nadimi, M. (1961). Am. J. Medicine. 31, 532-546.

Punsar, S and Karvonen, M.J. 1979. Drinking water quality and sudden death observations from vest and east Finland. Cardiology. 54: 24.

Ramalingaswami, V. (1995). Am. J. Clin. Nutr. 61, 259-263.

Ray, S.N., Dutt, B. and Majumdar, B.N. (1959). Final Report. Trace Elements Scheme 1952-1959. Animal Nutr. Div., Indian Vet. Res. Inst., Izatnagar.

Ringstad, J., Aaseth, J and Alexander, J. (1990). In: Geomedicine (ED. J. Lag). CRC, Boca Raton. Pp. 25-36.

Rivera, J.A., Ruel, M.T., Santizo, M.C. and Lonnerdal, B. (1998). J. Nutr. 128, 556.

Robson, A. D. (1993). Zinc in Soils and Plants.(Ed A.D. Robson). Kluwer Academic Publishers, London. Pp 206.

Spears, A.B., Kaufman, B.M,. Mathock, M.B., Saharia, S., Wig, J.D., Sachdeva, H.S., Takkar, P.N. and Randhawa, N.S. (1974). Bull. Post Graduate Institute of Medical and Education and Research.Chandigarh. 8, 21-25.

SSSA (Soil Sci. Soc. Am.).(1985). A survey of micronutrient deficiencies in the USA and means of correcting them. Maidison, Wisc.

Takkar, P.N. (1991). In: Zinc in Crop Nutrition. Int.Lead Zinc Res. Organization, Inc. and Indian Lead Zinc Information Center, New Delhi 110029 (India). Pp 55-64.

Takkar, P.N. (1996). J. Indian Soc. Soil Sci. 44, 562-581.

Takkar,P.N.. (2003). Geomedical problems of animal and human health related to trace elements. Fertilizer. News. 48:95-109.

Takkar, P.N., Chhibba, I.M. and Mehta, S.K. (1989). Twenty Years of Coordinated Research on Micronutrients in Soils and Plants. 1967-187. Bulletin 1. Indian Institute of Soil Science, Bhopal, India.

Takkar, P.N. and Randhawa, S.S. 1990. Specific geomedical problems in Asia. In:. Geomedicine (Ed. J. Lag ). CRC, Bosa Raton. Pp. 245-255.

Takkar, P.N. and Walker, C. D. (1993). In: Zinc in Soils and Plants. (Ed A. D. Robson). Kluwer Academic Publishers, London.

United Nation. (1991). Some options for improving nutrition in the 1990s. *SCN News* no. 7, Supplement, 16-18.

United Nation ACCSN (1992). Second report on the World Nutrition Situation. Vol. 1. Global and Regional Results., Geneva, Switzerland. Pp. 1-80.

Varo, P., Alfthan, G., Huttunen, J.K. and Aro, A. (1994).. In: Selenium in Biology and Human Health (Ed. R.F. Burk), Springer, New York. pp. 197-218.

Virtamo, J and Huttunen, J.K. 1988. Mineral, trace elements and cardiovascular disease. Ann. Clin. Res. 20: 102.

Wang, D., Alfthan, G., Aro,, Kauppi, L. and Soveri, J. (1991 In: Trace Elements in Health and Disease (ed. A. Aitio, A. Aro, J. Jarvisalo and H. Vainio). The Royal Society of Chemistry, Cambridge. Pp. 49-56.

Welch, R.M., Coombs G.F., Jr., and Duxbury, J.M. (1997). Toward a "Greener" revolution. Issues in Science and Technology. 14, 50-58.

Welch, R. M. (2001). In: Prospectives on the Micronutrient Nutrition of Crops (Eds Kalyan Singh, S Mori and R.M Walsh. Scientific Publishers, Jodhpur, India.

WHO. (1996). Trace Elements in Human Nutrition and Health. World Health Organization, Geneva.

Xia, Y., Hill, K.E. and Burk, R.F. (1989) J. Nutr. 119, 1318-1326.

Xu, G.L. and Jiang, Y.F. (1986). In: Proceedings of the first international Symposium on Geochemistry and Health. (Ed. I Thornton) Science Reviews limited. Northwood, UK.

Yang, G. Q. (1978). In: Selenium in Biology and Medicine Par B. (In. G. F. Coombs Jr.,et al.eds.) New York, Van Nostrand.